SPECIAL ISSUE: **PALLIATIVE CARE**

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ALSO IN THIS ISSUE

PREVENTING HAIR LOSS

Scalp cooling has been successful in preventing alopecia in patients with solid tumors who are on chemotherapy. The FDA approval of DigniCap scalp cooling technology last year will hopefully expand patient access, with an increase in provider and payer confidence in this technology (**SP602**).

ASCO UPDATES PALLIATIVE CARE GUIDELINE

The American Society of Clinical Oncology (ASCO) has updated its recommendations to integrate palliative care with active cancer treatment and refer caregivers to these services, among others (**SP609**).

MCANENY

SAGAR

OCM AT THE COA PAYER EXCHANGE SUMMIT

At the Community Oncology Alliance (COA) Payer Exchange Summit, community practitioners were provided a 101 on adopting the Oncology Care Model (OCM). In addition to private payers and providers who are participating in the model, a representative from the Innovation Center who was actively involved in developing the model, also participated on a panel discussion (**SP615**).

PROVIDER PERSPECTIVE

Welcome to the Future: Telemedicine and Value-Based Payment

Michael D. Fratkin, MD, and Stephen G. Franey, MBA

RECENTLY, MICHAEL WAS CALLED TO the hospital for a transitional palliative care consult. He walked into the room to see a Native American man in bed, surrounded by 8 people and a laptop computer on a cart. This man had been a lawyer, activist, probation officer, and more—a defender of his people. At his side was Aggie Pilgrim, chairperson of the International Council of 13 Indigenous Grandmothers, now 92, but still traveling the world with other elder women of First Nation communities to disseminate and preserve their cultures and healing traditions. The others in the room were all ages: from a babe in arms to millennials to baby boomers.

DOCTOR MEASURES BLOOD PRESSURE ONLINE © VERBASKA/FOTOLIA

At the end of the bed, the laptop screen showed 8 more family members gathered in support, from Maryland, Los Angeles, Sacramento, and elsewhere. Aggie said a beautiful prayer, pulled out a bundle of white sage, lit it, and passed it around—while, frankly, Michael worried it would set off the hospital's smoke alarm.

Welcome to the future. This was a videoconference that we, at ResolutionCare,[1] had no role in setting up. It was set up by empowered people who used ubiquitous, readily available technology to bridge geographic distance and provide family support. Clearly, there's a disruption afoot.

Telemedicine's Evolution

The arc of remote consultation support through videoconferencing, or telemedicine, is an evolution from high-cost, technologically complex systems to readily available, low-cost technology that is easily used by both physicians and people receiving care.

Telemedicine 1.0

Fifteen years ago, Telemedicine 1.0 was the first effort to connect subspecialists in tertiary referral centers to satellite clinics. It involved

CONTINUED ON SP621

VALUE-BASED PAYMENT

Achieving Value Through Palliative Care

Allison Silvers, MBA; Stacie Sinclair, MPP; and Diane E. Meier, MD, FACP

MOVING TO VALUE IN HEALTHCARE MEANS improving the quality of care delivered and the outcomes achieved while reducing unnecessary spending. Most healthcare organizations are pursuing value and the benefits that accrue under value-based payment, but too few are turning to palliative care to help achieve these goals.

Palliative care—which focuses on relieving the pain, symptoms, and stresses of a serious illness—changes healthcare delivery for both patients and their caregivers. Multiple studies and meta-analyses have shown that not only does palliative care improve patient experience and satisfaction,[1-3] but that it also reduces emergency department (ED) visits, hospitalizations, and days spent in intensive care,[4,5] thus reducing total spending.[6,7] It does this through:

- Safe and effective techniques for managing pain, shortness of breath, and other symptoms which would otherwise lead to ED and inpatient hospital use
- Communication expertise needed for long, often difficult discussions with patients and families about prognosis, goals of care, and the patient's wishes and values.

CONTINUED ON SP623

POLICY

Palliative Care for Patients With Advanced Illness: A Changing Policy Landscape

Sharon Pearce

EVERY DAY, 10,000 AMERICANS join the Social Security and Medicare rolls. Moreover, individuals 80 and older are the fastest growing demographic among older adults, with their ranks forecast to grow from 5.6 million in 2010 to more than 19 million by 2050.[1]

The rising number of aging Americans creates a commensurate increase in the costs for healthcare. While they constitute only 24% of Medicare beneficiaries, seniors 80 and up account for more than 33% of Medicare expenditures; much of that spending stems from the prevalence of chronic diseases and high end-of-life (EOL) costs.[2] In 2012, half of all individuals

CONTINUED ON SP635

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ANNOUNCING

A Permanent J-code for EMPLICITI™ (elotuzumab) – J9176

for injection, for intravenous use (300 mg and 400 mg vials)

J-code for EMPLICITI

HCPCS Code	Description	Effective
J9176[1]	Injection, elotuzumab, 1 mg	January 1, 2017

J9176 replaces HCPCS code C9477, injection, elotuzumab 1 mg, and also miscellaneous codes J9999, J3590, and J3490.[1]

NDC Codes for EMPLICITI[2]

0003-2291-11, 00003-2291-11	Single-dose vial containing 300 mg of lyophilized powder
0003-4522-11, 00003-4522-11	Single-dose vial containing 400 mg of lyophilized powder

For more information:

- Contact your **Area Reimbursement Manager** for general assistance and to schedule an office visit
- Call Bristol-Myers Squibb Access Support® at **1-800-861-0048** 8 AM to 8 PM ET, Monday-Friday, to speak with your dedicated team of regionally assigned specialists
- Visit **www.BMSAccessSupport.com** for information and resources, including the BMS Access Support program enrollment form, to help your patients with access to Bristol-Myers Squibb oncology products

The accurate completion of reimbursement- or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol-Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item. This coding guidance is not intended to provide specific directions on requesting prior authorization or submitting claims for EMPLICITI and does not provide a guarantee of receiving prior authorization or reimbursement. Coding for EMPLICITI is dependent on the insurer and the care setting in which the drug will be administered. Oncology practices need to make coding decisions based on the diagnosis and treatment of each patient and the specific insurer requirements.

Indication

EMPLICITI is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.

Select Important Safety Information

EMPLICITI with lenalidomide and dexamethasone is associated with the following Warnings and Precautions: Infusion Reactions, Infections, Second Primary Malignancies, Hepatotoxicity, Interference with Determination of Complete Response, Pregnancy/Females and Males of Reproductive Potential, and Adverse Reactions.

References

1. American Medical Association. *2016 HCPCS Level II, Professional Edition*. Chicago, IL: American Medical Association; 2016.
2. EMPLICITI [package insert]. Princeton, NJ: Bristol-Myers Squibb Company.

Please see additional Important Safety Information and brief summary of Full Prescribing Information on the following pages.

IMPORTANT SAFETY INFORMATION

Infusion Reactions

- EMPLICITI™ (elotuzumab) can cause infusion reactions. Common symptoms include fever, chills, and hypertension. Bradycardia and hypotension also developed during infusions. In the trial, 5% of patients required interruption of the administration of EMPLICITI for a median of 25 minutes due to infusion reactions, and 1% of patients discontinued due to infusion reactions. Of the patients who experienced an infusion reaction, 70% (23/33) had them during the first dose. If a Grade 2 or higher infusion reaction occurs, interrupt the EMPLICITI infusion and institute appropriate medical and supportive measures. If the infusion reaction recurs, stop the EMPLICITI infusion and do not restart it on that day. Severe infusion reactions may require permanent discontinuation of EMPLICITI therapy and emergency treatment.
- Premedicate with dexamethasone, H1 Blocker, H2 Blocker, and acetaminophen prior to infusing with EMPLICITI.

Infections

- In a clinical trial of patients with multiple myeloma (N=635), infections were reported in 81.4% of patients in the EMPLICITI with lenalidomide/dexamethasone arm (ERd) and 74.4% in the lenalidomide/dexamethasone arm (Rd). Grade 3-4 infections were 28% (ERd) and 24.3% (Rd). Opportunistic infections were reported in 22% (ERd) and 12.9% (Rd). Fungal infections were 9.7% (ERd) and 5.4% (Rd). Herpes zoster was 13.5% (ERd) and 6.9% (Rd). Discontinuations due to infections were 3.5% (ERd) and 4.1% (Rd). Fatal infections were 2.5% (ERd) and 2.2% (Rd). Monitor patients for development of infections and treat promptly.

Second Primary Malignancies

- In a clinical trial of patients with multiple myeloma (N=635), invasive second primary malignancies (SPM) were 9.1% (ERd) and 5.7% (Rd). The rate of hematologic malignancies were the same between ERd and Rd treatment arms (1.6%). Solid tumors were reported in 3.5% (ERd) and 2.2% (Rd). Skin cancer was reported in 4.4% (ERd) and 2.8% (Rd). Monitor patients for the development of SPMs.

Hepatotoxicity

- Elevations in liver enzymes (AST/ALT greater than 3 times the upper limit, total bilirubin greater than 2 times the upper limit, and alkaline phosphatase less than 2 times the upper limit) consistent with hepatotoxicity were 2.5% (ERd) and 0.6% (Rd). Two patients experiencing hepatotoxicity discontinued treatment; however, 6 out of 8 patients had resolution and continued treatment. Monitor liver enzymes periodically. Stop EMPLICITI upon Grade 3 or higher elevation of liver enzymes. After return to baseline values, continuation of treatment may be considered.

Interference with Determination of Complete Response

- EMPLICITI is a humanized IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis and immunofixation assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein.

Pregnancy/Females and Males of Reproductive Potential

- There are no studies with EMPLICITI with pregnant women to inform any drug associated risks.
- There is a risk of fetal harm, including severe life-threatening human birth defects associated with lenalidomide and it is contraindicated for use in pregnancy. Refer to the lenalidomide full prescribing information for requirements regarding contraception and the prohibitions against blood and/or sperm donation due to presence and transmission in blood and/or semen and for additional information.

Adverse Reactions

- Infusion reactions were reported in approximately 10% of patients treated with EMPLICITI with lenalidomide and dexamethasone. All reports of infusion reaction were Grade 3 or lower. Grade 3 infusion reactions occurred in 1% of patients.
- Serious adverse reactions were 65.4% (ERd) and 56.5% (Rd). The most frequent serious adverse reactions in the ERd arm compared to the Rd arm were: pneumonia (15.4%, 11%), pyrexia (6.9%, 4.7%), respiratory tract infection (3.1%, 1.3%), anemia (2.8%, 1.9%), pulmonary embolism (3.1%, 2.5%), and acute renal failure (2.5%, 1.9%).
- The most common adverse reactions in ERd and Rd, respectively (>20%) were fatigue (61.6%, 51.7%), diarrhea (46.9%, 36.0%), pyrexia (37.4%, 24.6%), constipation (35.5%, 27.1%), cough (34.3%, 18.9%), peripheral neuropathy (26.7%, 20.8%), nasopharyngitis (24.5%, 19.2%), upper respiratory tract infection (22.6%, 17.4%), decreased appetite (20.8%, 12.6%), and pneumonia (20.1%, 14.2%).

Please see brief summary of Full Prescribing Information on following pages.

EMPLICITI™ (elotuzumab) for injection, for intravenous use ℞ ONLY

Brief Summary of Prescribing Information. For complete prescribing information consult official package insert.

INDICATIONS AND USAGE

EMPLICITI (elotuzumab) is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.

CONTRAINDICATIONS

There are no contraindications to EMPLICITI. Because EMPLICITI is indicated for use in combination with lenalidomide and dexamethasone, healthcare providers should consult the prescribing information of these products for a complete description of contraindications before starting therapy.

WARNINGS AND PRECAUTIONS

Infusion Reactions

EMPLICITI can cause infusion reactions. Infusion reactions were reported in approximately 10% of patients treated with EMPLICITI with lenalidomide and dexamethasone in the randomized trial in multiple myeloma. All reports of infusion reaction were Grade 3 or lower. Grade 3 infusion reactions occurred in 1% of patients. The most common symptoms of an infusion reaction included fever, chills, and hypertension. Bradycardia and hypotension also developed during infusions.

In the trial, 5% of patients required interruption of the administration of EMPLICITI for a median of 25 minutes due to infusion reactions, and 1% of patients discontinued due to infusion reactions. Of the patients who experienced an infusion reaction, 70% (23/33) had them during the first dose.

Administer premedication consisting of dexamethasone, antihistamines (H1 and H2 blockers) and acetaminophen prior to EMPLICITI infusion *[see Dosage and Administration (2.2) in full Prescribing Information]*.

Interrupt EMPLICITI infusion for Grade 2 or higher infusion reactions and institute appropriate medical management *[see Dosage and Administration (2.3) in full Prescribing Information]*.

Infections

In a clinical trial of patients with multiple myeloma (N=635), infections were reported in 81.4% of patients in the EMPLICITI combined with lenalidomide and dexamethasone (E-Ld) arm and 74.4% in lenalidomide and dexamethasone (Ld). Grade 3 to 4 infections were noted in 28% and 24.3% of E-Ld- and Ld-treated patients, respectively. Discontinuations due to infections occurred in 3.5% of E-Ld-treated and 4.1% of Ld-treated patients. Fatal infections were reported in 2.5% and 2.2% of E-Ld- and Ld-treated patients.

Opportunistic infections were reported in 22% of patients in the E-Ld arm and 12.9% of patients in the Ld arm. Fungal infections occurred in 9.7% of patients in the E-Ld arm and 5.4% of patients in the Ld arm. Herpes zoster was reported in 13.5% of patients treated with E-Ld and 6.9% of patients treated with Ld. Monitor patients for development of infections and treat promptly.

Second Primary Malignancies

In a clinical trial of patients with multiple myeloma (N=635), invasive second primary malignancies (SPM) have been observed in 9.1% of patients treated with E-Ld and 5.7% of patients treated with Ld. The rate of hematologic malignancies were the same between E-Ld and Ld treatment arms (1.6%). Solid tumors were reported in 3.5% and 2.2% of E-Ld- and Ld-treated patients, respectively. Skin cancer was reported in 4.4% and 2.8% of patients treated with E-Ld and Ld, respectively. Monitor patients for the development of second primary malignancies.

Hepatotoxicity

Elevations in liver enzymes (aspartate transaminase/alanine transaminase [AST/ALT] greater than 3 times the upper limit, total bilirubin greater than 2 times the upper limit, and alkaline phosphatase less than 2 times the upper limit) consistent with hepatotoxicity were reported in 2.5% and 0.6% of E-Ld- and Ld-treated patients in a clinical trial of patients with multiple myeloma (N=635). Two patients experiencing hepatotoxicity were not able to continue treatment; however, 6 out of 8 patients had resolution and were able to continue treatment. Monitor liver enzymes periodically. Stop EMPLICITI upon Grade 3 or higher elevation of liver enzymes. After return to baseline values, continuation of treatment may be considered.

Interference with Determination of Complete Response

EMPLICITI is a humanized IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPEP) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein *[see Drug Interactions]*. This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein.

ADVERSE REACTIONS

The following adverse reactions are described in detail in other sections of the label:

- Infusion reaction *[see Warnings and Precautions]*.
- Infections *[see Warnings and Precautions]*.
- Second Primary Malignancies *[see Warnings and Precautions]*.
- Hepatotoxicity *[see Warnings and Precautions]*.
- Interference with Determination of Complete Response *[see Warnings and Precautions]*.

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described in this section are based on a randomized, open-label clinical trial in patients with previously treated multiple myeloma. In this study, EMPLICITI 10 mg/kg was administered with lenalidomide and dexamethasone *[see Clinical Studies (14) in full Prescribing Information]*. For adverse reaction evaluation, EMPLICITI combined with lenalidomide and dexamethasone was compared with lenalidomide and dexamethasone alone.

The mean age of the population was 66 years and 57% of patients were 65 years of age or older. Sixty percent (60%) of the population were male, 84% were white, 10% were Asian, and 4% were black. The Eastern Cooperative Oncology Group (ECOG) performance status was 0 in 47%, 1 in 44%, and 2 in 9% of patients.

These data reflect exposure of 318 patients to EMPLICITI and 317 to control with a median number of cycles of 19 for EMPLICITI and 14 for control.

Serious adverse reactions were reported in 65.4% of patients treated on the EMPLICITI arm and 56.5% for patients treated on the control arm. The most frequent serious adverse reactions in the EMPLICITI arm compared to the control arm were: pneumonia (15.4% vs. 11%), pyrexia (6.9% vs. 4.7%), respiratory tract infection (3.1% vs. 1.3%), anemia (2.8% vs. 1.9%), pulmonary embolism (3.1% vs. 2.5%), and acute renal failure (2.5% vs. 1.9%).

The proportion of patients who discontinued any component of the treatment regimen due to adverse reactions as listed below was similar for both treatment arms; 6.0% for patients treated on the EMPLICITI (elotuzumab) arm and 6.3% for patients treated on the control.

Adverse reactions occurring at a frequency of 10% or higher in the EMPLICITI arm and 5% or higher than the lenalidomide and dexamethasone arm for the randomized trial in multiple myeloma are presented in Table 1.

Table 1: Adverse Reactions with a 10% or Higher Incidence for EMPLICITI-Treated Patients and a 5% or Higher Incidence than Lenalidomide and Dexamethasone-Treated Patients [All Grades]

	EMPLICITI + Lenalidomide and Dexamethasone N=318		Lenalidomide and Dexamethasone N=317	
Primary Term	**All Grades**	**Grade 3/4**	**All Grades**	**Grade 3/4**
Fatigue*	61.6	12.6	51.7	11.7
Diarrhea	46.9	5.0	36.0	4.1
Pyrexia	37.4	2.5	24.6	2.8
Constipation	35.5	1.3	27.1	0.3
Cough†	34.3	0.3	18.9	0
Peripheral Neuropathy‡	26.7	3.8	20.8	2.2
Nasopharyngitis	24.5	0	19.2	0
Upper Respiratory Tract Infection	22.6	0.6	17.4	1.3
Decreased Appetite	20.8	1.6	12.6	1.3
Pneumonia§	20.1	14.2	14.2	9.5
Pain in Extremities	16.4	0.9	10.1	0.3
Headache	15.4	0.3	7.6	0.3
Vomiting	14.5	0.3	8.8	0.9
Weight Decreased	13.8	1.3	6.0	0
Lymphopenia	13.2	8.8	6.9	3.2
Cataracts	11.9	6.3	6.3	2.8
Oropharyngeal Pain	10.1	0	4.4	0

* The term fatigue is a grouping of the following terms: fatigue and asthenia.
† The term cough is a grouping of the following terms: cough, productive cough, and upper airway cough.
‡ The term peripheral neuropathy is a grouping of the following terms: peripheral neuropathy, axonal neuropathy, peripheral motor neuropathy, peripheral sensory neuropathy, and polyneuropathy.
§ The term pneumonia is a grouping of the following terms: pneumonia, atypical pneumonia, bronchopneumonia, lobar pneumonia, bacterial pneumonia, fungal pneumonia, pneumonia influenza, and pneumococcal pneumonia.

Other clinically important adverse reactions reported in patients treated with EMPLICITI that did not meet the criteria for inclusion in Table 1 but occurred at a frequency of 5% or greater in the EMPLICITI group and at a frequency at least twice the control rate for the randomized trial in multiple myeloma are listed below:

General disorders and administration site conditions: chest pain

Immune system disorders: hypersensitivity

Nervous system disorders: hypoesthesia

Psychiatric disorders: mood altered

Skin and subcutaneous tissue disorders: night sweats

Laboratory abnormalities worsening from baseline and occurring at a frequency of 10% or higher in the EMPLICITI group and 5% or higher than the lenalidomide and dexamethasone group (criteria met for all Grades or Grade 3/4) for the randomized trial in multiple myeloma are presented in Table 2.

Table 2: Laboratory Abnormalities Worsening from Baseline and with a 10% or Higher Incidence for EMPLICITI-Treated Patients and a 5% Higher Incidence than Lenalidomide and Dexamethasone-Treated Patients [Criteria met for All Grades or Grade 3/4]

	EMPLICITI + Lenalidomide and Dexamethasone N=318		Lenalidomide and Dexamethasone N=317	
Laboratory Parameter	**All Grades**	**Grade 3/4**	**All Grades**	**Grade 3/4**
Hematology				
Lymphopenia	99.4	76.7	98.4	48.7
Leukopenia	90.6	32.4	88.3	25.6
Thrombocytopenia	83.6	19.2	77.8	20.3
Liver and Renal Function Tests				
Hypoalbuminemia	73.3	3.9	65.6	2.3
Elevated Alkaline Phosphatase	38.7	1.3	29.8	0
Chemistry				
Hyperglycemia	89.3	17.0	85.4	10.2
Hypocalcemia	78.0	11.3	76.7	4.7
Low Bicarbonate	62.9	0.4	45.1	0
Hyperkalemia	32.1	6.6	22.2	1.6

Vital sign abnormalities were assessed by treatment arm for the randomized trial in multiple myeloma and are presented in Table 3. Percentages are based on patients who had at least one on-treatment vital sign abnormality any time during the course of therapy.

Table 3: Vital Sign Abnormalities

Vital Sign Parameter	EMPLICITI + Lenalidomide and Dexamethasone N=318 %	Lenalidomide and Dexamethasone N=317 %
Systolic Blood Pressure ≥160 mmHg	33.3	20.9
Diastolic Blood Pressure ≥100 mmHg	17.3	11.7
Systolic Blood Pressure <90 mmHg	28.9	8.2
Heart Rate ≥100 bpm	47.8	29.7
Heart Rate <60 bpm	66	31.3

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity to EMPLICITI (elotuzumab).

Of 390 patients across four clinical studies who were treated with EMPLICITI and evaluable for the presence of anti-product antibodies, 72 patients (18.5%) tested positive for treatment-emergent anti-product antibodies by an electrochemiluminescent (ECL) assay. In 63 (88%) of these 72 patients, anti-product antibodies occurred within the first 2 months of the initiation of EMPLICITI treatment. Anti-product antibodies resolved by 2 to 4 months in 49 (78%) of these 63 patients. Neutralizing antibodies were detected in 19 of 299 patients in the randomized trial in multiple myeloma. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to EMPLICITI with the incidences of antibodies to other products may be misleading.

DRUG INTERACTIONS

Drug Interactions

No formal drug-drug interaction studies have been conducted with EMPLICITI. However, EMPLICITI is used in combination with lenalidomide and dexamethasone. Refer to the prescribing information for those products for important drug-drug interactions.

Laboratory Test Interference

EMPLICITI may be detected in the SPEP and serum immunofixation assays of myeloma patients and could interfere with correct response classification. A small peak in the early gamma region on SPEP that is IgGk on serum immunofixation may potentially be attributed to EMPLICITI, particularly in patients whose endogenous myeloma protein is IgA, IgM, IgD, or lambda light chain restricted. This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein *[see Warnings and Precautions]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no studies with EMPLICITI with pregnant women to inform any drug associated risks. Animal reproduction studies have not been conducted with elotuzumab.

EMPLICITI is administered in combination with lenalidomide and dexamethasone. Lenalidomide can cause embryo-fetal harm and is contraindicated for use in pregnancy. Refer to the lenalidomide and dexamethasone prescribing information for additional information. Lenalidomide is only available through a REMS program.

The background risk in the U.S. general population of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

Lactation

Risk Summary

There is no information on the presence of EMPLICITI in human milk, the effect on the breast-fed infant, or the effect on milk production. Because of the potential for serious adverse reactions in breast-fed infants from elotuzumab administered with lenalidomide/dexamethasone, breastfeeding is not recommended. Refer to the lenalidomide and dexamethasone prescribing information for additional information.

Females and Males of Reproductive Potential

Pregnancy Testing

Refer to the lenalidomide labeling for pregnancy testing requirements prior to initiating treatment in females of reproductive potential.

When EMPLICITI (elotuzumab) is used with lenalidomide, there is a risk of fetal harm, including severe life-threatening human birth defects associated with lenalidomide, and the need to follow requirements regarding pregnancy avoidance, including testing.

Contraception

Refer to the lenalidomide labeling for contraception requirements prior to initiating treatment in females of reproductive potential and males.

Lenalidomide is present in the blood and semen of patients receiving the drug. Refer to the lenalidomide full prescribing information for requirements regarding contraception and the prohibitions against blood and/or sperm donation due to presence and transmission in blood and/or semen and for additional information.

Pediatric Use

Safety and effectiveness have not been established in pediatric patients.

Geriatric Use

Of the 646 patients across treatment groups in the randomized trial in multiple myeloma, 57% were 65 years of age or older; the number of patients 65 years or older was similar between treatment groups. No overall differences in efficacy or safety were observed between patients 65 years or older and younger patients (less than 65 years of age).

OVERDOSAGE

The dose of EMPLICITI at which severe toxicity occurs is not known. EMPLICITI does not appear to be removed by dialysis as determined in a study of patients with renal impairment.

In case of overdosage, monitor patients closely for signs or symptoms of adverse reactions and institute appropriate symptomatic treatment.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Infusion Reactions

- EMPLICITI may cause infusion reactions. Advise patients to contact their healthcare provider if they experience signs and symptoms of infusion reactions, including fever, chills, rash, or breathing problems within 24 hours of infusion *[see Warnings and Precautions]*.
- Advise patients that they will be required to take the following oral medications prior to EMPLICITI dosing to reduce the risk of infusion reaction *[see Dosage and Administration (2.2) in full Prescribing Information]*:
  - Dexamethasone orally as prescribed
  - H1 blocker: diphenhydramine or equivalent (if oral)
  - H2 blocker: ranitidine or equivalent (if oral)
  - Acetaminophen (650-1000 mg orally)

Pregnancy

- Advise patients that lenalidomide has the potential to cause fetal harm and has specific requirements regarding contraception, pregnancy testing, blood and sperm donation, and transmission in sperm. Lenalidomide is only available through a REMS program *[see Use in Specific Populations]*.

Infections

- Inform patients of the risk of developing infections during treatment with EMPLICITI, and to report any symptoms of infection *[see Warnings and Precautions]*.

Second Primary Malignancies

- Inform patients of the risk of developing SPM during treatment with EMPLICITI *[see Warnings and Precautions]*.

Hepatotoxicity

- Inform patients of the risk of hepatotoxicity during treatment with EMPLICITI and to report any signs and symptoms associated with this event to their healthcare provider for evaluation *[see Warnings and Precautions]*.

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SPECIAL ISSUE / Palliative Care

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SP602. Good contact between the cooling cap and the scalp and maintenance of a consistent temperature throughout treatment are key factors to scalp cooling effectiveness. Source: Digitana.

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SP598. Palliative care services provide an umbrella of care for cancer patients.

FROM THE CHAIRMAN

Defining Palliation From the Patient's Perspective


MIKE HENNESSY, SR

THERE IS NO DOUBT THAT with increased conversations around symptom management, palliative care has finally managed to escape its once-dreaded identity, that of care at the end of life. More frequent, and more open, discussions—initiated by clinical care providers, the patient's family members, or by the patients themselves—have proven immensely important to moving the field in the right direction. Patients and their families are willing to speak about palliative care with their oncologists, or with a palliative care specialist, soon after their diagnosis. The conversation extends much beyond pain management and touches upon various aspects of managing the patient as a whole. It's a team effort of course, and as you will read in our end-of-year issue, a lot remains to be achieved in this field.

ResolutionCare is a community-based provider of palliation. Founded by Michael Fratkin, MD, the clinic provides palliative support, in person or remotely via telehealth, to cancer patients. By using telemedicine and relocating the center of care to where a person lives, the ResolutionCare model provides an opportunity to address more unmet demand for palliative care, while giving more control to the seriously ill to meet their stated needs.

Karen Mulvihill, DNP, APRN, FNP-BC, ACHPN, director of palliative care services at Danbury Hospital, writes about some of the challenges of integrating palliative care in a community cancer center. She also provides a case study, which was a pilot that evaluated the impact of integrating a palliative care advanced practice registered nurse in a health network in the state of Connecticut. An important lesson gained from the pilot was that educating patients, their family members, and care providers (oncologists), on what palliative care has to offer, is crucial.

However, public policy efforts are needed to maintain the momentum in the field. Sharon Pearce, vice president for public policy at the National Hospice and Palliative Care Organization (NHPCO) writes that despite a growing body of evidence supporting the integration of palliative care into treatment plans for individuals with advance illness, public policy has lagged behind and has led to significant variation across palliative care programs. Recent policy changes are, however, allowing small-scale testing of community-based palliative care delivery and some innovations in other delivery systems. Acknowledging that recent changes in the political climate could slow down the entire healthcare transformation, Pearce writes that NHPCO "Will continue to push for Medicare hospice benefit, and will support policies that allow hospice and palliative care providers to innovate and refine patient care services and ensure that all patients with advanced and terminal illness have access to the pain and symptom relief, psychosocial services and supports, and spiritual care that they need."

Along those lines, The Center to Advance Palliative Care (CAPC) is working to highlight the merits of concurrent palliative care under value-based payments. In their article, CAPC reviews published evidence and highlights exactly how Medicare Advantage plans, accountable care organizations, and oncology practices can benefit from integrating palliative care into standard treatment plans.

From the patient's perspective, their physical appearance is also extremely important. It has been documented that women have refused chemotherapy for their breast cancer for fear of losing their hair. That is quite astounding, but more importantly, there now is an FDA-approved option to preventing alopecia associated with chemotherapy—a form of palliation that could reduce unnecessary stress for the patient. However, coverage policies continue to define these preventive treatments as "experimental."

We hope this last issue of the year 2016 opens up conversations among oncology care teams on improving their care plans, with the patient placed front and center. As always, thank you to our readers for their continuous support, and we at *The American Journal of Managed Care®* would like to wish everyone a wonderful new year! ◆

Sincerely,
Mike Hennessy, Sr
CHAIRMAN AND CEO

Interesting Times in Healthcare


JOSEPH ALVARNAS, MD

IN HIS "RIPPLES OF HOPE" speech at the University of Cape Town, Robert F. Kennedy challenged his audience by telling them, "There is a Chinese curse which says, 'May he live in interesting times.' Like it or not we live in interesting times."[1] While the origins of this curse are likely apocryphal,[2] the sense of anxiety associated with coping with the uncertainty of changing circumstance seems appropriate as we contemplate the potential repeal of the Affordable Care Act (ACA).

Since it was signed into law on March 23, 2010, the ACA has provided a deeply detailed roadmap for the remaking of American healthcare.[3] For the past 6 years, stakeholders throughout the United States have participated in a mass reorganization of the healthcare system. This has included large-scale consolidation of providers and hospitals, development of the federal and state insurance exchange markets, restructuring of insurance products, realignment of payment policies, industry-wide restructuring of care processes, and a shift toward creating sustainable value-based care models. In the domain of cancer care, we have seen physicians, payers, advocacy groups, pharma, pharmacy benefits managers, employers, and the government collaborate on the reinvention of our cancer care delivery system. Given the relentless pace of therapeutic innovation, the meteoric rise in the cost of pharmaceuticals, and the rapidly changing standards of care for virtually every cancer diagnostic category, the complexity of this process and the level of stakeholder investment would be difficult to overstate. A glance at the topics featured in *Evidence-Based Oncology*™ (*EBO*™) over the past year reveals few areas in cancer care left untouched by the ACA.

Despite the breadth of engagement in this industry-wide reorganization, the ACA has been deeply polarizing. While for some it was an essential path toward equitable care access and sustainable healthcare expenditures, for others it was another example of federal micromanagement and overregulation of care delivery that led toward more costly, less-effective care with less consumer choice.[4,5] On the heels of an election whose results were surprising to many, we now find ourselves at the threshold of a potential repeal of this law, without a clear articulation of what might replace it.[6] The likely nomination of a highly vocal critic of the ACA (Georgia Congressman Tom Price) as Secretary of HHS signals that dramatic change rather than a nuanced evolution of the ACA is quite likely. Interesting times, indeed!

As we look to grapple with what is likely to be another period of extraordinary change in healthcare, there are some clues to the potential evolution of the ACA. Political promises notwithstanding, an immediate repeal would be extraordinarily difficult to achieve. Some have proposed that the actual undoing of the ACA might happen relatively slowly, over the course of several years, as a replacement strategy and legislation are crafted. Moreover, President-elect Donald Trump has indicated that some of the more popular portions of the law might remain in effect, including a ban against consideration of preexisting health conditions in coverage denials.[7]

The best clues to what healthcare strategy might look like under the incoming congress and Trump White House come from House Speaker Paul Ryan's recent healthcare policy paper, A Better Way: Our Vision for a Confident America.[8] In reviewing this policy paper, several important themes stand out. The focus upon value delivery in healthcare will remain an extraordinarily important driver in the evolution of cancer care. A recognition of the importance of innovation in care delivery ensures that the challenges of integrating rapidly evolving standards of care and novel therapeutics remains a central challenge in the cancer care domain. The reiteration of the importance of patient choice in healthcare reaffirms that care delivery systems will need to become increasingly patient-centered.

Undoubtedly, there are many interesting times ahead. At its core, however, the issues that we have highlighted throughout the past year in *EBO*™ remain the essential terrain that we will have to navigate in order to ultimately move toward sustainable, patient-centered, and innovation-driven cancer care delivery in the post-ACA era.

From the editorial staff, and me we wish you a wonderful holiday season. ◆

REFERENCES

1. RFK in the land of apartheid: a ripple of hope. Rfksafilm.org website. http://www.rfksafilm.org/html/speeches/unicape.php. Accessed November 28, 2016.
2. Kristof ND. A Chinese curse? *The New York Times* website. http://kristof.blogs.nytimes.com/2008/09/24/a-chinese-curse/?_r=0. Published September 24, 2008. Accessed November 28, 2016.
3. Read the law. Department of Health and Human Services website. https://www.hhs.gov/healthcare/about-the-law/read-the-law/#. Accessed November 28, 2016.
4. Rivlin AM. What the ACA has achieved and what's next. Brookings Institution website. https://www.brookings.edu/opinions/what-the-aca-has-achieved-and-whats-next/.Published December 21, 2015. Accessed November 28, 2016.
5. Epstein RA. Unaffordable care act. Hoover Institution website. http://www.hoover.org/research/unaffordable-care-act. Published October 31, 2016. Accessed November 28, 2016.
6. Goldstein A. Obamacare's future in critical condition after Trump's victory. *The Washington Post* website. https://www.washingtonpost.com/national/health-science/acas-future-in-critical-condition-with-trumps-victory/2016/11/09/7c5587e8-a684-11e6-ba59-a7d93165c6d4_story.html. Published November 9, 2016. Accessed November 28, 2016.
7. Pearlstein S. Donald Trump is about to face a rude awakening over Obamacare. *The Washington Post* website. https://www.washingtonpost.com/news/wonk/wp/2016/11/12/donald-trump-is-beginning-to-face-a-rude-awakening-over-obamacare/. Published November 12, 2016. Accessed November 28, 2016.
8. A better way: our vision for a confident America. A Better Way website. https://abetterway.speaker.gov/_assets/pdf/ABetterWay-HealthCare-PolicyPaper.pdf. Published June 22, 2016. Accessed November 28, 2016.

EDITORIAL MISSION

To present policy makers, payers, and providers with the clinical, pharmacoeconomic, and regulatory information they need to improve efficiency and outcomes in cancer care.

Integrating Palliative Care Into Outpatient Oncology: A Case Study

Karen Mulvihill, DNP, APRN, FNP-BC, ACHPN

MULVIHILL

Karen Mulvihill, DNP, APRN, FNP-BC, ACHPN, is director of palliative care services at Danbury Hospital.

ALTHOUGH A SIGNIFICANT EVIDENCE BASE EXISTS to support the integration of palliative care in the care of cancer patients, difficulty comes from how to actually operationalize it. There is no standard method for integrating palliative care into outpatient oncology practices, and no examples of how cancer centers are doing it. The 2016 edition of the Commission on Cancer standard 2.4 states, "Palliative care services are available to patients either on-site or by referral."[1] Further, clinical organizations like the American Society of Clinical Oncology support the integration of palliative care into the care of "any patient with metastatic cancer and/or high symptom burden."[2] This article will present, as a case study, one program's integration of palliative care services into outpatient community oncology. The benefits and challenges will be explored, as well as evidence for why palliative care clinicians are an integral part of the outpatient oncology care team.

Defining the Expanse of Palliative Care Services

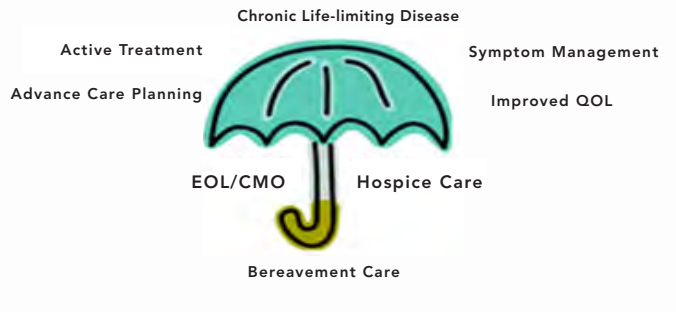
The first step in successful integration should be defining what palliative care is and is not. Palliative care is a fairly new specialty, having started as an inpatient consult service that recently expanded into the outpatient community. The National Quality Forum developed a consensus report in 2006 on the preferred practices for Palliative Care and Hospice Quality,[3] where they defined palliative care as, "Patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. Palliative care throughout the continuum of illness involves addressing physical, intellectual, emotional, social, and spiritual needs and to facilitate patient autonomy, access to information, and choice."[3,4]

The following are features of the philosophy and delivery of palliative care:

- Care is provided and services are coordinated by an interdisciplinary team
- Patients, families, and palliative and nonpalliative healthcare providers collaborate and communicate on care needs
- Services are available concurrently with, or independent of, curative or life-prolonging care
- Patient and family hopes for peace and dignity are supported throughout the course of illness, during the dying process, and after death[5]

Palliative care can be thought of as an umbrella, with the umbrella representing the protection palliation can provide for patients with serious illness.[6] Palliative care addresses the patients' quality of life (QOL), symptom management, advance care planning, and goals of care. Once the patient is under the protection of the umbrella, hospice care and comfort are the goals of care. The handle of the umbrella represents bereavement services for families (see **FIGURE**). This model helps with the understanding that palliative care is not hospice or end-of-life (EOL) care alone (hospice is a type of palliative care, but palliative care is much broader). Palliative care should be integrated into care from the time of diagnosis of a serious illness, and it works as an extra layer of support for patients, families, and staff dealing with serious illness.[6]

FIGURE. Palliative Cares Services Provide an Umbrella of Care for Cancer Patients



EOL/CMO indicates end-of-life/comfort measures; QOL, quality of life.

Case Study

A health network in western Connecticut is home to a robust inpatient palliative care service, which was established late in 2003 and continued to expand over the next decade. In 2013, the palliative care team and the community cancer center decided to explore the trial integration of palliative care into the outpatient oncology practice. Designated cancer centers tend to have more robust palliative care service but largely use consulting services to provide their palliative care.[7] Although the physicians were familiar with the palliative care advanced practice registered nurse (APRN) from the inpatient service, they still expressed concern and had some misunderstanding regarding the role of palliative care. There was concern that the palliative care team would tell patients they were dying before the patients were ready to discuss death. Some oncologists felt, too, that their patients would get upset hearing the word "palliative."

As a first step, an APRN with expertise in palliative care was assigned to the cancer center for 1 afternoon every week. The interdisciplinary team included the oncology team, palliative care APRN, oncology social worker, and other support services available in the cancer center. Initially, patients were seen by

the palliative care service while they were an inpatient and were subsequently seen in the outpatient oncology office for follow-up care. This was a good way to start to get to know the practice and team members and begin to gain trust. The APRN also attended lung and gastrointestinal (GI) tumor boards and completed a palliative care screening on newly diagnosed patients, with the goal being able to identify appropriate patients and see them soon after diagnosis.

The focus of this pilot was on diagnoses that were stage IIIb and above, recurrent or metastatic disease, and solid organ tumors. The patients identified by the tumor board often fell through the cracks due to difficulty in obtaining the oncologist's approval and lack of a clear process for arranging appointments following tumor boards. The barriers identified included:

- Lack of understanding of the APRN's role
- Fear that the patients would not want to hear the term "palliative care"
- Trying to fit another appointment into the patients' already full schedules

A Team Effort

The APRN and the oncology team brainstormed to carve out an ongoing education program for the oncology team, which would cover the role of palliative care in improving clinical outcomes. Further, it was collaboratively decided that the best way to fully integrate the palliative program was to have the APRN meet the patient with the oncologist on their initial consult visit in the outpatient oncology office. The palliative care APRN introduced herself as "another member of the oncology team to provide you with an extra layer of support." The benefit of this model was the oncologist got to experience exactly how the APRN introduced the topic of palliative care to a newly diagnosed patient prior to treatment initiation. This created trust with the oncologists, and referrals started coming in.

Initially, the APRN had enough flexibility within her schedule to be able to see most patients when they were already in the office for other appointments, including for chemotherapy or radiation therapy. Eventually, however, the patient load became too large and patients were being missed. This called for another brainstorming session, so the team sat down again and decided the best way to integrate was to have a palliative care APRN on staff in the practice. Trust with providers about the palliative care service now exists. Once patients are identified by tumor boards, the APRN can see patients once they are identified in tumor boards by scheduling the appointment sooner.

Many lessons were learned as the program grew, with the most important lesson being the oncologist must have full trust in the palliative care provider. For the program to be effective, trust needs to be built with the palliative care team, and the oncologist must witness the interactions that the palliative care providers have with patients and their families. Another lesson learned is how many stage IV patients actually want to know about hospice on their initial visit. This was a shocking discovery and very refreshing. The most frequent question asked was, "How am I going to know when it is time for hospice?" These patients were accepting treatment but had not started it, yet they were already thinking about their EOL care.

All of the palliative care APRN visits were billable, as long as another APRN had not seen the patient on the same day. Over time, we also learned that it is important to continue to provide education on palliative care and assess the model of care being provided. The model may need to change over time, and palliative care teams need to be able to flex their services based on the needs of their patients and families.

Evidence-Based Integration of Palliative Care

So, what does the evidence support? From a clinical perspective, a vast amount of research supports the benefits of palliative care in outpatient oncology. Patients are living longer with a serious illness and heavy symptom burden. Nearly half of patients diagnosed with a metastatic cancer will live for years following diagnosis,[2] and those years may be riddled with multiple on-going symptoms that may have a negative impact on the patients' QOL. According to a study by Ferrell et al, patients with non–small cell lung cancer (NSCLC) who received palliative care intervention had significantly better QOL scores, better symptom control, better spiritual well-being, and lower psychological distress.[8] The intervention group had a higher advance directive completion rate and higher referrals to supportive services, with greater improvements in their stage IV disease. A study by Greer et al had similar results, showing higher QOL scores and less depression in patients with incurable lung and GI cancers when palliative care was included in the treatment plan.[9] This group also reported discussing their EOL preferences more than patients who were not seen by a palliative care specialist.

The benefits of quality palliative care on patient survival remains a topic of ongoing research. A groundbreaking study by Temel and others was the first to show the survival benefit of palliation in patients with NSCLC—up to 2.7 months longer for patients who received palliative care compared with those who did not.[10] The "why" of these results, however, is yet to be determined.

A heavy symptom burden can affect patients: physically, psychologically, spiritually, and existentially. Uncontrolled pain and symptoms can lead to poor QOL, loss of purpose, loss of financial resources, and lack of sleep and can prevent the body from functioning optimally. Palliative care looks at the whole patient and addresses all aspects of care to assist with better symptom control and better QOL, resulting in patients living longer.

Educating Providers

Education has been identified as a barrier to quality palliative care services in oncology. The 2014 Institute of Medicine (IOM) report, Dying in America, recommends that "Educational institutions, professional societies, accrediting organizations, certifying bodies, healthcare delivery organizations, and medical centers take measures to both increase the number of palliative care specialists and expand the knowledge base for all clinicians."[11] Physicians and nurses often feel ill-prepared to discuss palliative or EOL care with their patients and families. A study among 675 nurses and physicians identified need for more basic information on palliative care, improved training on communication skills, and knowledge of how to take better care of the patient's caregivers.[12] When Horlait et al examined what oncologists identified as barriers in discussing palliative care with their patients, they found that these discussions were perceived as a "complex and emotional task," which in turn led to palliative care referrals being made late in the course of the illness.[13]

The benefits of palliative care can be seen at any age level. Mahmood et al found that not only is palliative care feasible for children with high-risk cancer, but was also acceptable to the children, families, and pediatric oncologists.[14] Caring for older adults with cancer can be challenging because they often suffer multiple co-morbidities and decreasing functional status, which need to be taken

FROM A CLINICAL PERSPECTIVE, A VAST AMOUNT OF RESEARCH SUPPORTS THE BENEFITS OF PALLIATIVE CARE IN OUTPATIENT ONCOLOGY. PATIENTS ARE LIVING LONGER WITH A SERIOUS ILLNESS AND HEAVY SYMPTOM BURDEN.

into consideration when discussing treatment options. Palliative care should be provided from the moment of diagnosis to ensure adequate symptom management and to ensure that treatments are aligned with the patient's preferences and values.[15] Palliative care can prove beneficial to a host of individuals, including cancer survivors,[16] hematopoietic transplant patients,[17] patients with hematological malignancies,[18] adolescents and young adults,[19] as well as patients participating in clinical trials.[20]

Cost of Care

Another barrier identified in the literature is cost. Several studies have identified a perceived barrier related to the cost involved in implementing palliative care programs in cancer centers. Palliative care programs have struggled to provide cost benefit analysis of their services. Cost savings are a secondary outcome and can be realized when patient preferences are documented and obeyed. Palliative care does not convince patients to follow a conservative plan of care or sign-on to hospice. To the contrary, palliative care practitioners are expert at eliciting the patient's goals and values and helping integrate them in the treatment plan. Patients may identify not wanting that "last resort" treatment or not wanting to go to the hospital any longer. Some patients may decide they want everything done so they can see their first grandchild born. Patients and families often do not understand that they have a choice in treatments—they may even feel guilty about wanting to stop treatment and expressing this to their oncologist. Also, it is often difficult for patients to tell their own family members that they have had enough treatment and that they would like the focus of their care to be comfort only. Palliative care teams have the skill to advocate for their patients' preferences and assist the patient in discussing those preferences with their oncologist and family. Aligning treatment with patient goals can also save costs via reduced hospitalizations and by avoiding expensive treatments and procedures that are not aligned with the patient preferences.

PALLIATIVE CARE TEAMS HAVE THE SKILL TO ADVOCATE FOR THEIR PATIENTS' PREFERENCES AND ASSIST THE PATIENT IN DISCUSSING THOSE PREFERENCES WITH THEIR ONCOLOGIST AND FAMILY.

In conclusion, there is a strong evidence to support integrating palliative care into cancer centers. However, an understanding of what palliative care is and what it isn't is crucial for this integration. A majority of patients with cancer consider their disease a "serious illness," and they will most definitely benefit from a palliative care intervention. A standard approach will also decrease the misunderstanding that palliative care is hospice or EOL care, and ensure that patients benefit from palliative care programs. Early palliative care can prolong survival for some diagnoses, improve QOL, decrease symptom burden, and improve patient and family satisfaction. The example in this paper reviewed some of the challenges that may be encountered during integration, and some solutions to overcome them. As the field of palliative care continues to grow, cancer centers should share examples of how they have successfully integrated palliative care into their centers, so others can learn from their successes and challenges. ◆

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REFERENCES

1. Cancer program standards: ensuring patient-centered care. 2016;standard 2.4;54. American College of Surgeons website. https://www.facs.org/quality%20programs/cancer/coc/standards. Accessed October 20, 2016.
2. Smith TJ, Temin S, Alesi ER, et al. American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care. *J Clin Onc.* 2012:30(8):880-887. doi: 10.1200/JCO.2011.38.5161.
3. Nation Quality Forum. A national framework and preferred practices for palliative and hospice care quality. NQF website. http://www.qualityforum.org/publications/2006/12/A_National_Framework_and_Preferred_Practices_for_Palliative_and_Hospice_Care_Quality.aspx. Published December 2006. Accessed October 15, 2016.
4. Centers for Medicare & Medicaid Services. Medicare and Medicaid programs: hospice conditions of participation. *Federal Register.* 2008;73(109). US Government Publishing Office website. https://www.gpo.gov/fdsys/pkg/FR-2008-06-05/pdf/08-1305.pdf. Published June 5, 2008. Accessed November 1, 2016.
5. National Consensus Project for Quality Palliative Care. Clinical practice guidelines for quality palliative care. HPNA website. https://www.hpna.org/multimedia/NCP_Clinical_Practice_Guidelines_3rd_Edition.pdf. Published 2013. Accessed November 1, 2016.
6. Mulvihill K. Emmi website. http://engagingthepatient.com/2014/10/21/palliative-care-but-i-am-not-dying/. Published October 21, 2014. Accessed October 15, 2016.
7. Davis MP, Strasser F, Cherny N. How well is palliative care integrated into cancer care? A MASCC, ESMO, and EAPC project. *Support Care Cancer.* 2015;23(9):2677-2685. doi: 10.1007/s00520-015-2630-z.
8. Ferrell B, Sun V, Hurria A, et al. Interdisciplinary palliative care for patients with lung cancer. *J Pain Symptom Manage.* 2015;50(6):758-767. doi: 10.1016/j.jpainsymman.2015.07.005.
9. Greer JA, El-Jawahri A, Pirl WF, et al. Randomized trial of early integrated palliative and oncology care. *J Clin Onc* 2016;34. Suppl 26S; abstr 104.
10. Temel J, Greer J, Muzikansky A, et al. Early palliative care for patients with metastatic non-small cell lung cancer. *N Engl, J Med.* 2010;363(8):733-742. doi: 10.1200/JCO.2010.32.4459.
11. Committee on Approaching Death: addressing key end-of-life issues. Dying in America: improving quality and honoring individual preferences near the end of life. National Academies website. http://www.nationalacademies.org/hmd/~/media/Files/Report%20Files/2014/EOL/Report%20Brief.pdf. Published September 2014. Accessed on October 24, 2016.
12. Jors K, Seibel K, Bardenheuer H, et al. Education in end-of-life care: what do experienced professionals find important? *J Cancer Educ.* 2016;31(2):272-278. doi: 10.1007/s13187-015-0811-6.
13. Horlait M, Chambaere K, Pardon K, Deliens L, Belle S. What are the barriers faced by medical oncologists in initiating discussion of palliative care? A qualitative study in Flanders, Belgium. *Support Care Cancer.* 2016;24(9):3873-3881. doi: 10.1007/s00520-016-3211-5.
14. Mahmood LA, Casey D, Dolan JG, Dozier AM, Korones DN. Feasibility of early palliative care consultation for children with high-risk malignancies. *Pediatr Blood Cancer.* 2016;63(8):1419-1422. doi: 10.1002/pbc.26024.
15. Balducci L, Dolan D, Hoffe SE, Hoffe SA. Palliative care in older patients with cancer. *Cancer Control.* 2015;22(4):480-488.
16. Economou D. Palliative care needs of cancer survivors. *Semin Oncol Nurs.* 2014;30(4):262-267. doi: 10.1016/j.soncn.2014.08.008.
17. Tierney DK, Passaglia J, Jenkins P. Palliative care of hematopoietic cell transplant recipients and families. *Semin Oncol Nurs.* 2014;30(4):253-261. doi: 10.1016/j.soncn.2014.08.007.
18. LeBlanc TW, O'Donnell JD, Crowley-Matoka M, et al. Perceptions of palliative care among hematologic malignancy specialists: a mixed-methods study. *J Oncol Pract.* 2015;11(2):e230-e238. doi: 10.1200/JOP.2014.001859.
19. Donovan KA, Knight D, Quinn GP. Palliative care in adolescents and young adults with cancer. *Cancer Control.* 2015;22(4):475-479.
20. Sun V, Cooke L, Chung V, Uman G, Smith TJ, Ferrell B. Feasibility of a palliative care intervention for cancer patients in phase I clinical trials. *J Palliat Med.* 2014;17(12):1365-1368. doi: 10.1089/jpm.2014.0108.

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Preventing Chemotherapy-Associated Alopecia: A Case for Palliation?

Surabhi Dangi-Garimella, PhD

A PATIENT UNDERGOING TREATMENT FOR a chronic or debilitating illness has enough to deal with, with respect to their treatment and care, and challenges with their appearance should be the least of their worries. However, chemotherapy-induced alopecia (CIA) is real, and it can dishearten patients and their attitude toward their care.

Physicians consider alopecia an eventuality of chemotherapy, and very few can offer any advice to patients on how to manage this side effect. However, hair loss, which drastically changes how a person looks and feels, can significantly impact the patient's quality of life (QOL), over and above the physical exhaustion associated with their treatment.

The incidence and severity of CIA varies based on the drug being used, from 65% to 100%. For patients, alopecia ranks high, next to nausea and vomiting, as the most distressing side effect of treatment. A literature review of the impact of alopecia on a patient's QOL found that this side effect of cancer treatment can impact patients in a variety of ways—it can cause anxiety and distress; trigger issues with body image, self-esteem, perception of sexuality, and social functioning; and influence the ability to return to work.[1]

A survey conducted 25 years ago found that slightly less than 10% of women diagnosed with cancer, in the 24 to 66 age group, were actually ready to forego chemotherapy due to the impending threat of losing their hair.[2] A more recent study in newly diagnosed cancer patients found that a little over 15% of participants refused cancer treatment partially or completely, and of those, a majority were women refusing adjuvant chemotherapy for their breast cancer.[3]

To measure this stress, researchers have developed the Chemotherapy-induced Alopecia Distress Scale (CADS). CADS quantifies the distress experienced by patients undergoing treatment for breast cancer. Used in 305 Korean women, the study found that CADS moderately correlated with body image ($r = -0.47$; $P < .001$), weakly correlated with the patient's overall quality of life ($r = -0.28$; $P < .001$), but did not correlate with self-esteem ($r = -0.07$; $P = 0.23$).[4]

Preventing hair loss would be a game changer for patients, and one way of achieving this is by using scalp cooling technology.

Potential Solution: Scalp Cooling Systems

Several scalp cooling or cold cap systems have been developed for use in patients with solid tumors while they are being treated with chemotherapy agents. Cold cap technology helps alleviate the damage of chemotherapy agents on hair follicles via vasoconstriction—reducing blood flow to follicles. This significantly lowers the dose of the chemotherapy agent that reaches the hair follicles, potentially reducing alopecia.

A few of the products that are currently being marketed include:

FIGURE 1. DigniCap Cooling System

The DigniCap cooling system has 2 inbuilt sensors for temperature regulation, and a third safety sensor to ensure that the scalp temperature never falls below 32°F (0°C). Source: Digitana.

1. The Paxman Scalp Cooling System[5]
2. DigniCap[6]
3. Chemo Cold Caps[7]
4. Penguin Cold Caps[8]

Clinical trials have evaluated the efficacy of these devices.[6] One such trial compared the Paxman system with cold caps in patients

receiving treatment with docetaxel in a palliative setting. Of the 238 patients who were enrolled, 128 were on the Paxman system, 71 were on cold cap, and 39 patients were the control group that did not receive any scalp cooling treatment. The primary outcome was benchmarked as alopecia World Health Organization III or IV, or the need to wear a wig.[9]

Although alopecia was observed across all 3 groups being compared, cooling was found to reduce the risk of alopecia by 78% (HR 0.22; 95% CI, 0.12-0.41). Both systems, the study found, were equally effective in preventing alopecia. The intense cold sensation, however, was unbearable for 13% of patients and they subsequently dropped out of the study.

A literature review by Shin et al of articles published in PubMed, EMBASE, and the Cochrane Library, between June 20, 2013, and August 31, 2013, concluded that scalp cooling can prevent CIA in patients receiving chemotherapy; however, long-term safety studies are warranted. Out of 691 articles retrieved by the study authors, a total of 8 randomized control trials and 9 controlled clinical trials involving 1098 participants (616 interventions and 482 controls) were included in the final analyses, a majority of whom were breast cancer patients receiving doxorubicin- or epirubicin-containing chemotherapy. Scalp cooling, the most popular preventive method, significantly reduced the risk of CIA (RR, 0.38; 95 % CI, 0.32-0.45), whereas topical 2 % minoxidil and other interventions did not, the authors confirmed based on their analysis.[10]

Device manufacturers, however, contraindicate the use of scalp cooling technology in individuals with:

- Hematological conditions
- Cold allergy
- Cold agglutinins
- Manifest scalp metastases
- Imminent bone marrow ablation chemotherapy
- Imminent skull irradiation

Of the available scalp cooling systems, DigniCap is the first one to be granted FDA approval to reduce alopecia in breast cancer patients receiving chemotherapy.[11] Digitana, the manufacturer of the device, told *Evidence-Based Oncology™* (*EBO™*) in an e-mail, that the DigniCap System is the only scalp cooling device to complete FDA-approved multi-center clinical trials at several medical centers within the United States, including the Helen Diller Family Comprehensive Cancer Center, University of California San Francisco; Wake Forest Baptist Medical Center; Weill Cornell Breast Center; Mount Sinai Beth Israel Comprehensive Cancer Center; and Jonsson Comprehensive Cancer Center, University of California, Los Angeles.

DigniCap System

The DigniCap cooling system (**FIGURE 1**) has 2 inbuilt sensors for temperature regulation, and a third safety sensor to ensure that the scalp temperature never falls below 32ºF (0ºC). Safe and effective across multiple ethnicities, clinical studies found that the DigniCap scalp cooling system prevented hair loss in 70.3% of patients with breast cancer receiving adjuvant chemotherapy, compared with the control group that experienced significant hair loss. "Good contact between the cooling cap and the scalp and maintenance of a consistent temperature throughout treatment are key factors to scalp cooling effectiveness," according to Digitana (**FIGURE 2**).

FIGURE 2. Contact Ensures Appropriate Scalp Cooling

Good contact between the cooling cap and the scalp and maintenance of a consistent temperature throughout treatment are key factors to scalp cooling effectiveness. Source: Digitana.

The company either directly charges the patient or leases the cooling system (**FIGURE 1**) to clinics and cancer care facilities, with additional payment attached per use. Following FDA clearance, the past year has seen more than 40 medical centers across the United States offer this preventive intervention to their patients.

Challenges With Using the Technology

According to Nancy Marshall, cofounder of The Rapunzel Project,[12] patient tolerance with using these extremely cold caps may vary. Patients could become numb to the cold after the first cap is placed on their head but may become comfortable by the time of the next change. "Exposed skin (such as forehead, ears, and scalp) can get freezer burn, but patients are taught to change hair part lines and protect other exposed skin with moleskin or similar covering," Marshall told *EBO™*. Additionally, the process needs to be well coordinated by a very capable helper who can safely handle the extremely cold caps, while ensuring the schedule of cap changes is maintained, according to Marshall.

"INSURANCE REIMBURSEMENT HAS OCCURRED IN A FEW INSTANCES, BUT IS STILL HIGHLY UNLIKELY."

-Nancy Marshall, cofounder, The Rapunzel Project

The Rapunzel Project finds its inspiration in the experiences of its cofounders, Shirley Billigmeier and Marshall, both breast cancer survivors. Billigmeier, with the support of her oncologist, used the cold caps when she was being treated for her breast cancer. Marshall supported her friend by organizing fundraisers that helped the hospital, where Billigmeier was being treated, purchase a freezer. Motivated by this experience, the 2 women then decided to raise awareness among cancer patients, their physicians, and their hair stylists about this new technology, and The Rapunzel Project was born.

Smaller clinics may not have access to biomedical freezers, which would mean the patient has to bring in dry ice to freeze the individual caps, an added cost of up to $150, according to Marshall. Their organization assists these clinics by donating freezers.

FOLLOWING FDA CLEARANCE, NEARLY 40 MEDICAL CENTERS NOW OFFER DIGNICAP AS A PREVENTIVE INTERVENTION.

Health Plan Coverage Not Yet Standard Practice

Digitana is working with third-party payers to establish coverage for use of their cooling device. According to the company, each medical center decides what percentage of the cost of the device and its operation it will absorb, and how much will be shouldered by the patient. Medical and philanthropic foundations are also lending monetary support to patients.

Aetna considers "scalp cooling (ie, using ice-filled bags/bandages, cryogenic packs, or specially designed devices) experimental and investigational as a means to prevent hair loss during chemotherapy because the effectiveness of this process has not been established."[13]

The UnitedHealth policy brief on scalp cooling states, "While ice-filled bags or bandages or other devices used for scalp hypothermia during chemotherapy may be covered as supplies of the kind commonly furnished without a separate charge, no separate charge for them would be recognized."[14]

"Insurance reimbursement has occurred in a few instances, but is still highly unlikely," explained Marshall. She argues that if insurance companies are ready to pay for a wig, paying for these cold caps to avoid wearing a wig should be a no-brainer. She would like to see organizations like the Susan G. Komen Foundation and the American Cancer Society lend support to this cause.

Raising Awareness

Marshall told *EBO™* that there is a gap in knowledge, between both patients and care providers, on the efficiency of this technology. "Doctors and clinics were understandably wary of supporting an unapproved product, though many recognized the importance of this issue to patients," Marshall said. This was compounded by the fact that most manufacturers of these systems were small businesses and the FDA process is expensive.

Marshall acknowledged the persistence of both patients and providers—doctors reviewed the literature and research and concluded they had no issue with their patients trying cold caps, and when the caps worked, the physicians became believers. "This has really led to considerable support, particularly in California, Florida, and New York," Marshall said.

In a statement, Digitana told *EBO™*, "We have been working with our clinical partners to share patient success stories and increase awareness among patients at the community level. Digitana is also supporting several charities and philanthropic initiatives within the breast cancer community to increase awareness that cost need not be a deterrent with this therapeutic option." Additionally, educating oncologists and health center staff on the benefits of scalp cooling is also a part of the company's awareness campaign. The company is also a supporter of HairToStay, a nonprofit that provides financial assistance to those women who cannot afford the cost of hair cooling systems.[16]

The Rapunzel Project also reaches out to hair stylists. "We discovered that hair stylists are all too familiar with the trauma prospective hair loss represents for their clients. Faced with the prospect of chemo, many patients consult a stylist (with whom they often have a personal relationship) regarding shaving their head and/or acquiring a wig. This is a critical time window—after diagnosis and before treatment," Marshall told *EBO™*. They have partnered with Kenra Professional, a hair care products manufacturer out of Indianapolis, to distribute the project's literature to Kenra's salon clients, as well as to educate the stylists.

Digitana believes their treatment to prevent alopecia in women receiving chemotherapy for their breast cancer is a form of palliative care. "Patients who have been able to save their hair through scalp cooling describe the greater sense of control and well-being that has come along with being able to save their hair during their chemotherapy. This is definitely in keeping with the palliative care goal to improve quality of life for both the patient and the family," the company told *EBO™*.

According to Marshall, "The DigniCap system is definitely more user friendly, and, hopefully, there will be cost efficiencies, as well, as volume builds." She also thinks that having a nurse handle the caps will make the process easier and hassle free for patients and their families.

"We know cold cap therapy is not for everyone, but we strongly believe you can't make a choice if you don't know you have a choice," Marshall continued. "Patients should be informed there is a viable option to save their hair, so they can make the decision that is best for them. And, of course, the process needs to be affordable for all." ◆

REFERENCES

1. Dmytriw AA, Morzycki W, Green PJ. Prevention of alopecia in medical and interventional chemotherapy patients. *J Cutan Med Surg.* 2015;19(1):11-16. doi: 10.2310/7750.2014.13200.

2. Tierney AJ, Taylor J, Closs SJ. Knowledge, expectations and experiences of patients receiving chemotherapy for breast cancer. *Scand J Caring Sci.* 1992;6(2):75-80. doi: 10.1111/j.1471-6712.1992.tb00128.x.

3. Puts MT, Monette J, Girre V, et al. Characteristics of older newly diagnosed cancer patients refusing cancer treatments. *Support Care Cancer.* 2010;18(8):969-74. doi: 10.1007/s00520-010-0883-0.

4. Cho J, Choi EK, Kim IR, et al. Development and validation of Chemotherapy-induced Alopecia Distress Scale (CADS) for breast cancer patients. *Ann Oncol.* 2014;25(2):346-351. doi: 10.1093/annonc/mdt476.

5. What is scalp cooling? Paxman Scalp Cooling website. http://paxmanscalpcooling.com/scalp-cooling. Accessed November 14, 2016.

6. DigniCap website. https://www.dignicap.com/. Accessed November 14, 2016.

7. Chemo Cold Caps website. http://chemocoldcaps.com/. Accessed November 14, 2016.

8. Penguin Cold Caps website. https://penguincoldcaps.com/us/. Accessed November 14, 2016.

9. Betticher DC, Delmore G, Breitenstein U, et al. Efficacy and tolerability of two scalp cooling systems for the prevention of alopecia associated with docetaxel treatment. *Support Care Cancer.* 2013;21(9):2565-2573. doi: 10.1007/s00520-013-1804-9.

10. Shin H, Jo SJ, Kim DH, Kwon O, Myung SK. Efficacy of interventions for prevention of chemotherapy-induced alopecia: a systematic review and meta-analysis. *Int J Cancer.* 2015;136(5):E442-E454. doi: 10.1002/ijc.29115.

11. FDA allows marketing of cooling cap to reduce hair loss during chemotherapy [news release]. Silver Spring, MD: FDA; December 8, 2015. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm476216.htm. Accessed November 15, 2016.

12. The Rapunzel Project. Rapunzel Project website. http://www.rapunzelproject.org/OurStory.aspx. Accessed November 16, 2016.

13. Scalp cooling (hypothermia) to prevent hair loss during chemotherapy. Aetna website. http://www.aetna.com/cpb/medical/data/200_299/0290.html. Reviewed May 27, 2016. Accessed November 15, 2016.

14. Scalp hypothermia during chemotherapy to prevent hair loss (NCD 110.6). UnitedHealthcare website.

15. https://www.unitedhealthcareonline.com/ccmcontent/ProviderII/UHC/en-US/Main%20Menu/Tools%20&%20Resources/Policies%20and%20Protocols/Medicare%20Advantage%20Policy%20Guidelines/Scalp_Hypothermia_During_Chemo_Prevent_Hair_Loss.pdf. Approved August 10, 2016. Accessed November 16, 2016.

16. HairToStay website. http://www.hairtostay.org/. Accessed November 16, 2016.

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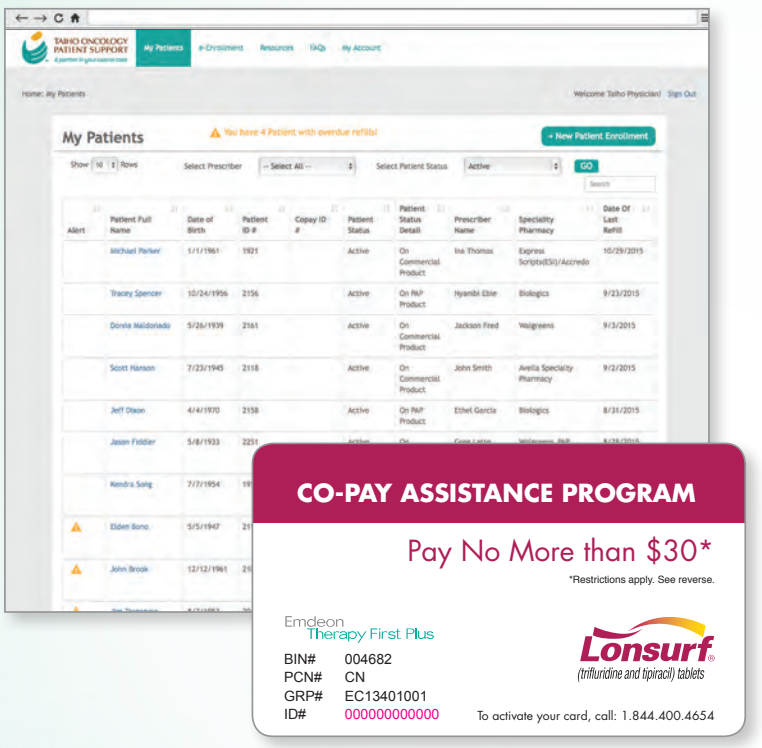

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Please see Important Safety Information and brief summary of Prescribing Information on the following pages.

Lonsurf® (trifluridine and tipiracil) tablets

TAIHO ONCOLOGY

Lonsurf®
(trifluridine and tipiracil) tablets

Indication

LONSURF is indicated for the treatment of patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if *RAS* wild type, an anti-EGFR therapy.

Important Safety Information

WARNINGS AND PRECAUTIONS

Severe Myelosuppression: In Study 1, LONSURF caused severe and life-threatening myelosuppression (Grade 3-4) consisting of anemia (18%), neutropenia (38%), thrombocytopenia (5%), and febrile neutropenia (3.8%). One patient (0.2%) died due to neutropenic infection. In Study 1, 9.4% of LONSURF-treated patients received granulocyte-colony stimulating factors.

Obtain complete blood counts prior to and on day 15 of each cycle of LONSURF and more frequently as clinically indicated. Withhold LONSURF for febrile neutropenia, Grade 4 neutropenia, or platelets less than 50,000/mm^3. Upon recovery, resume LONSURF at a reduced dose.

Embryo-Fetal Toxicity: LONSURF can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with LONSURF.

USE IN SPECIFIC POPULATIONS

Lactation: It is not known whether LONSURF or its metabolites are present in human milk. There are no data to assess the effects of LONSURF or its metabolites on the breast-fed infant or the effects on milk production. Because of the potential for serious adverse reactions in breast-fed infants, advise women not to breast-feed during treatment with LONSURF and for 1 day following the final dose.

Male Contraception: Advise males with female partners of reproductive potential to use condoms during treatment with LONSURF and for at least 3 months after the final dose.

Geriatric Use: Grade 3 or 4 neutropenia and thrombocytopenia and Grade 3 anemia occurred more commonly in patients 65 years or older who received LONSURF.

Renal Impairment: Patients with moderate renal impairment may require dose modifications for increased toxicity. No patients with severe renal impairment were enrolled in Study 1.

Hepatic Impairment: Patients with moderate or severe hepatic impairment were not enrolled in Study 1.

ADVERSE REACTIONS

Most Common Adverse Drug Reactions in Patients Treated With LONSURF (≥5%): The most common adverse drug reactions in LONSURF-treated patients vs placebo-treated patients with refractory mCRC, respectively, were asthenia/fatigue (52% vs 35%), nausea (48% vs 24%), decreased appetite (39% vs 29%), diarrhea (32% vs 12%), vomiting (28% vs 14%), abdominal pain (21% vs 18%), pyrexia (19% vs 14%), stomatitis (8% vs 6%), dysgeusia (7% vs 2%), and alopecia (7% vs 1%).

Additional Important Adverse Drug Reactions: The following occurred more frequently in LONSURF-treated patients compared to placebo: infections (27% vs 15%) and pulmonary emboli (2% vs 0%).

Interstitial lung disease (0.2%), including fatalities, has been reported in clinical studies and clinical practice settings in Asia.

Laboratory Test Abnormalities in Patients Treated With LONSURF: Laboratory test abnormalities in LONSURF-treated patients vs placebo-treated patients with refractory mCRC, respectively, were anemia (77% vs 33%), neutropenia (67% vs 1%), and thrombocytopenia (42% vs 8%).

Please see brief summary of Prescribing Information on the following pages.

Learn more at LONSURFhcp.com

TAIHO ONCOLOGY

LONSURF (trifluridine and tipiracil) tablets, for oral use
Initial U.S. Approval: 2015

Brief Summary of Prescribing Information
For complete Prescribing Information, consult official package insert.

1 INDICATIONS AND USAGE
LONSURF is indicated for the treatment of patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS
5.1 Severe Myelosuppression
In Study 1, LONSURF caused severe and life-threatening myelosuppression (Grade 3-4) consisting of anemia (18%), neutropenia (38%), thrombocytopenia (5%) and febrile neutropenia (3.8%). One patient (0.2%) died due to neutropenic infection. In Study 1, 9.4% of LONSURF-treated patients received granulocyte-colony stimulating factors.

Obtain complete blood counts prior to and on Day 15 of each cycle of LONSURF and more frequently as clinically indicated. Withhold LONSURF for febrile neutropenia, Grade 4 neutropenia, or platelets less than 50,000/mm^3. Upon recovery resume LONSURF at a reduced dose. *[*see *Dosage and Administration (2.2) in the full Prescribing Information]*

5.2 Embryo-Fetal Toxicity
Based on animal studies and its mechanism of action, LONSURF can cause fetal harm when administered to a pregnant woman. Trifluridine/tipiracil caused embryo-fetal lethality and embryo-fetal toxicity in pregnant rats when orally administered during gestation at dose levels resulting in exposures lower than those achieved at the recommended dose of 35 mg/m^2 twice daily.

Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with LONSURF. *[*see *Use in Specific Populations (8.1, 8.3), Clinical Pharmacology (12.1) in the full Prescribing Information]*

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below are from Study 1, a randomized (2:1), double-blind, placebo-controlled trial in which 533 patients (median age 63 years; 61% men; 57% White, 35% Asian, 1% Black) with previously treated metastatic colorectal cancer received LONSURF as a single agent at a dose of 35 mg/m^2/dose administered twice daily on Days 1 through 5 and Days 8 through 12 of each 28-day cycle. The mean duration of LONSURF therapy was 12.7 weeks.

The most common adverse drug reactions or laboratory abnormalities (all Grades and greater than or equal to 10% in incidence) in patients treated with LONSURF at a rate that exceeds the rate in patients receiving placebo were anemia, neutropenia, asthenia/fatigue, nausea, thrombocytopenia, decreased appetite, diarrhea, vomiting, abdominal pain, and pyrexia.

In Study 1, 3.6% of patients discontinued LONSURF for an adverse event and 13.7% of patients required a dose reduction. The most common adverse reactions leading to dose reduction were neutropenia, anemia, febrile neutropenia, fatigue, and diarrhea.

Table 1 Per Patient Incidence of Adverse Drug Reactions (≥5%) in Study 1 Occurring More Commonly (>2%) than in Patients Receiving Placebo.

Adverse Reactions	LONSURF (N=533)		Placebo (N=265)	
	All Grades	Grades 3-4*	All Grades	Grades 3-4*
Gastrointestinal disorders				
Nausea	48%	2%	24%	1%
Diarrhea	32%	3%	12%	<1%
Vomiting	28%	2%	14%	<1%
Abdominal pain	21%	2%	18%	4%
Stomatitis	8%	<1%	6%	0%
General disorders and administration site conditions				
Asthenia/fatigue	52%	7%	35%	9%
Pyrexia	19%	1%	14%	<1%
Metabolism and nutrition disorders				
Decreased appetite	39%	4%	29%	5%
Nervous system disorders				
Dysgeusia	7%	0%	2%	0%
Skin and subcutaneous tissue disorders				
Alopecia	7%	0%	1%	0%

*No Grade 4 definition for nausea, abdominal pain, or fatigue in National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.

Table 2 Laboratory Test Abnormalities

Laboratory Parameter	LONSURF (N=533*)			Placebo (N=265*)		
	Grade†			Grade†		
	All %	3 %	4 %	All %	3 %	4 %
Blood and lymphatic system disorders						
Anemia‡	77	18	N/A#	33	3	N/A
Neutropenia	67	27	11	1	0	0
Thrombocytopenia	42	5	1	8	<1	<1

*% based on number of patients with post-baseline samples, which may be less than 533 (LONSURF) or 265 (placebo)
† Common Terminology Criteria for Adverse Events (CTCAE), v4.03
‡ Anemia: No Grade 4 definition for these laboratory parameters in CTCAE, v4.03
# One Grade 4 anemia adverse reaction based on clinical criteria was reported

In Study 1, infections occurred more frequently in LONSURF-treated patients (27%) compared to those receiving placebo (15%). The most commonly reported infections which occurred more frequently in LONSURF-treated patients were nasopharyngitis (4% versus 2%), and urinary tract infections (4% versus 2%).

In Study 1, pulmonary emboli occurred more frequently in LONSURF-treatment patients (2%) compared to no patients on placebo.

Additional Clinical Experience
Interstitial lung disease was reported in fifteen (0.2%) patients, three of which were fatal, among approximately 7,000 patients exposed to LONSURF in clinical studies and clinical practice settings in Asia.

7 DRUG INTERACTIONS
No pharmacokinetic drug-drug interaction studies have been conducted with LONSURF.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
Based on animal data and its mechanism of action, LONSURF can cause fetal harm. LONSURF caused embryo-fetal lethality and embryo-fetal toxicity in pregnant rats when given during gestation at doses resulting in exposures lower than or similar to exposures at the recommended dose in humans. [see *Data*] There are no available data on LONSURF exposure in pregnant women. Advise pregnant women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

Trifluridine/tipiracil was administered orally once daily to female rats during organogenesis at dose levels of 15, 50, and 150 mg/kg [trifluridine (FTD) equivalent]. Decreased fetal weight was observed at FTD doses greater than or equal to 50 mg/kg (approximately 0.33 times the exposure at the clinical dose of 35 mg/m^2 twice daily). At the FTD dose of 150 mg/kg (approximately 0.92 times the FTD exposure at the clinical dose of 35 mg/m^2 twice daily) embryolethality and structural anomalies (kinked tail, cleft palate, ectrodactyly, anasarca, alterations in great vessels, and skeletal anomalies) were observed.

8.2 Lactation

Risk Summary

It is not known whether LONSURF or its metabolites are present in human milk. In nursing rats, trifluridine and tipiracil or their metabolites were present in breast milk. There are no data to assess the effects of LONSURF or its metabolites on the breastfed infant or the effects on milk production. Because of the potential for serious adverse reactions in breastfeeding infants, advise women not to breastfeed during treatment with LONSURF and for one day following the final dose.

Data

Radioactivity was excreted in the milk of nursing rats dosed with trifluridine/tipiracil containing ^{14}C-FTD or ^{14}C-tipiracil (TPI). Levels of FTD-derived radioactivity were as high as approximately 50% of the exposure in maternal plasma an hour after dosing with trifluridine/tipiracil and were approximately the same as those in maternal plasma for up to 12 hours following dosing. Exposure to TPI-derived radioactivity was higher in milk than in maternal plasma beginning 2 hours after dosing and continuing for at least 12 hours following administration of trifuridine/tipiracil.

8.3 Females and Males of Reproductive Potential

Contraception

Females

LONSURF can cause fetal harm when administered to a pregnant woman. *[*see *Use in Specific Populations (8.1)]*

Advise females of reproductive potential to use effective contraception during treatment.

Males

Because of the potential for genotoxicity, advise males with female partners of reproductive potential to use condoms during treatment with LONSURF and for at least 3 months after the final dose. *[*see *Nonclinical Toxicology (13.1) in the full Prescribing Information]*

8.4 Pediatric Use

Safety and effectiveness of LONSURF in pediatric patients have not been established.

Animal Data

Dental toxicity including whitening, breakage, and malocclusion (degeneration and disarrangement in the ameloblasts, papillary layer cells and odontoblasts) were observed in rats treated with trifluridine/tipiracil at doses greater than or equal to 50 mg/kg (approximately 0.33 times the exposure at the clinical dose of 35 mg/m^2 twice daily).

8.5 Geriatric Use

In Study 1, 533 patients received LONSURF; 44% were 65 years of age or over, while 7% were 75 and over. No overall differences in effectiveness were observed in patients 65 or older versus younger patients, and no adjustment is recommended for the starting dose of LONSURF based on age.

Patients 65 years of age or older who received LONSURF had a higher incidence of the following compared to patients younger than 65 years: Grade 3 or 4 neutropenia (48% vs 30%), Grade 3 anemia (26% vs 12%), and Grade 3 or 4 thrombocytopenia (9% vs 2%).

8.6 Hepatic Impairment

No dedicated clinical studies have been conducted to evaluate the effect of hepatic impairment on the pharmacokinetics of LONSURF. No dose adjustment is recommended for patients with mild hepatic impairment (total bilirubin (TB) less than or equal to the upper limit of normal (ULN) and AST greater than ULN or TB less than 1 to 1.5 times ULN and any AST). Patients with moderate (TB greater than 1.5 to 3 times ULN and any AST) or severe (TB greater than 3 times ULN and any AST) hepatic impairment were not enrolled in Study 1. *[*see *Clinical Pharmacology (12.3) in the full Prescribing Information]*

8.7 Renal Impairment

No dedicated clinical studies have been conducted to evaluate the effect of renal impairment on the pharmacokinetics of LONSURF.

In Study 1, patients with moderate renal impairment (CLcr = 30 to 59 mL/min, n= 47) had a higher incidence (difference of at least 5%) of ≥ Grade 3 adverse events, serious adverse events, and dose delays and reductions compared to patients with normal renal function (CLcr ≥ 90 mL/min, n= 306) or patients with mild renal impairment (CLcr = 60 to 89 mL/min, n= 178).

No dose adjustment to the starting dose of LONSURF is recommended in patients with mild or moderate renal impairment (CLcr of 30 to 89 mL/min); however patients with moderate renal impairment may require dose modification for increased toxicity. No patients with severe renal impairment (CLcr < 30 mL/min) were enrolled in Study 1. *[*see *Clinical Pharmacology (12.3) in the full Prescribing Information]*

8.8 Ethnicity

There were no clinically meaningful differences in Study 1 between Western and Asian subgroups with respect to overall incidence of adverse events or ≥ Grade 3 adverse events in either the LONSURF or placebo groups.

10 OVERDOSAGE

The highest dose of LONSURF administered in clinical studies was 180 mg/m^2 per day.

There is no known antidote for LONSURF overdosage.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Severe Myelosuppression:

Advise the patient to immediately contact their healthcare provider if they experience signs or symptoms of infection and advise patients to keep all appointments for blood tests. *[*see *Warnings and Precautions (5.1)]*

Gastrointestinal toxicity:

Advise patients to contact their healthcare provider for severe or persistent nausea, vomiting, diarrhea, or abdominal pain. *[*see *Adverse Reactions (6.1)]*

Administration Instructions:

Advise the patient that LONSURF is available in two strengths and they may receive both strength tablets to provide the prescribed dose. Advise the patient of the importance of reading prescription labels carefully and taking the appropriate number of tablets.

Advise the patient to take LONSURF within 1 hour after eating their morning and evening meals. *[*see *Dosage and Administration (2.1) in the full Prescribing Information]*

Advise the patient that anyone else who handles their medication should wear gloves. *[*see *References (15) in the full Prescribing Information]*

Embryo-Fetal Toxicity:

Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with LONSURF. *[*see *Warnings and Precautions (5.2)* and *Use in Specific Populations (8.3)]*

Lactation:

Advise women not to breastfeed during treatment with LONSURF and for one day following the final dose. *[*see *Use in Specific Populations (8.2)]*

TAIHO ONCOLOGY, INC.

GUIDELINE UPDATE

ASCO Guideline Upgrade Integrates Palliative Care in Standard Oncology Care

Surabhi Dangi-Garimella, PhD

CANCER PATIENTS SHOULD RECEIVE palliative care early and in parallel with their active treatment plan. Referral to interdisciplinary palliative care teams is optimal and can complement existing palliative care services. Caregivers for patients may be referred to these services. These are the most significant recommendations of the American Society of Clinical Oncology (ASCO)'s Ad Hoc Palliative Care Expert Panel.

The panel worked on the guideline, which has been published in the *Journal of Clinical Oncology*,[1] to update the 2012 ASCO provisional clinical option on integrating palliative care into standard oncology care. The update includes a review of 9 randomized clinical trials (RCTs), 1 quasiexperimental study, and 5 secondary publications from previously reviewed RCTs, all published between March 2010 and January 2016.

The studies included patients with advanced or metastatic disease, patients with early-stage non–small cell lung cancer, and a study that compared early with delayed palliative care. All studies included nurses in the intervention, and 5 studies also included palliative care specialists. All studies included outpatients. The primary outcomes of the trials included quality of life (QOL), symptom relief, psychological outcomes, survival, and satisfaction.

Senior author and guideline co-chair Thomas J. Smith, MD, FACP, FASCO, FAAHPM, professor of palliative medicine and professor of oncology, Johns Hopkins School of Medicine, told *Evidence-Based Oncology*™ that the publication is only the beginning. "We plan to hold a major education session at the 2017 [ASCO] annual meeting, with an emphasis on how oncologists can use the same techniques and listening skills as palliative care team specialists." Smith indicated that ASCO University,[2] the society's e-learning website, as well as ASCO's patient-information website, Cancer.Net,[3] already have a lot of this information accessible.

Recommendations

Based on their review of evidence, the panel has developed the following specific recommendations:

1. Individuals given an advanced cancer diagnosis should be referred to an interdisciplinary team of palliative care consultants early in the course of their disease, in parallel with the active treatment plan.
2. Patients with advanced cancer should have access to interdisciplinary palliative care teams in the outpatient and inpatient settings.
3. Palliative care services for patients with advanced cancer may include the following:
    a. Building a relationship with the patient and family caregivers
    b. Symptom, distress, and functional status management
    c. Investigate patient understanding of their disease and diagnosis
    d. Clarification of treatment goals
    e. Assessment and support of coping needs
    f. Assistance with medical decision making
    g. Coordination of care with other providers
    h. Referrals to other providers as needed
4. Patients who are newly diagnosed with advanced cancer should receive a palliative care consult within 8 weeks of their diagnosis.
5. For patients who have a high symptom burden or unmet physical or psychosocial needs, outpatient programs should ensure patient access to palliative care clinicians who can complement existing program tools.
6. Family caregivers caring for patients with cancer, either in the early or advanced stage, should have access to a caregiver-tailored palliative care support, such as telephone coaching, education, referrals, and face-to-face meetings.

In their paper, the authors emphasize that their evidence review supported guidelines for patients who have advanced cancer and that existing evidence is insufficient to make strong recommendations for individuals given an early-stage disease diagnosis.

SMITH

Thomas J. Smith, MD, FACP, FASCO, FAAHPM

Palliation Saves Healthcare Dollars

Palliative and hospice care have had a billing code since 2008, and although physicians and advance care practitioners can bill Medicare for time spent in delivering necessary care, currently, chaplains, social workers, and other participants on the interdisciplinary palliative care team cannot.

Beyond the most important role of palliation—improving the patient's QOL—it also has a significant impact on the overall cost of care. The first such study, conducted by Kaiser Permanente, in more than 800 patients, found that palliative care in the last stages of life prevented hospital and intensive care without any difference in survival; in fact, there was reportedly better satisfaction and a cost savings of $7550.[5] Integrating palliative care saved the Veteran's Administration 38% in direct costs compared with patients who did not receive palliative care, resulting in a system-wide emphasis on palliation. The average daily total direct hospital costs were reduced by $464 for 606 of the 3321 patients who were receiving palliative care ($P < .001$).[6]

THE AUTHORS EMPHASIZE THAT EXISTING EVIDENCE IS INSUFFICIENT TO MAKE STRONG RECOMMENDATIONS FOR INDIVIDUALS WITH AN EARLY-STAGE DIAGNOSIS.

Dissemination of Guidelines and Filling the Gaps

Smith believes that one way of measuring the impact of these guidelines would be via ASCO's Quality Oncology Practice Initiative, or QOPI,[4] which has developed measures on palliative care that ASCO members are using to monitor their practice. "The easiest is to see what percentage are referred, or not, by practitioner. Make it a quality-improvement project." In his opinion, physician behavior is most influenced when their they are compared with their peers, "If others are doing it to improve quality of care, I will, too."

"THE GOAL IS TO START HAVING DISCUSSIONS WHEN PEOPLE ARE STILL WELL, SO THAT THEY CAN PLAN."

—Thomas J. Smith, MD, FACP, FASCO, FAAHPM

The study itself has several limitations, as the authors point out:

1. Being a fairly new field, research funding is limited and, therefore, outcome data are limited.
2. The field lacks sufficient studies on palliative care in patients with hematological cancer.
3. Data on health disparities in palliative care are lacking.
4. Single-site studies limit their generalizability.

In their paper, the authors also propose a few recommendations to help fill out existing gaps in research around palliation in oncology:

1. Identification of triggers for palliative care
2. Inclusion of patients with cancer types that were left out of previous trials, including hematological cancers
3. Palliative care in patients with early-stage disease and
   including these patients in clinical trials
4. Research on family caregivers
5. Research to identify disparities in palliative care and evidence-based interventions to address disparities.

The authors conclude that while interventional studies support early specialty palliative care referrals for patients with advanced-stage cancer, other triggers should be considered to ensure patients receive prompt referral to specialty palliative care services. Additionally, they emphasize the need for training oncologists in primary palliative care competencies and assessing triggers for palliative care specialty services as part of their routine caregiving to patients and their family caregivers.

Despite efforts, a mental barrier remains around early discussions on palliative care, among patients, their caregivers, and providers. A chief reason is that people continue to equate palliation with hospice and end-of-life care. When asked about this, Smith, a veteran in this field, said that the evidence speaks for itself. "The data are clear that palliative care is associated with longer survival, not shorter survival. So, if people want to maximize their length and QOL, they should be seeking out palliative care."

He added, however, that studies have found that hospice care also extends survival. "We want to emphasize that palliative care can be given anywhere along the spectrum. Hospice, if you need it, is the best way to help people lead their lives well until they die. And it might be a longer and better time."

Smith believes that patients and caregivers need to be kept cognizant of the fact that each of us is mortal and that every disease may not be medically curable. "The goal is to start having discussions when people are still well, so that they can plan. It won't help those with terrible death anxiety, except to plan. But for most people, having a discussion about what the future might hold, and how to plan for it, is tough but good. I had several of those conversations today." ◆

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REFERENCES

1. Ferrell BR, Temel JS, Temin S, et al. Integration of palliative care into standard oncology care: American Society of Clinical Oncology Clinical Practice Guideline update [published online October 28, 2016]. *J Clin Oncol.* doi: 10.1200/JCO.2016.70.1474.
2. ASCO University website. http://university.asco.org/. Accessed November 20, 2016.
3. Cancer.Net website. http://www.cancer.net/. Accessed November 20, 2016.
4. ASCO Institute for Quality website. http://www.instituteforquality.org/. Accessed November 20, 2016.
5. Brumley R, Enguidanos S, Jamison P, et al. Increased satisfaction with care and lower costs: results of a randomized trial of in-home palliative care. *J Am Geriatr Soc.* 2007; ;55(7):993-1000.
6. Penrod JD, Deb P, Dellenbaugh C, et al. Hospital-based palliative care consultation: effects on hospital cost. *J Palliat Med.* 2010;13(8):973-979. doi: 10.1089/jpm.2010.0038.

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Produced by Nicole Beagin and Laura Joszt

Dr Toby Campbell Explains That Palliative Care Discussions Are Difficult but Necessary

Bringing up palliative care is inherently difficult for providers, because it means bringing up death and dying, said Toby C. Campbell, MD, MSCI, associate professor of medicine, hematology-oncology; chief of Palliative Care and program director of the Hospice and Palliative Medicine Fellowship Training Program, at the University of Wisconsin School of Medicine and Public Health.

How early in the cancer care process can palliative care be introduced?

Palliative care, ideally, comes up pretty early, actually. We know from the research that the earlier we talk about integrating palliative care into the management of an individual and their family's cancer care, the better the outcomes are. So, when we see improved symptom management, when we see improved adherence to advance care planning and goals of care, when we see people live longer, that's when we've brought it up early. Early can be at any time that someone has a serious illness to face. It might even be a curable problem—bone marrow transplant, for example—or it might be a metastatic end-of-life issue. But I think, really, if you want to realize the true benefits of palliative care, you've got to give these providers time to work with the patients and families.

Has patient and caregiver understanding of palliative care changed over time?

Patients and families have a pretty limited understanding of palliative care. In general, when surveys have been done, patients and families are neutral on the topic. Generally speaking, the majority of individuals has never heard the term before. So, I think oncologists can rest assured that some patients will have a familiarity with palliative care, but that most will have a very open mind about it or actually may have no concept of what the term means at all, giving the oncologist the opportunity to introduce it in the way that makes the most sense for them. Bringing up strategies such as symptom management or an extra layer of support can be easy ways to get into a conversation about palliative care.

Do you find the that topic of palliative care is more commonly brought up by a nurse or other caregiver on the patient's team?

Palliative care comes up in a variety of circumstances. Sometimes it's the nurse in the chemotherapy room. Sometimes it's the provider. So, I think discussions of a palliative nature come up in lots of different contexts. Sometimes it rises to the level where a subspecialist in palliative care becomes a part of the team. And that, too, can be brought up by any number of individuals, including the patients and families themselves.

How difficult is it for healthcare providers to bring up the topic of palliative care?

Talking about palliative care means acknowledging someone's mortality. It means, by some measure, beginning to talk about an incurable disease, beginning to talk about dying. And so I think it is inherently difficult.

I want to make it clear, though, that patients are already worried about it. From the very beginning when they hear the word "cancer," they're already scared. They're already worried; their minds have already gone to the question, "Is this going to take my life? Am I going to die?" So, this won't be the first time that they've brought it up. But for many patients and families, they will not bring it up without some prompting from the oncologist.

And so, what we have learned in survey data and other places is that patients and families want to talk about this. In fact, they expect to talk about it. But they, generally speaking, won't bring it up themselves. So, it is important, actually, for the oncologist to be comfortable with bringing this up, to talk both about palliative care and about life expectancy, about what happens when you're dealing with an advanced cancer.

Dr Sophia Smith Advocates for Introducing Palliative Care as Early as Possible

Palliative care should be introduced as early as possible, even as early as diagnosis, so patients hear about it early and not during a late stage of their disease when they might need hospice, said Sophia K. Smith, PhD, MSW, associate professor at the Duke School of Nursing.

How early in the cancer care process should palliative care be introduced?

As early as possible. The feeling among providers is that the earlier it is introduced, even at diagnosis, palliative care can provide symptom management and psychosocial supportive care to the patient throughout their [disease] trajectory. That way the patient hears about it early on and it's not thrown at them late in their disease process when, perhaps, their condition has deteriorated and they need to seek out specialty services, like hospice. So, I'm a big proponent of having the discussion early on, so the patient can take advantage of the services, as well. Palliative care is not just hospice—hospice is just one form of palliative care. Palliative care really, if done right, [should ideally be] done across providers by a multi-disciplinary team that's focused on the entire patient and not just their disease. So, it's all about "How do we maximize quality of life throughout the cancer trajectory?"

Can the introduction of patient-centeredness in clinical trials, such as measures of patient-reported outcomes (PROs), be considered palliative care?

I'm a big proponent of hearing from the patient. I think PROs are extremely important, particularly in clinical trials. There's different ways to collect this information. I think that we should really look at technology to help leverage that with electronic PRO systems.

(continued on SP614)

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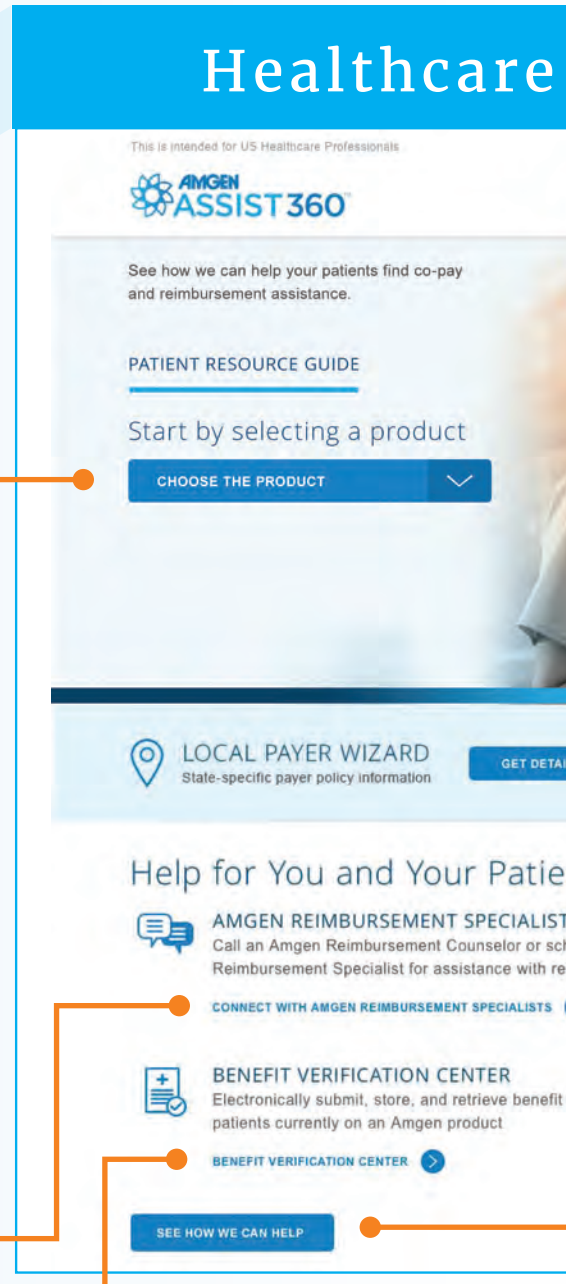

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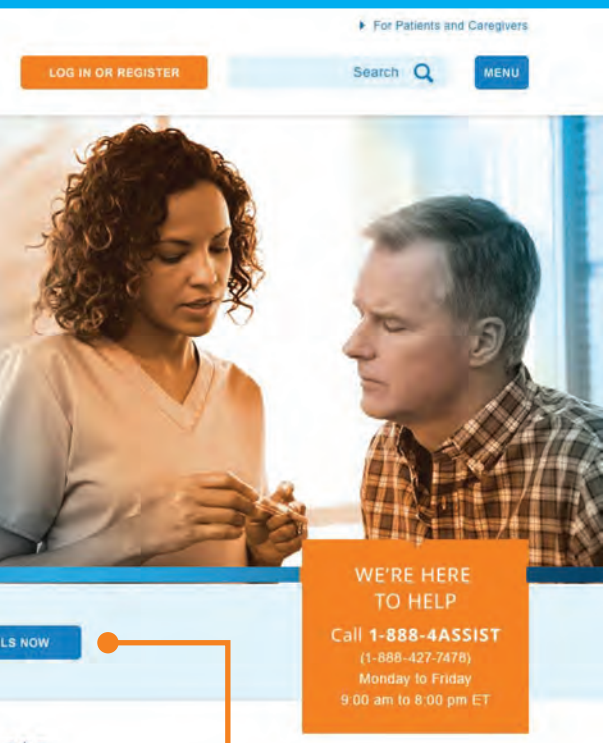

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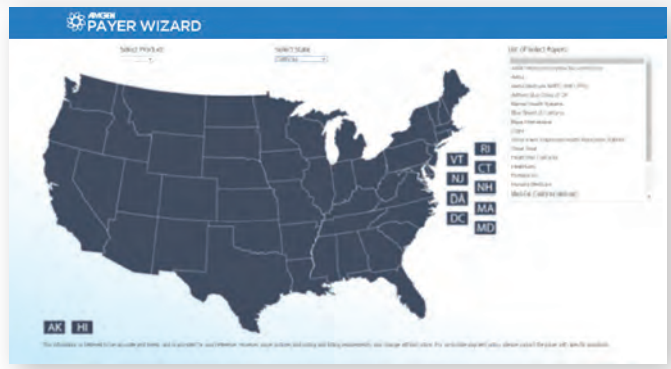

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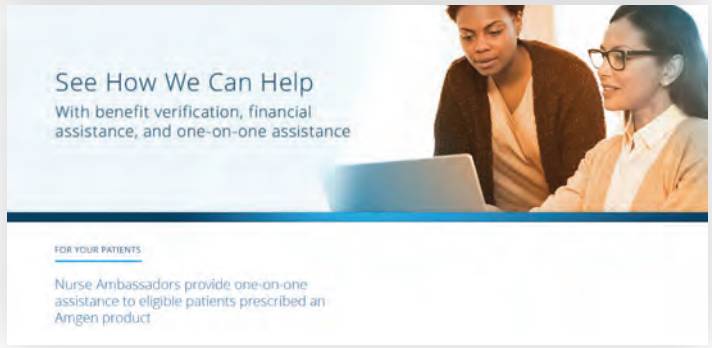

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(continued from SP611)

I know that a lot of our medical systems have electronic health records now, such as Epic, and they actually have survey capability built in. There's other tools such as Apple Research Kit, where we can provide surveys on mobile devices, so a lot of our patients—particularly our younger patients and our patients who may use their smartphone as their only connection to the internet—being able to put these PROs out there for them to use on their mobile devices is really important.

"PALLIATIVE CARE [SHOULD IDEALLY BE] DONE ACROSS PROVIDERS BY A MULTI-DISCIPLINARY TEAM THAT'S FOCUSED ON THE ENTIRE PATIENT AND NOT JUST THEIR DISEASE."

—Sophia K. Smith, PhD, MSW

I am also a big proponent of the distress thermometers, so you could probably characterize that as a PRO, but each time our cancer patients come in for their treatment or a visit, we ask them how distressed they are and then we list a series of areas that they might be distressed in. For example, financial distress, emotional distress, maybe relationship problems, and maybe some spiritual crisis. So, that's another form of PROs and, again, as early in the process as you can introduce these things, the better.

How important is psychosocial support for patients with cancer? And is there something that the oncologist can refer patients to as a standard practice?

A lot depends on the institution where the patient is seen. I can speak to how it's provided at Duke: at the Duke Cancer Institute, we have different avenues for psychosocial support. We have the department of social work, and we also have a cancer patient support program that's funded partially through philanthropy where we provide counseling support for free to our patients and their family members.

I think for psychosocial support, it's very important to include the whole family in the support. A lot of support for the patient comes through the family. A lot of our caregivers are stressed; they add the financial implications of the treatment. A lot of the caregivers maybe have to miss work to help care for the patient, they're under tremendous stress, there may be children involved. We have various programs within our cancer center that focus on the patient support system, in addition to the patients themselves.

You know, some of our support groups are disease-specific. Right now, through my research, we're testing interventions that are delivered online; so a lot of our patients are from out of state and they can access these services if they have a computer, or internet access, or a mobile device, or whatever. So, I think, in answer to your question, psychosocial support is critical. Our patients tell us it's critical. I hear directly from patients that so much attention is gone into curing the disease and extending life. A lot of people feel that psychosocial needs or emotional needs are often overlooked in busy clinics.

You know your clinical appointment now, your standard appointment, is 15 minutes. It's so important during that short visit that we collect the PROs, so we ask them, just with a distress thermometer or whatever. The tool is less important, but the fact is, we have the conversation with the patient, and you've got to have that conversation each time because the situation changes.

So, yes, it's very important. I recognize that our nurses and our physicians are very busy during that 15-minute visit, but if we can get that team working together—that multidisciplinary team where we're administering the PRO, and then the nurse in our institution collects the distress thermometer and then refers to psychosocial care based upon what the patient identifies as their need. ◆

How Can Practices Seek Success With Oncology Payment Reform?


GOULD

AT THE PAYER EXCHANGE SUMMIT V, sponsored by the Community Oncology Alliance (COA), and held October 24-25, 2016, in Tyson's Corner, Virginia, Bruce Gould, MD, president and medical director, Northwest Georgia Oncology Center, and president of COA, presented an overview of how cancer care has improved over the years and what the current challenges are.

"The number of new cancer cases and survivors is expected to rise," Gould said. "Survivors will increase from 11.7 million in 2007 to 18 million in 2020. Patients are living longer, especially with multiple treatment options available—however, the new treatments are expensive." In melanoma, for example, patients have seen a significant improvement in survival, especially after the checkpoint inhibitors arrived on the scene. "But these drugs come with a significant price tag," Gould said.

Gould went on to share the findings of a Milliman report,[1] commissioned by COA, that did an analysis to identify drivers of cancer care costs. "Hospitals—academic ones in particular, were identified as major cost drivers," he said. "There's a significant consolidation of [community] practices with hospitals, and cost of care is definitely much higher in hospitals than in private practice."

What is COA doing about this? Gould described the Oncology Medical Home (OMH) model, which was initiated by COA, as well as the associated accreditation program.

"We have been speaking about the OMH concepts across the country with various practices, and several institutions have bene adopting this care model," Gould said. The OMH model assures practices better value for their dollars spent, provides patients care at home, and is a path to cost savings, he added.

The OMH accreditation program helps validate compliance standards, appropriate structures and processes, and the need to have an electronic health record, Gould told the audience. "Further, there are 5 domains of care that are the primary focus of the program, namely: patient engagement, expanded access, comprehensive team-based care, evidence-based medicine, and quality-improvement projects," Gould said. He then highlighted some of the nuances of the various domains:

1. *Patient engagement* includes financial counseling, patient education on OMH benefits, engaging patients in treatment planning, a patient portal to allow communication with the practice, and actively including specialty trained nurses in patient care.
2. *Expanded access* comprises assurance of same day appointments, structured triage, and 24-hour patient access to a doctor or nurse.
3. *Team-based care* means dividing a care navigator's job among the practice staff. The practice also sets up relationships with outside providers for nonurgent care, psychosocial care, discussions on end-of-life care, etc.
4. *Quality improvement projects* include quality improvement methods that are developed and implemented, patient surveys to get feedback, and evaluation of how the survey results inform practice performance.

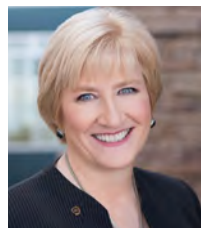
"COA has multiple ongoing projects and has commissioned several studies to address these issues," Gould said. ◆

REFERENCE

1. Dangi-Garimella S. Cancer care has not overtaken overall healthcare costs, clarifies Milliman study. *The American Journal of Managed Care®* website. http://www.ajmc.com/newsroom/cancer-care-has-not-overtaken-overall-healthcare-costs-clarifies-milliman-study. Published April 5, 2016. Accessed October 26, 2016.

Strategies for OCM Implementation at the COA Payer Summit


PATTON


MCANENY

WHAT ARE THE CHALLENGES THAT clinical practices will face as they implement the Medicare Oncology Care Model (OCM)? What are some of the strategies that have worked for practices using similar payment models? How does The Center for Medicare & Medicaid Innovation (CMMI), also known as the Innovation Center, hope to work with oncologists for the success of the OCM? These were some of the questions that were discussed at the Payer Exchange Summit V.

Sponsored by the Community Oncology Alliance (COA), the Summit was held October 24-25, 2016, in Tyson's Corner, Virginia. Experts on the panel included Jeffrey Patton, MD, chief executive officer, Tennessee Oncology; Barbara McAneny, MD, chief executive officer, New Mexico Hematology Oncology Consultants; and Ron Kline, MD, medical officer, CMMI.

Patton provided the perspective of a practice that has 3 monthss experience with the OCM. "It's been good with respect to investing the dollars," he said. "We used Via Oncology [clinical] pathways; nurse triage is important, and we built it on a Salesforce platform. We have also developed a relationship with a palliative care company. Additionally, care coordination is the last thing with respect to the OCM that we had to include as part of our practice transformation."

"CARE COORDINATION OCCURS WITH THE SIMPLEST THINGS IN THE CLINIC, SUCH AS WHEN A DOCTOR SPEAKS TO A NURSE ABOUT ADJUSTING A CHEMOTHERAPY DOSE. IT'S THEREFORE A MATTER OF DOCUMENTING THESE DAILY COORDINATION ACTIVITIES."

—Barbara McAneny, MD

Patton told the audience that at their cancer clinics, the focus is on the top 10% of patients that may need hospitalization. These patients are expected to have a significant impact on care costs. He added that with 85 doctors and 32 sites of care delivery, "We try to take care of patients where they are."

"With COME HOME,[1] our first year was spent on ramping up practices," McAneny said. "So, with the OCM, practices that might already have a similar model in place might need about 6 months to gear up. We don't yet know what the 'targets' will be; it's still a blur." COME HOME is an oncology medical home model that McAneny pioneered at New Mexico Hematology Oncology Consultants.

McAneny firmly believes that clinical pathways are critical to adequately implement cost-saving reimbursement models. "With COME HOME, we created pathways in a collaborative way—they are a very important decision support tool. Triage pathways are important, too," she said.

Kline said he was delighted to see that oncology practices have started developing innovative ways to implement the OCM, which, he added, is the objective of this pilot phase. "We have 95 practices with $6 billion in oncology spending, 3200 physicians, and 5000 providers under the OCM," Kline told the audience, adding that he hoped that through their work, "We are changing oncology care in the country."

Speaking to the significant impact of drugs on the cost of care, he said that with drugs, there are 2 categories: game-changing drugs are essential, but most of those are expensive. Then there are those that can be replaced by

equally effective, but cheaper alternatives. "It comes down to making financially stable choices on treatments," Kline said.

The OCM requires physicians to include data on staging and molecular characterization of patient tumors in the electronic health record (EHR). "We want to identify EHRs that will minimize physician burden and include them in the OCM system," Kline said.

So, what are some of the challenges with meeting OCM requirements, and what specific changes do clinics need to adopt to? Kline said that staging and mutations data are not a part of the claims system. "For a better model, we need to include this information in the system." He added that the first year of quality reporting is "pay-for-improvement, not pay-for-performance. So, the statute is that you have to do this … submit the data."

Patton expressed concern with quicker access to outcomes data. "Technology platforms, like [those developed by] Flatiron Health, can help us understand where we are lagging," he said.

Speaking about the importance of care coordination in improving outcomes, McAneny said, "Care coordination occurs with the simplest things in the clinic, such as when a doctor speaks to a nurse about adjusting a chemotherapy dose. It's therefore a matter of documenting these daily coordination activities." She told the audience that the unique experience with the OCM is that she felt she was on the same page with CMS on this. "We, at our clinics, have now set up a way for patients to sit down with a mid-level provider to talk about the care plan, their goals of care, and distress issues that we can help them with." She emphasized, however, that vendors need to create a platform that does not interfere with the practice workflow or make the oncologist a data-entry operator.

"The government really wants this to work … if we don't succeed they don't succeed," Patton added.

Speaking to the aspect of financial risks associated with the OCM, which are 1-sided in the first 2 years and then become 2-sided, McAneny said that she has very smart data managers working for her "who used a Monte Carlo scenario." Using this model, they try to identify those patients whose cost of care would result in the practice paying back to Medicare. "Through the National Cancer Care Alliance, we are trying to develop a process where we share a larger group of patients and reinsure these patients to balance the associated actuarial risk," McAneny said.

"You don't have to assume a 2-sided risk at all during the entire 5-year period. But with 1-sided risk, you have to show savings after 2 years," Kline told the audience. ◆

REFERENCE

1. McAneny BL. The future of oncology? COME HOME, the oncology medical home. *Am J Manag Care*. 2013;19(spec no 1):SP41-SP42.

Will a Payer-Provider Collaboration Guarantee OCM Success?

THE ONCOLOGY CARE MODEL (OCM) IS in its infancy right now, but participating practices have been preparing for its implementation for several months. Following the launch of the pilot phase, and as practices and payers start accruing data, identifying the keys for success becomes vital. At the Payer Exchange Summit V, in Tyson's Corner, Virginia, oncologists and payers came together to discuss the role of collaboration and data sharing for the successful implementation of the OCM.


GOULD


JORDAN


SAGAR

Panelists at the summit, which was sponsored by the Community Oncology Alliance (COA), included Bruce Gould, MD, medical director, Northwest Georgia Oncology Centers, who also serves as the president of COA; Terrill Jordan, president and chief executive officer, Regional Cancer Care Associates (RCCA); Bhuvana Sagar, MD, medical director, Cigna; and Maria Sipala, director, strategic planning, Aetna.

Speaking about the extent to which payers and providers can collaborate on OCM, Gould said, "[They] are working together, but they need to identify each other's limitations. It's a Herculean task to pull actionable data out of the haystack, and it requires that we keep those lines of communication open."

"Both [payers and providers] ultimately want the same thing … we want to do the right thing for the patient," said Sagar. "We, as payers, try to understand where the practice is coming from—we try to have conversations with providers over time, and it's almost about building the trust," she added. Despite the efforts to marry what is important for the 2 stakeholders, Sagar acknowledged that there are limitations and challenges.

Jordan said that, historically, there was a constant battle with payers. "That has changed now. While understanding the data is key to improving outcomes, payers do not know everything," he said. Jordan believes that the road to better healthcare outcomes and improvements in care delivery is via understanding the data at hand and asking the right questions.

Explaining the need-based progress in data mining by Aetna, Sipala said, "A few years back, we had the metrics, but we lacked the tools needed to scour through the data. That's when we developed the necessary tools. So, now we have the metrics, the tools, and we are sharing it with the providers. But we are still not where we would like to be in the process."

Several clinical practices have worked out different payment models with health plans, some of which can inform participation in the OCM. One such model is COME HOME, which was developed by McAneny's practice in New Mexico. "We have had processes in place from COME HOME, and for the OMH, so we did not need too much work to adapt to private payer models," said Gould. "When we started promulgating the OMH concept, the common message was already out there, with slight variations in the theme." He added that although the program looks similar across all payers, differences might arise in what we get back from the payers. "How we interpret it and then act on it might be the challenge."

Speaking about Cigna's Collaborative Care program, Sagar explained that when the program expanded to oncology, it continued to work on risk adjustment and reporting. "We have, however, tried to align with the OCM at least on quality measures that made sense for our patient demographic. We have tried to make it easy for the groups to transition to our model. But there have been challenges," she said. "The bottom line is to work toward keeping the costs low and improving outcomes."

Jordan explained that for RCCA, which was not a part of COME HOME, they had to start with the basics. "We needed significant infrastructure changes. We also looked at the program, and we spoke to our payers to look at our model and critique it for us. This allowed us the flexibility to tweak the model before implementing it in the clinic," Jordan said. He acknowledged that the payers they worked with were very accommodating and flexible, because they realized that the successful implementation of the model hinged on this collaboration.

So, what are some of the prime items needed for practice redesign, and how can they be prioritized? At RCCA, there were 2 main buckets of changes, said Jordan. The first was changes within the administrative structure, including changes with respect to value, quality, and cost, in addition to the need for care

coordination. "The second was improving things that we were already doing in the clinic, but doing them better. So, looking at it from a different lens. With respect to physician engagement, it was imperative to not change their workflow or at least to find common ground and include them into discussions on why those changes were important," Jordan said.

Sagar pointed out the importance of ensuring an adequate cancer care team, as well as knowledge sharing. "Exchange of ideas is critical for practice improvement," she said.

Sipala agreed, adding that as a payer, they have significant access to resources, which may not always be available to providers, particularly the smaller practices. "So, we need to understand where they need assistance."

Sagar told the audience that payers seek a better understanding of the clinical data to understand the cost-of-care distribution for a practice. "We need to stratify this data. We need the details to understand the potential source of cost savings for the practice. With oncology, there are so many different cancer types and different staging for the same cancer. And add to that the complexity of regional differences."

Sagar and Sipala agreed that identifying actionable data is very important—data that can feed back into the clinic and help make improvements. Providers seek data, as well. "Practices need more information on benchmarks that they need to meet to be able to bring about practice improvement," Gould responded. ◆

Employers Express Their Concerns With Cancer Care at the COA Summit


MCABEE


FAZEN


RUSSO

WITH DISCUSSIONS AROUND CANCER CARE QUALITY AND cost, payers—either health plans or employers—are concerned with what it means for them and for their patients. At the Payer Exchange Summit V, sponsored by the Community Oncology Alliance (COA), held October 24-25, 2016, in Tyson's Corner, Virginia, 2 employer groups and a provider participated on a panel to provide practical insight into the extraordinary challenges and decisions that employers and employees with a cancer diagnosis are faced with. Panel participants included Alice McAbee, CEBS, CCP, SPHR, SHRM-SCP, DynCorp International; Marianne Fazen, PhD, Texas Business Group on Health; and Barry Russo, The Center for Cancer & Blood Disorders.

"Cancer is a top condition that concerns employers, because of cost, the quality of care, and the complexity associated with managing the disease," Fazen said. "Employers are interested in helping their employees. With our coalition, we want to talk about the entire journey for the employee patient and also for employers to have access to the patient information." Fazen then shared a video of a stage production on the entire cancer journey, which she said helped make a very significant impact in getting the message across to their employees.

According to Fazen, the top 3 challenges for employees are cost, the quality of care, and supporting employees who have cancer as they try to return to work and a sense of normalcy. "The employer needs to accommodate them at the workplace, providing options such as rest time, changing their job profile to avoid heavy lifting, etc."

Representing a care provider organization, Russo presented another aspect of cancer care: the delivery of care itself. "One of several challenges is the complexity of the delivery system. Because we have so many sub-networks, keeping patients informed is a difficult task," he said. According to Russo, the preauthorization process adds a significant challenge to care delivery. "Having the patient wait 7 to 14 days to initiate therapy, as we try to go through the hoops, is difficult for us, in addition to what the patient endures as they wait. Meeting an ideal timeframe is a significant challenge," he said. "Our third challenge is getting connected to the employers to explain to them what the [Quality Oncology Practice Initiative] certification means, along with other aspects of care. So, the coalition has provided us a great opportunity for this."

"For us, curbing our healthcare costs impacts whether someone has a job next year," McAbee told the attendees. "So, while cost is important, we are struggling with whether our employee has the right care at the right time." She added that even if the employee does not raise this concern, having an advocacy model at play ensures that employees and their families have adequate care.

> **"WE NEED TO LISTEN TO WHAT EMPLOYERS ARE LOOKING FOR AND WHAT THEIR NEEDS ARE.WE CAN ALSO HELP EMPLOYERS CREATE A CHECKLIST OF THINGS THAT EMPLOYEES DIAGNOSED WITH CANCER MIGHT NEED."**
> —Barry Russo

Fazen is a firm believer in the potential of education programs to align the different issues faced by employees. "For example, during one such program on precision medicine, one on the benefit managers in attendance said that if this is so valuable, 'How come my benefit plan does not offer precision medicine?' It turned out that they did offer employees the option of genetic testing, but the information was provided only if the employee asked about it. So, that is a care gap … a communication gap," Fazen said.

Russo said, "We need to listen to what employers are looking for and what their needs are. We can also help employers create a checklist of things that employees might need once they are diagnosed with cancer."

"Too often it's easy for those in my role to lose sight of what patients and providers are looking for," McAbee said. "So, the answer is in the individual patient experience and being mindful of what they need."

Fazen agreed and emphasized the important support of a nurse navigator for the process. "Having a nurse navigator at the workplace, who is a patient advocate and a navigator, can have a significant impact, as can a convenient site for drug administration," she said. "Working with the coalition helps cross-educate providers, payers, and employees on what options are available for the employee patients."

"We have to start trusting each other for a better outcome for the patient and a better outcome for the process of better outcome," according to Russo. "And benefit literacy is extremely important for this. The continuous learning process is ultimately going to deliver a better product to the patient. Ultimately, we will be at risk as a provider, but we have to understand the pieces to deliver better on the care we provide," he said. ◆

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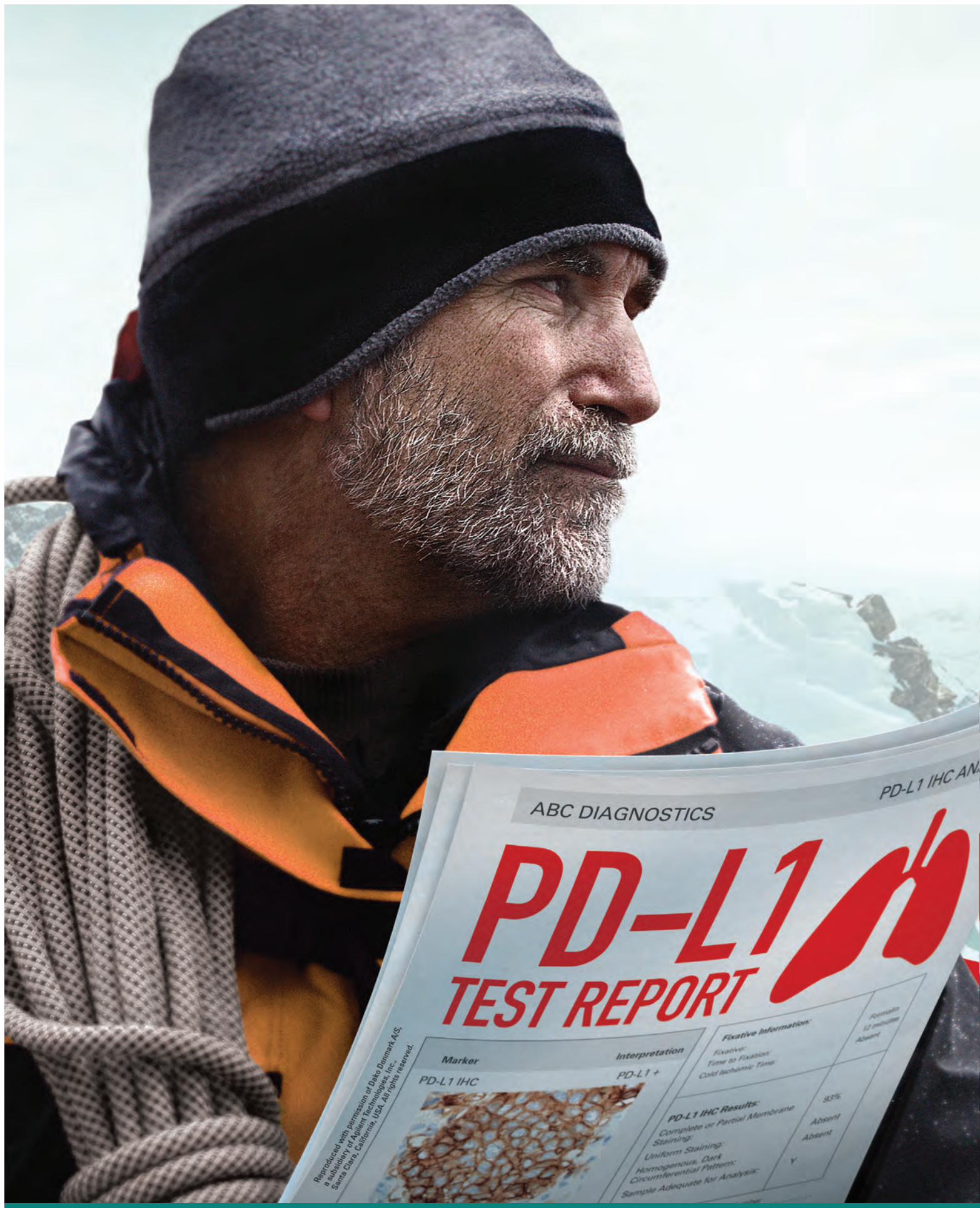
New Digital Tool to Compare Insurance Coverage for Cancer Screening Tests

Surabhi Dangi-Garimella, PhD

A REVIEW BY THE PREVENT CANCER FOUNDATION HAS found that insurance coverage of cancer screening tools varies based on the health plan. With this in mind, the foundation has developed a digital tool that can compare coverage of screening tests for breast, cervical, colorectal, lung, and prostate cancers across health insurance plans available in a specific state. »



The review, Cancer Screening: A Review of Guidelines and Insurance Coverage, summarizes current screening options and provides an overview of screening guidelines issued by the American Cancer Society, the National Comprehensive Cancer Network, and the US Preventive Services Task Force (USPSTF), in addition to a comparison of screening coverage by the 30 biggest health insurers in the United States. The following are a few key findings of this report:

Only 13 of the 30 plans cover 3D mammography for breast cancer screening.

Virtually every plan covers low-dose computed tomography for lung cancer screening; Pap tests alone or in combination with HPV tests for cervi- »

cal cancer screening; and fecal occult blood test, stool-based DNA testing, colonoscopy, and flexible sigmoidoscopy for colorectal cancer screening.

Twenty-eight plans cover prostate-specific antigen (PSA) test for prostate cancer screening, even though the USPSTF does not recommend this test for men at average risk of the disease.

While the USPSTF has assigned a D rating for using the PSA test to screen for prostate cancer, healthcare providers and health plans do not necessarily follow these recommendations. Carolyn R. Aldigé, president of the Prevent Cancer Foundation, told *The American Journal of Managed Care®* (*AJMC*) in an e-mail that the Foundation's annual meeting, Dialogue for Action, helps convene a variety of stakeholders to discuss such issues "and to provide information for individuals to engage in shared decision making with their providers."

The study observed the following trend with breast cancer screening:

TABLE. Coverage for Screening

SCREENING TEST	PLANS COVERING	PLANS NOT COVERING	PLANS WITHOUT POLICY
MAMMOGRAPHY (2D)	132	0	274
BREAST TOMOSYNTHESIS (3D)	47	45	313

In an associated press release, the Prevent Cancer Foundation recommends that patients should discuss these inconsistencies, which could be a result of the guideline discrepancies across organizations.[1] Aldigé told *AJMC®* that the foundation strives to educate and inform the public on the differences in guidelines and to clear any confusion that exists with using them.

"Effective cancer screening can lead to early detection of these potentially deadly diseases—but the variation between guidelines allows insurance companies to adopt cancer screening policies that may adversely affect patients' access to preventive services," Bernard Levin, MD, co-chair of the Prevent Cancer Foundation Scientific Review Panel, said in a statement.

The tool and the e-book are available on the Prevent Cancer Foundation website.[2] ◆

REFERENCES

1. Insurance policies have inconsistent coverage for cancer screening [press release]. Alexandria, VA: Prevent Cancer Foundation; November 1, 2016. http://preventcancer.org/uncategorized/insurance-policies-have-inconsistent-coverage-for-cancer-screening/. Accessed November 8, 2016.

2. Cancer screening coverage. Prevent Cancer Foundation website. http://preventcancer.org/our-work/cancer-screening-coverage/. Accessed November 8, 2016.

ICU Admission Reduces Survival, Augments Costs Among Patients With AML

Surabhi Dangi-Garimella, PhD

A STUDY PUBLISHED BY researchers from the Fred Hutchinson Cancer Research Center in Seattle, Washington, has found that admission to the intensive care unit (ICU) reduced survival and increased the cost of care among patients undergoing treatment for acute myeloid leukemia (AML).

AML is a disease with dismal outcomes, and about 75% of those diagnosed do not survive for more than 5 years. With the objective of examining the risk factors, mortality, length of stay (LOS), and cost associated with admission to the ICU for patients with AML, scientists at Fred Hutch extracted data from the University HealthSystem Consortium database on adult patients diagnosed

HOSPITAL THROUGH THE EYES OF PATIENT. © SUDOK1/FOTOLIA

with AML and who were hospitalized between January 1, 2004 and December 21, 2012. The primary outcomes being evaluated were admission to the ICU and inpatient mortality among patients who needed ICU care. Secondary outcomes included LOS in ICU, total LOS, and cost.

During the study period, a little more than 25% (11,277) of patients diagnosed with AML were admitted to the ICU. Risk factors for admissions included:

- Younger than 80 years of age (odds ratio [OR], 1.56; 95% CI, 1.42-1.70)
- Hospitalization in the South (OR, 1.81; 95% CI, 1.71-1.92)
- Hospitalization at a low- or medium-volume hospital (OR, 1.25; 95% CI, 1.19-1.31)
- Number of comorbidities (OR, 10.64; 95% CI, 8.89-12.62, for 5 vs none)
- Sepsis (OR, 4.61; 95% CI, 4.34-4.89)
- Invasive fungal infection (OR, 1.24; 95% CI, 1.11-1.39)
- Pneumonia (OR, 1.73; 95% CI, 1.63-1.82)

DURING THE STUDY PERIOD, A LITTLE MORE THAN 25% OF PATIENTS DIAGNOSED WITH AML WERE ADMITTED TO THE INTENSIVE CARE UNIT.

In-hospital mortality was significantly greater in patients who needed ICU care (4857 of 11,277 [43.1%] vs 2959 of 31,972 [9.3%]). The authors identified the following risk factors for death in the ICU-admitted cohort:

- Older than 60 years of age (OR, 1.16; 95% CI, 1.06-1.26)
- Ethnicity (nonwhite) (OR, 1.18; 95% CI, 1.07-1.30)
- Hospitalization on the West Coast (OR, 1.19; 95% CI, 1.06-1.34)
- Number of comorbidities (OR, 18.76; 95% CI, 13.7-25.67, for 5 vs none)
- Sepsis (OR, 2.94; 95% CI, 2.70-3.21)
- Invasive fungal infection (OR, 1.20; 95% CI, 1.02-1.42)
- Pneumonia (OR, 1.13; 95% CI, 1.04-1.24)

Simultaneous with the increased ICU admission was the increased cost of care—patients who needed the intensive care treatment incurred nearly double the cost of those who were not in the ICU ($83,354 vs $41,973, respectively). Presence of comorbidities further accentuated treatment costs, from $50,543 for no comorbidities, all the way to $124,820 in patients with at least 5 comorbidities.

The authors conclude that although comorbidities increase the risk of mortality and cost of care in patients with AML, appropriate interventions by identifying patients at high risk for ICU use could reduce fatalities. ◆

REFERENCE

Halpen AB, Culakova E, Walter RB, Lyman GH. Association of risk factors, mortality, and care costs of adults with acute myeloid leukemia with admission to the intensive care unit [published online November 10, 2016]. *JAMA Oncol.* doi: 10.1001/jamaoncol.2016.4858.

PROVIDER PERSPECTIVE

ResolutionCare

Welcome to the Future: Telemedicine and Value-Based Payment

Michael D. Fratkin, MD, and Stephen G. Franey, MBA

continued from cover

the use of fiber-optic cables, expensive carts at both ends, and dedicated telemedicine centers. Because it was so capital-intensive, it never really took off in northern California, our home base. Although it did provide a great service for many remote communities outside of major metropolitan areas, its high barrier to entry limited its use.

Telemedicine 2.0

Telemedicine 2.0 has leveraged the rise of ubiquitous smartphones, always-on connectivity, and cloud-based processing to deliver a sizable impact on how physicians provide care. Organizations like Doctor on Demand, Teladoc, and American Well have activated networks of remote-working primary care physicians to provide low-cost, effective telemedicine encounters for episodic problems (such as a sniffy nose or sore throat). Both consumers and employers see huge value when someone can see a doctor while on a coffee break and go back to work. The low barrier to entry has been responsible for an explosion in service providers and locations—including kiosks in CVS and Walgreens. This is driving growth in teledermatology and behavioral health, among other fields.

Telemedicine 3.0

What we're doing, as palliative care specialists at ResolutionCare, is what we call Telemedicine 3.0. In some ways, version 3.0 represents the evolution of the technology so that it can disappear—and thus allow for the return of the deep relational work that's always been at the heart of caring. We're using these technologies to reach people with ease via technology they already have at their fingertips (or that we provide) to reach them in their homes, to unburden them from travel and transport, and to offer a patient- and home-centered locus of care. We're discovering substantial benefits for the patients, unanticipated efficiencies, and surprising nuances that are intrinsic to this new medium.

Telemedicine and the Seriously Ill

The evolution from the episodic care of Telemedicine 2.0 to the use of telemedicine for the longer-term, chronic issues faced by individuals who are seriously ill (Telemedicine 3.0) eases the burdens of both sick patients and their doctors, and lets us go back to the raison d'être of most physicians: caring for people.

The Patient Experience

Some cancer patients will make more than 150 trips in their last year of life for infusions, physician appointments, lab draws, imaging, and fractionated radiotherapy. Removing the need for yet another clinic visit can have an immeasurable impact on that patient's quality of life (QOL). When people must drag their tired, broken bodies into clinics to satisfy every stakeholder *but themselves*, when they have to take time off work, deal with parking, and leave their own turf to sit in a doctor's office and wait (and wait) to be seen—while surrounded by other really sick people—you can imagine the negative effect on their physical, mental, and spiritual states.

Home Visits

Home visits, by contrast, remove many of those burdens for sick people. For the physician, seeing individuals where they live, and gaining all the extra information gleaned just by walking into their homes, has many real benefits that can improve care. However, the doctor may be viewed as an invader—there's a power dynamic, and simply by being a doctor and walking into a person's home, you shift the control from them to you. When sick people know the doctor is coming, they work really hard to get the home all cleaned up, to appear a certain way, to take a shower and fluff themselves up. Even though a home visit frees them from certain burdens, they burden themselves in other ways because they have a sense of what's acceptable for the doctor to see.

Telemedicine Visits

Now compare that to telemedicine and a videoconference using a cloud-based platform, where the person doesn't need to travel or clean up, and simply needs a wall that looks presentable. The burden of preparation and getting everything ready has been removed. From the doctor's perspective, you don't have to allow for commute time and traffic—the "house call" can seamlessly fit into your day without disruption.

Surprisingly—at least for those who haven't done it yet—the intimacy, the immediacy, the feeling of being right there in the room together, is palpable. One would think that the technology might get in the way somehow, but instead, it disappears. The call is an interaction between 2 people, face-to-face, sharing and talking intimately. Yet, that connection takes less time overall. Whereas an in-person home visit for a new-patient consult takes between 90 to 120 minutes, a telemedicine first consult takes 60 to 70 minutes.

Because we work as part of an integrated, multidisciplinary team, some of our telemedicine sessions include just the sick person and the physician, while other sessions might include other care providers, such as a nurse, social worker, chaplain, or family members. The needs of the person we're caring for tell us what to do, whom to involve, and when. As we often say at ResolutionCare, "We do what makes sense." This doesn't, however, totally remove the need for in-person visits. The information gained in those visits is brought back to the interdisciplinary team and helps us understand the full context of this person's living situation. We do a better job of shared decision making when we have that complete picture.

Locus of Control

Besides improving a person's QOL and gaining efficiency for the physician, one of the most important benefits of telemedicine for palliative care is that it helps the sick person retain a feeling of control over his or her life. This is in sharp contrast to the market view that takes sick people and makes them "patients," subject to

FRATKIN

FRANEY

Michael D. Fratkin, MD, is founder and chief medical officer, ResolutionCare.

Stephen G. Franey, MBA, is chief financial officer and chief strategy officer, ResolutionCare.

TABLE. Difference in Focus: From Volume to Value-Based Payment

FROM	TO
Physician-based care >80% of the time	Team-based care, with 20% use of physician and 80% use of mid- or low-level providers in a multidisciplinary team: • Physician • Nurse practitioner • Nurse • Chaplain • Social worker • Community health worker • Patient care coordinator • Pharmacist • Mental health specialist
In-person visit (patient goes to provider, or provider to patient)	Combined in-person and telemedicine visits
Payment by visit	Payment for patient care by month (per patient per month) for team-based care
Quality care standard: length of life	Quality defined as patient satisfaction and/or quality outcomes, with payment for these outcomes

the rules of our medical world, where they often have procedures done *to* them rather than *for* them.

Sick people aren't patients; they're people. Over the past 50 years, we've medicalized illness and our natural progression toward death. We've constructed our technology-intensive, industrial model around "fix it, fix it, fix it"—and that model fails sick people miserably. By relocating the center of care to where a person lives, we release them from being patients and offer them guidance within the medical landscape that we're familiar with and they're not. How ironic that innovative technology is responsible for bringing us back to the human-centered, relational model of care that's been subverted for the past 50 years. Our experience at ResolutionCare suggests that our use of telemedicine in palliation will increase—because of the efficiency of the approach, the opportunity to address more unmet demand, and the increased control afforded patients.

Value-Based Payment for Telemedicine

Much of the fix-it model, and the reason we do procedures *to* people rather than for them, has come about because of how payers traditionally reimbursed for services. The fee-for-service (FFS) model is a one-size-fits-all, check-the-box, and move-on-to-the-next-patient approach. Each person receiving palliative care has the same menu of possible services, and his or her individual situation or needs have no place in the formula. This assumed homogeneity does not match our experience in practice, as differences in socioeconomic class, disease type, and length of time on service can greatly impact the depth and scope of care required and the patient census each multidisciplinary team can accommodate.

But the landscape is changing. Payers, providers, and people receiving care are seeing the need and are demanding that palliative care be available as a covered benefit. In California, Senate Bill 1004 requires Medi-Cal managed care plans to offer access to palliative care programs—and 4 other states have similar laws either in place or on the horizon. This is occurring while the supply of specialty palliative care resources is overwhelmed by the number of sick people who are clinically appropriate for care.

In contrast to FFS, value-based payment allows for coverage of the entire multidisciplinary palliative care team, rather than just the physician and nurse practitioner. This, in turn, helps increase the capacity of subspecialty palliative care across all disciplines and is an investment strategy by insurance partners to entice more providers into the field. With value-based payment payers say, "We'll pay you not on the basis of doing X, Y, and Z—but on how you address the life goals articulated by the patient and family." You can then use an adaptable and nimble response to the individual circumstances of an individual person to try and reach those goals. It's outcomes-based (see **Table**).

ResolutionCare's value-based reimbursement is in the form of per-patient-per-month (PPPM) payment. Our current PPPM reimbursement model reflects the challenges associated with the rural population we serve and provides support for experimenting with the use of new delivery resource models, new approaches to care, and new community affiliations and partnerships. Some of our PPPM payments are unencumbered, meaning they are a flat fee with no strings attached. Other value-based reimbursement models provide a base rate, with bonuses associated with the achievement of select quality measures and the reduction in select utilization indicators.

When it comes to metrics, payers are looking at quality and satisfaction. But in the end, the most important metric to them is decreased cost. Adding kind, person-centered care always increases satisfaction; we are committed to the value of the person's QOL. The costs of care go down when you provide an alternative to high-cost, low-value, and high-stress interventions.[2] Palliative care increases the length of a person's life and decreases payers' net costs.[3] Those people who move on to hospice after a palliative care intervention have longer lengths of stay in hospice.[2]

We anticipate that value-based reimbursement will both grow and change over time as we better understand population needs and differences, and have greater consensus in the field regarding the critical indicators of quality. Multiple forms of value-based payment are likely, with future reimbursement to include a base rate plus quality and shared cost savings components.

Where We Go From Here

Eighteen months ago, at the time of ResolutionCare's last article for this journal,[4] we talked about a looming seismic change that would make the healthcare system spawned by our current FFS model unrecognizable in 5 years. At ResolutionCare, where we have cared for more than 500 souls to date, the exploding demand for palliative care and the potency of value-based payments allows us to address medical symptoms, anticipatory planning, social determinants of health, and whatever yields value for each patient.

We began a successful pilot program with Partnership Health Plan in September 2015 that will go until California Senate Bill 1004 takes effect in April 2017. At that point, we expect to continue the value-based system of payment established by the pilot, with a capitation rate to be decided. Through our newly formed ResolutionCare Institute, a 501(c)3 organization, we will continue our affiliation with the University of New Mexico's Project ECHO[5] to provide palliative care education to primary care practices in our region and beyond. Working with Project ECHO and with academics for the development of a palliative care curriculum, we're creating affiliations that will offer our environment as an educational experience for physicians and other professionals in training. It will also be a source for our publications and research activity, and allow us to participate in important research to advance our field.

Where we need to go, and still have work to do, is involving

community partners in our work with seriously ill people. Healthcare has been very narrowly defined as hospital-based care and invasive procedures. With the communities we serve, we're finding that the populations we care for need much more than procedures: the palliative care social workers at ResolutionCare could spend 50% of their time on housing issues alone.

As value-based payment becomes the norm, where we're given a block amount of money to create value for our clients, we may sometimes find that the best use of that money is to buy them food, transport them to their appointments, find them transitional or permanent housing, or get them to the dentist for a painful tooth. These services may not be covered under anyone's plan, but they're central—and critical—to that person's well-being and QOL.

In the end, telemedicine and value-based payment returns us to soulful, person-centered care that is based on how we can best serve each individual's very specific needs. Payers are realizing that this approach leads to higher satisfaction, fewer unnecessary interventions, and lower cost. ◆

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REFERENCES

1. ResolutionCare website. http://www.resolutioncare.com. Accessed October 30, 2016.
2. Brian Cassel J, Kerr KM, McClish DK, et al. Effect of a home-based palliative care program on healthcare use and costs [published online September 2, 2016]. *J Am Geriatr Soc.* doi: 10.1111/jgs.14354.
3. Temel J, Greer J, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med.* 2010;363(8):733-742. doi: 10.1056/NEJMoa1000678.
4. Fratkin MD. Trading conflict for synergy: the new normal for oncology and palliative care. *Am J Manag Care.* 2015;21(6):SP211-SP212.
5. Project ECHO. The University of New Mexico website. http://echo.unm.edu/. Accessed October 31, 2016.

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Achieving Value Through Palliative Care

Allison Silvers, MBA; Stacie Sinclair, MPP; and Diane E. Meier, MD, FACP

continued from cover

These skills and expertise benefit both the patients and the healthcare system. Standardized access to palliative care for hospitalized patients with advanced cancer has been shown to significantly reduce receipt of chemotherapy after discharge, as well as oncology service mortality and 30-day readmission rates.[8] However, the most effective results are produced when palliative care is introduced early in the disease trajectory and is provided concurrent with treatment. For example, randomized controlled trials involving patients with cancer found that early and concurrent palliative care:

- Results in a dramatic reduction in major depression (16% vs 38%)[9]
- Increases survival by an average of nearly 3 months[9]
- Results in fewer hospital admissions (33% vs 66%), fewer ED visits (34% vs 54%), reduced intensive care unit (ICU) use (5% vs 20%), and lower direct costs of inpatient care in the last 6 months of life ($19,067 vs $25,754).[10]

A recent analysis by DataGen found that oncology episodes for cancer of the esophagus, liver, pancreas, lung, testes, and brain have the greatest likelihood of hospital admission and ED visits.[11] Not surprisingly, this list correlates with cancer types that report the greatest prevalence of pain[12]— patients and families turn to emergency services when symptoms are poorly managed. Yet expert palliative care mitigates the need for crisis intervention, thus simultaneously improving patient quality of life and cost-effectiveness.

In recognition of these results, the American Society of Clinical Oncology (ASCO) issued a provisional clinical opinion in 2012, stating that "combined standard oncology care and palliative care should be considered early in the course of illness for any patient with metastatic cancer and/or high symptom burden."[13] Despite the weight of the evidence and the ASCO opinion, barriers continue to exist to expanding the integration of palliative care into cancer care. These include:

- The persistent confusion between palliative care and hospice (particularly on the part of physicians)
- Insufficient clinician training in skilled communication and expert symptom management
- A limited understanding of how palliative care can contribute to the value equation

In response, the Center to Advance Palliative Care (CAPC) is working to highlight the merits of concurrent palliative care under value-based payments (VBPs), and to educate payers and providers

(continued on SP628)

Center to Advance Palliative Care
capc

SILVERS

Allison Silvers, MBA, is vice president, payment and policy, Center to Advance Palliative Care.

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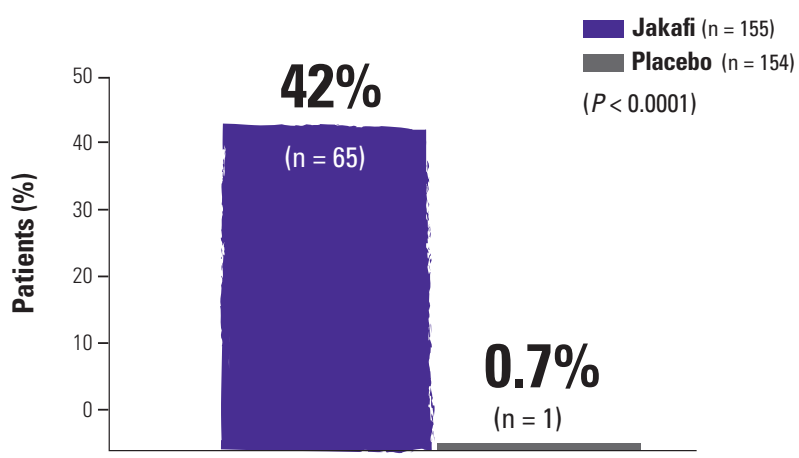
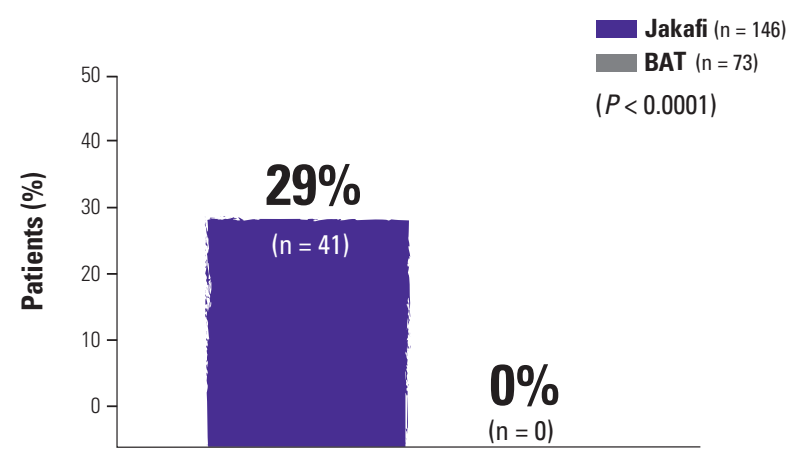
- The primary end point was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline at week 24 as measured by CT or MRI[1,2]

COMFORT-I Primary End Point: Spleen Volume Reduction at Week 24[1,2]



- The primary end point was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline at week 48[1,3]

COMFORT-II Primary End Point: Spleen Volume Reduction at Week 48[1,3]



BAT, best available therapy.

* COMFORT-I (COntrolled MyeloFibrosis study with ORal JAK inhibitor Treatment-I) was a randomized, double-blind, placebo-controlled phase 3 study with 309 patients with intermediate-2–risk and high-risk myelofibrosis.[1,2]

† Best available therapy in COMFORT-II included hydroxyurea (46.6%) and glucocorticoids (16.4%), as well as no medication, anagrelide, epoetin alfa, thalidomide, lenalidomide, mercaptopurine, thioguanine, danazol, peginterferon alfa-2a, interferon-α, melphalan, acetylsalicylic acid, cytarabine, and colchicine.[4]

‡ COMFORT-II (COntrolled MyeloFibrosis study with ORal JAK inhibitor Treatment-II) was a randomized, open-label phase 3 study with 219 patients with intermediate-2–risk and high-risk myelofibrosis.[1,3]

Important Safety Information

- Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia, which are each dose-related effects. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated
- Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary
- Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi
- Severe neutropenia (ANC $<0.5 \times 10^9$/L) was generally reversible by withholding Jakafi until recovery
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly
- Tuberculosis (TB) infection has been reported. Observe patients taking Jakafi for signs and symptoms of active TB and manage promptly. Prior to initiating Jakafi, evaluate patients for TB risk factors and test those at higher risk for latent infection. Consult a physician with expertise in the treatment of TB before starting Jakafi in patients with evidence of active or latent TB. Continuation of Jakafi during treatment of active TB should be based on the overall risk-benefit determination
- Progressive multifocal leukoencephalopathy (PML) has occurred with ruxolitinib treatment for myelofibrosis. If PML is suspected, stop Jakafi and evaluate
- Advise patients about early signs and symptoms of herpes zoster and to seek early treatment
- Increases in hepatitis B viral load with or without associated elevations in alanine aminotransferase and aspartate aminotransferase have been reported in patients with chronic hepatitis B virus (HBV) infections. Monitor and treat patients with chronic HBV infection according to clinical guidelines

Incyte

Jakafi® ruxolitinib (tablets)

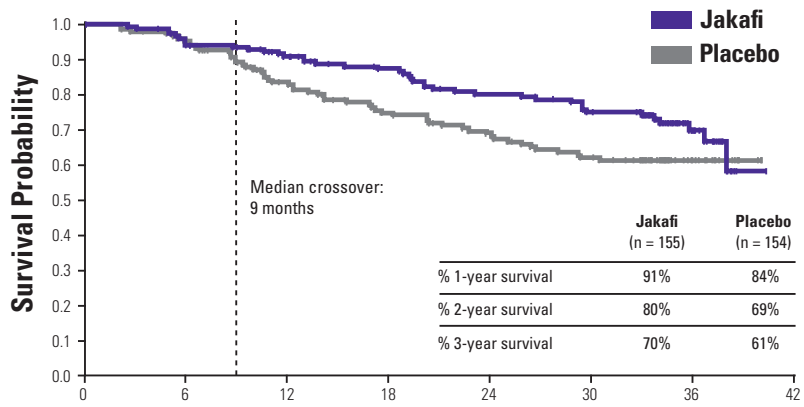
Indications and Usage

Jakafi is indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post–polycythemia vera myelofibrosis and post–essential thrombocythemia myelofibrosis.

Overall survival was a prespecified secondary end point in COMFORT-I and COMFORT-II[1]

- COMFORT-I: At 3 years, survival probability was 70% for patients originally randomized to Jakafi and 61% for those originally randomized to placebo[1]
- COMFORT-II: At 3 years, survival probability was 79% for patients originally randomized to best available therapy[1]

COMFORT-I Overall Survival: Kaplan-Meier Curves by Treatment Group[1]

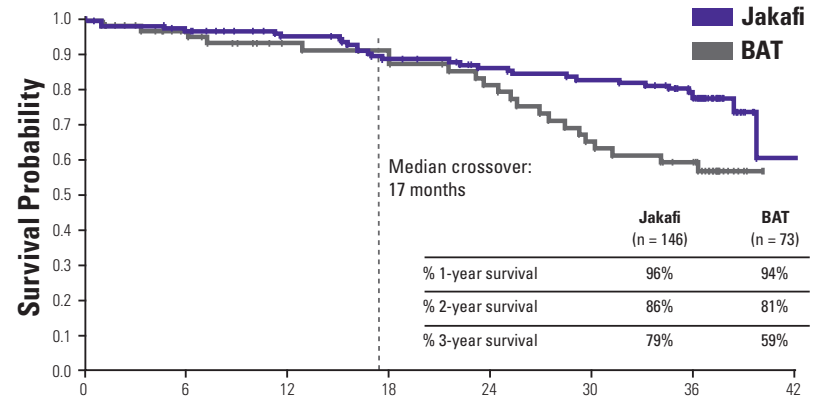


	Jakafi (n = 155)	Placebo (n = 154)
% 1-year survival	91%	84%
% 2-year survival	80%	69%
% 3-year survival	70%	61%

Number of patients at risk

Jakafi	155	145	134	122	111	102	29	0
Placebo	154	142	117	101	92	82	32	0

COMFORT-II Overall Survival: Kaplan-Meier Curves by Treatment Group[1]



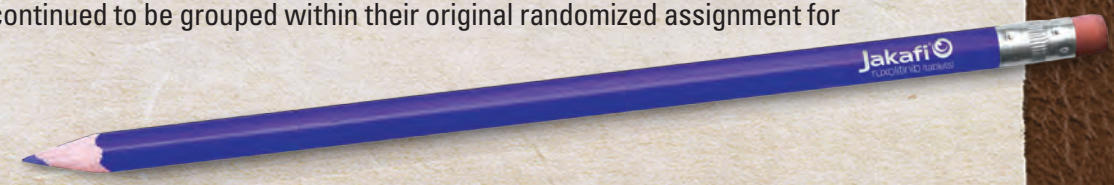
	Jakafi (n = 146)	BAT (n = 73)
% 1-year survival	96%	94%
% 2-year survival	86%	81%
% 3-year survival	79%	59%

Number of patients at risk

Jakafi	146	135	126	115	107	104	33	0
BAT	73	58	50	47	42	33	9	0

BAT, best available therapy.

- Because of progression-driven events or at the physician's discretion, patients randomized to placebo (COMFORT-I) or best available therapy (COMFORT-II) who crossed over to receive Jakafi continued to be grouped within their original randomized assignment for analysis purposes[4]



- When discontinuing Jakafi, myeloproliferative neoplasm-related symptoms may return within one week. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, DIC, or multi-organ failure. If any of these occur after discontinuation or while tapering Jakafi, evaluate and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi without consulting their physician. When discontinuing or interrupting Jakafi for reasons other than thrombocytopenia or neutropenia, consider gradual tapering rather than abrupt discontinuation
- Non-melanoma skin cancers including basal cell, squamous cell, and Merkel cell carcinoma have occurred. Perform periodic skin examinations
- Treatment with Jakafi has been associated with increases in total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Assess lipid parameters 8-12 weeks after initiating Jakafi. Monitor and treat according to clinical guidelines for the management of hyperlipidemia
- The three most frequent non-hematologic adverse reactions (incidence >10%) were bruising, dizziness and headache
- A dose modification is recommended when administering Jakafi with strong CYP3A4 inhibitors or fluconazole or in patients with renal or hepatic impairment. Patients should be closely monitored and the dose titrated based on safety and efficacy
- Use of Jakafi during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking Jakafi should not breast-feed

Please see Brief Summary of Full Prescribing Information for Jakafi on the following pages.

To learn more about Jakafi, visit **Jakafi.com/HCP**.

References: 1. Jakafi Prescribing Information. Wilmington, DE: Incyte Corporation. **2.** Verstovsek S, Mesa RA, Gotlib J, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. *N Engl J Med.* 2012;366(9):799-807. **3.** Harrison C, Kiladjian J-J, Al-Ali HK, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. *N Engl J Med.* 2012;366(9):787-798. **4.** Data on file. Incyte Corporation. Wilmington, DE.

Jakafi®
ruxolitinib (tablets)

BRIEF SUMMARY: For Full Prescribing Information, see package insert.

CONTRAINDICATIONS None.

WARNINGS AND PRECAUTIONS Thrombocytopenia, Anemia and Neutropenia Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia. [*see Dosage and Administration (2.1) in Full Prescribing Information*]. Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary [*see Dosage and Administration (2.1.1) and Adverse Reactions (6.1) in Full Prescribing Information*]. Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi. Severe neutropenia (ANC less than 0.5 X 10^9/L) was generally reversible by withholding Jakafi until recovery [*see Adverse Reactions (6.1) in Full Prescribing Information*]. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated. [*see Dosage and Administration (2.1.1) and Adverse Reactions (6.1) in Full Prescribing Information*].

Risk of Infection Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting therapy with Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly. *Tuberculosis* Tuberculosis infection has been reported in patients receiving Jakafi. Observe patients receiving Jakafi for signs and symptoms of active tuberculosis and manage promptly. Prior to initiating Jakafi, patients should be evaluated for tuberculosis risk factors, and those at higher risk should be tested for latent infection. Risk factors include, but are not limited to, prior residence in or travel to countries with a high prevalence of tuberculosis, close contact with a person with active tuberculosis, and a history of active or latent tuberculosis where an adequate course of treatment cannot be confirmed. For patients with evidence of active or latent tuberculosis, consult a physician with expertise in the treatment of tuberculosis before starting Jakafi. The decision to continue Jakafi during treatment of active tuberculosis should be based on the overall risk-benefit determination. *PML* Progressive multifocal leukoencephalopathy (PML) has occurred with ruxolitinib treatment for myelofibrosis. If PML is suspected, stop Jakafi and evaluate. *Herpes Zoster* Advise patients about early signs and symptoms of herpes zoster and to seek treatment as early as possible if suspected [*see Adverse Reactions (6.1) in Full Prescribing Information*]. *Hepatitis B* Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking Jakafi. The effect of Jakafi on viral replication in patients with chronic HBV infection is unknown. Patients with chronic HBV infection should be treated and monitored according to clinical guidelines. **Symptom Exacerbation Following Interruption or Discontinuation of Treatment with Jakafi** Following discontinuation of Jakafi, symptoms from myeloproliferative neoplasms may return to pretreatment levels over a period of approximately one week. Some patients with myelofibrosis have experienced one or more of the following adverse events after discontinuing Jakafi: fever, respiratory distress, hypotension, DIC, or multi-organ failure. If one or more of these occur after discontinuation of, or while tapering the dose of Jakafi, evaluate for and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi therapy without consulting their physician. When discontinuing or interrupting therapy with Jakafi for reasons other than thrombocytopenia or neutropenia [*see Dosage and Administration (2.5) in Full Prescribing Information*], consider tapering the dose of Jakafi gradually rather than discontinuing abruptly. **Non-Melanoma Skin Cancer** Non-melanoma skin cancers including basal cell, squamous cell, and Merkel cell carcinoma have occurred in patients treated with Jakafi. Perform periodic skin examinations. **Lipid Elevations** Treatment with Jakafi has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides. The effect of these lipid parameter elevations on cardiovascular morbidity and mortality has not been determined in patients treated with Jakafi. Assess lipid parameters approximately 8-12 weeks following initiation of Jakafi therapy. Monitor and treat according to clinical guidelines for the management of hyperlipidemia.

ADVERSE REACTIONS The following serious adverse reactions are discussed in greater detail in other sections of the labeling: • Thrombocytopenia, Anemia and Neutropenia [*see Warnings and Precautions (5.1) in Full Prescribing Information*] • Risk of Infection [*see Warnings and Precautions (5.2) in Full Prescribing Information*] • Symptom Exacerbation Following Interruption or Discontinuation of Treatment with Jakafi [*see Warnings and Precautions (5.3) in Full Prescribing Information*] • Non-Melanoma Skin Cancer [*see Warnings and Precautions (5.4) in Full Prescribing Information*]. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. **Clinical Trials Experience in Myelofibrosis** The safety of Jakafi was assessed in 617 patients in six clinical studies with a median duration of follow-up of 10.9 months, including 301 patients with myelofibrosis in two Phase 3 studies. In these two Phase 3 studies, patients had a median duration of exposure to Jakafi of 9.5 months (range 0.5 to 17 months), with 89% of patients treated for more than 6 months and 25% treated for more than 12 months. One hundred and eleven (111) patients started treatment at 15 mg twice daily and 190 patients started at 20 mg twice daily. In patients starting treatment with 15 mg twice daily (pretreatment platelet counts of 100 to 200 X 10^9/L) and 20 mg twice daily (pretreatment platelet counts greater than 200 X 10^9/L), 65% and 25% of patients, respectively, required a dose reduction below the starting dose within the first 8 weeks of therapy. In a double-blind, randomized, placebo-controlled study of Jakafi, among the 155 patients treated with Jakafi, the most frequent adverse drug reactions were thrombocytopenia and anemia [*see Table 2*]. Thrombocytopenia, anemia and neutropenia are dose related effects. The three most frequent non-hematologic adverse reactions were bruising, dizziness and headache [*see Table 1*]. Discontinuation for adverse events, regardless of causality, was observed in 11% of patients treated with Jakafi and 11% of patients treated with placebo. Table 1 presents the most common adverse reactions occurring in patients who received Jakafi in the double-blind, placebo-controlled study during randomized treatment.

Table 1: Myelofibrosis: Adverse Reactions Occurring in Patients on Jakafi in the Double-blind, Placebo-controlled Study During Randomized Treatment

	Jakafi (N=155)			Placebo (N=151)		
Adverse Reactions	**All Grades[a] (%)**	**Grade 3 (%)**	**Grade 4 (%)**	**All Grades (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Bruising[b]	23	<1	0	15	0	0
Dizziness[c]	18	<1	0	7	0	0
Headache	15	0	0	5	0	0
Urinary Tract Infections[d]	9	0	0	5	<1	<1
Weight Gain[e]	7	<1	0	1	<1	0
Flatulence	5	0	0	<1	0	0
Herpes Zoster[f]	2	0	0	<1	0	0

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0
[b] includes contusion, ecchymosis, hematoma, injection site hematoma, periorbital hematoma, vessel puncture site hematoma, increased tendency to bruise, petechiae, purpura
[c] includes dizziness, postural dizziness, vertigo, balance disorder, Meniere's Disease, labyrinthitis
[d] includes urinary tract infection, cystitis, urosepsis, urinary tract infection bacterial, kidney infection, pyuria, bacteria urine, bacteria urine identified, nitrite urine present
[e] includes weight increased, abnormal weight gain
[f] includes herpes zoster and post-herpetic neuralgia

Description of Selected Adverse Drug Reactions **Anemia** In the two Phase 3 clinical studies, median time to onset of first CTCAE Grade 2 or higher anemia was approximately 6 weeks. One patient (<1%) discontinued treatment because of anemia. In patients receiving Jakafi, mean decreases in hemoglobin reached a nadir of approximately 1.5 to 2.0 g/dL below baseline after 8 to 12 weeks of therapy and then gradually recovered to reach a new steady state that was approximately 1.0 g/dL below baseline. This pattern was observed in patients regardless of whether they had received transfusions during therapy. In the randomized, placebo-controlled study, 60% of patients treated with Jakafi and 38% of patients receiving placebo received red blood cell transfusions during randomized treatment. Among transfused patients, the median number of units transfused per month was 1.2 in patients treated with Jakafi and 1.7 in placebo treated patients. **Thrombocytopenia** In the two Phase 3 clinical studies, in patients who developed Grade 3 or 4 thrombocytopenia, the median time to onset was approximately 8 weeks. Thrombocytopenia was generally reversible with dose reduction or dose interruption. The median time to recovery of platelet counts above 50 X 10^9/L was 14 days. Platelet transfusions were administered to 5% of patients receiving Jakafi and to 4% of patients receiving control regimens. Discontinuation of treatment because of thrombocytopenia occurred in <1% of patients receiving Jakafi and <1% of patients receiving control regimens. Patients with a platelet count of 100 X 10^9/L to 200 X 10^9/L before starting Jakafi had a higher frequency of Grade 3 or 4 thrombocytopenia compared to patients with a platelet count greater than 200 X 10^9/L (17% versus 7%). **Neutropenia** In the two Phase 3 clinical studies, 1% of patients reduced or stopped Jakafi because of neutropenia. Table 2 provides the frequency and severity of clinical hematology abnormalities reported for patients receiving treatment with Jakafi or placebo in the placebo-controlled study.

Table 2: Myelofibrosis: Worst Hematology Laboratory Abnormalities in the Placebo-Controlled Study[a]

	Jakafi (N=155)			Placebo (N=151)		
Laboratory Parameter	**All Grades[b] (%)**	**Grade 3 (%)**	**Grade 4 (%)**	**All Grades (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Thrombocytopenia	70	9	4	31	1	0
Anemia	96	34	11	87	16	3
Neutropenia	19	5	2	4	<1	1

[a] Presented values are worst Grade values regardless of baseline
[b] National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0

Additional Data from the Placebo-controlled Study 25% of patients treated with Jakafi and 7% of patients treated with placebo developed newly occurring or worsening Grade 1 abnormalities in alanine transaminase (ALT). The incidence of greater than or equal to Grade 2 elevations was 2% for Jakafi with 1% Grade 3 and no Grade 4 ALT elevations. 17% of patients treated with Jakafi and 6% of patients treated with placebo developed newly occurring or worsening Grade 1 abnormalities in aspartate transaminase (AST). The incidence of Grade 2 AST elevations was <1% for Jakafi with no Grade 3 or 4 AST elevations. 17% of patients treated with Jakafi and <1% of patients treated with placebo developed newly occurring or worsening Grade 1 elevations in cholesterol. The incidence of Grade 2 cholesterol elevations was <1% for Jakafi with no Grade 3 or 4 cholesterol elevations.

Clinical Trial Experience in Polycythemia Vera In a randomized, open-label, active-controlled study, 110 patients with polycythemia vera resistant to or intolerant of hydroxyurea received Jakafi and 111 patients received best available therapy [*see Clinical Studies (14.2) in Full Prescribing Information*]. The most frequent adverse drug reaction was anemia. Table 3 presents the most frequent non-hematologic treatment emergent adverse events occurring up to Week 32. Discontinuation for adverse events, regardless of causality, was observed in 4% of patients treated with Jakafi.

Table 3: Polycythemia Vera: Treatment Emergent Adverse Events Occurring in ≥ 6% of Patients on Jakafi in the Open-Label, Active-controlled Study up to Week 32 of Randomized Treatment

	Jakafi (N=110)		Best Available Therapy (N=111)	
Adverse Events	**All Grades[a] (%)**	**Grade 3-4 (%)**	**All Grades (%)**	**Grade 3-4 (%)**
Headache	16	<1	19	<1
Abdominal Pain[b]	15	<1	15	<1
Diarrhea	15	0	7	<1
Dizziness[c]	15	0	13	0
Fatigue	15	0	15	3
Pruritus	14	<1	23	4
Dyspnea[d]	13	3	4	0
Muscle Spasms	12	<1	5	0
Nasopharyngitis	9	0	8	0
Constipation	8	0	3	0
Cough	8	0	5	0
Edema[e]	8	0	7	0
Arthralgia	7	0	6	<1
Asthenia	7	0	11	2
Epistaxis	6	0	3	0
Herpes Zoster[f]	6	<1	0	0
Nausea	6	0	4	0

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0
[b] includes abdominal pain, abdominal pain lower, and abdominal pain upper
[c] includes dizziness and vertigo
[d] includes dyspnea and dyspnea exertional
[e] includes edema and peripheral edema
[f] includes herpes zoster and post-herpetic neuralgia

Other clinically important treatment emergent adverse events observed in less than 6% of patients treated with Jakafi were: Weight gain, hypertension, and urinary tract infections. Clinically relevant laboratory abnormalities are shown in Table 4.

Table 4: Polycythemia Vera: Selected Laboratory Abnormalities in the Open-Label, Active-controlled Study up to Week 32 of Randomized Treatment[a]

	Jakafi (N=110)			Best Available Therapy (N=111)		
Laboratory Parameter	**All Grades[b] (%)**	**Grade 3 (%)**	**Grade 4 (%)**	**All Grades (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Hematology						
Anemia	72	<1	<1	58	0	0
Thrombocytopenia	27	5	<1	24	3	<1
Neutropenia	3	0	<1	10	<1	0
Chemistry						
Hypercholesterolemia	35	0	0	8	0	0
Elevated ALT	25	<1	0	16	0	0
Elevated AST	23	0	0	23	<1	0
Hypertriglyceridemia	15	0	0	13	0	0

[a] Presented values are worst Grade values regardless of baseline
[b] National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0

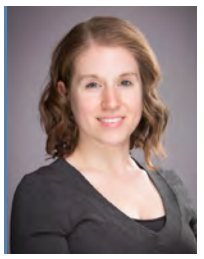
DRUG INTERACTIONS Drugs That Inhibit or Induce Cytochrome P450 Enzymes Ruxolitinib is metabolized by CYP3A4 and to a lesser extent by CYP2C9. **CYP3A4 inhibitors:** The C_{max} and AUC of ruxolitinib increased 33% and 91%, respectively following concomitant administration with the strong CYP3A4 inhibitor ketoconazole in healthy subjects. Concomitant administration with mild or moderate CYP3A4 inhibitors did not result in an exposure change requiring intervention [*see Pharmacokinetics (12.3) in Full Prescribing Information*]. When administering Jakafi with strong CYP3A4 inhibitors, consider dose reduction [*see Dosage and Administration (2.3) in Full Prescribing Information*]. **Fluconazole:** The AUC of ruxolitinib is predicted to increase by approximately 100% to 300% following concomitant administration with the combined CYP3A4 and CYP2C9 inhibitor fluconazole at doses of 100 mg to 400 mg once daily, respectively [*see Pharmacokinetics (12.3) in Full Prescribing Information*]. Avoid the concomitant use of Jakafi with fluconazole doses of greater than 200 mg daily [*see Dosage and Administration (2.3) in Full Prescribing Information*]. **CYP3A4 inducers:** The C_{max} and AUC of ruxolitinib decreased 32% and 61%, respectively, following concomitant administration with the strong CYP3A4 inducer rifampin in healthy subjects. No dose adjustment is recommended; however, monitor patients frequently and adjust the Jakafi dose based on safety and efficacy [*see Pharmacokinetics (12.3) in Full Prescribing Information*].

USE IN SPECIFIC POPULATIONS Pregnancy Pregnancy Category C: *Risk Summary* There are no adequate and well-controlled studies of Jakafi in pregnant women. In embryofetal toxicity studies, treatment with ruxolitinib resulted in an increase in late resorptions and reduced fetal weights at maternally toxic doses. Jakafi should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. *Animal Data* Ruxolitinib was administered orally to pregnant rats or rabbits during the period of organogenesis, at doses of 15, 30 or 60 mg/kg/day in rats and 10, 30 or 60 mg/kg/day in rabbits. There was no evidence of teratogenicity. However, decreases of approximately 9% in fetal weights were noted in rats at the highest and maternally toxic dose of 60 mg/kg/day. This dose results in an exposure (AUC) that is approximately 2 times the clinical exposure at the maximum recommended dose of 25 mg twice daily. In rabbits, lower fetal weights of approximately 8% and increased late resorptions were noted at the highest and maternally toxic dose of 60 mg/kg/day. This dose is approximately 7% the clinical exposure at the maximum recommended dose. In a pre- and post-natal development study in rats, pregnant animals were dosed with ruxolitinib from implantation through lactation at doses up to 30 mg/kg/day. There were no drug-related adverse findings in pups for fertility indices or for maternal or embryofetal survival, growth and development parameters at the highest dose evaluated (34% the clinical exposure at the maximum recommended dose of 25 mg twice daily). **Nursing Mothers** It is not known whether ruxolitinib is excreted in human milk. Ruxolitinib and/or its metabolites were excreted in the milk of lactating rats with a concentration that was 13-fold the maternal plasma. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Jakafi, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use** The safety and effectiveness of Jakafi in pediatric patients have not been established. **Geriatric Use** Of the total number of patients with myelofibrosis in clinical studies with Jakafi, 52% were 65 years and older, while 15% were 75 years and older. No overall differences in safety or effectiveness of Jakafi were observed between these patients and younger patients. **Renal Impairment** The safety and pharmacokinetics of single dose Jakafi (25 mg) were evaluated in a study in healthy subjects [CrCl 72-164 mL/min (N=8)] and in subjects with mild [CrCl 53-83 mL/min (N=8)], moderate [CrCl 38-57 mL/min (N=8)], or severe renal impairment [CrCl 15-51 mL/min (N=8)]. Eight (8) additional subjects with end stage renal disease requiring hemodialysis were also enrolled. The pharmacokinetics of ruxolitinib was similar in subjects with various degrees of renal impairment and in those with normal renal function. However, plasma AUC values of ruxolitinib metabolites increased with increasing severity of renal impairment. This was most marked in the subjects with end stage renal disease requiring hemodialysis. The change in the pharmacodynamic marker, pSTAT3 inhibition, was consistent with the corresponding increase in metabolite exposure. Ruxolitinib is not removed by dialysis; however, the removal of some active metabolites by dialysis cannot be ruled out. When administering Jakafi to patients with myelofibrosis and moderate (CrCl 30-59 mL/min) or severe renal impairment (CrCl 15-29 mL/min) with a platelet count between 50 X 10^9/L and 150 X 10^9/L, a dose reduction is recommended. A dose reduction is also recommended for patients with polycythemia vera and moderate (CrCl 30-59 mL/min) or severe renal impairment (CrCl 15-29 mL/min). In all patients with end stage renal disease on dialysis, a dose reduction is recommended [*see Dosage and Administration (2.4) in Full Prescribing Information*]. **Hepatic Impairment** The safety and pharmacokinetics of single dose Jakafi (25 mg) were evaluated in a study in healthy subjects (N=8) and in subjects with mild [Child-Pugh A (N=8)], moderate [Child-Pugh B (N=8)], or severe hepatic impairment [Child-Pugh C (N=8)]. The mean AUC for ruxolitinib was increased by 87%, 28% and 65%, respectively, in patients with mild, moderate and severe hepatic impairment compared to patients with normal hepatic function. The terminal elimination half-life was prolonged in patients with hepatic impairment compared to healthy controls (4.1-5.0 hours versus 2.8 hours). The change in the pharmacodynamic marker, pSTAT3 inhibition, was consistent with the corresponding increase in ruxolitinib exposure except in the severe (Child-Pugh C) hepatic impairment cohort where the pharmacodynamic activity was more prolonged in some subjects than expected based on plasma concentrations of ruxolitinib. When administering Jakafi to patients with myelofibrosis and any degree of hepatic impairment and with a platelet count between 50 X 10^9/L and 150 X 10^9/L, a dose reduction is recommended. A dose reduction is also recommended for patients with polycythemia vera and hepatic impairment [*see Dosage and Administration (2.4) in Full Prescribing Information*].

OVERDOSAGE There is no known antidote for overdoses with Jakafi. Single doses up to 200 mg have been given with acceptable acute tolerability. Higher than recommended repeat doses are associated with increased myelosuppression including leukopenia, anemia and thrombocytopenia. Appropriate supportive treatment should be given. Hemodialysis is not expected to enhance the elimination of ruxolitinib.

Revised: March 2016 RUX-1778a

(continued from SP623)



SINCLAIR

MEIER

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on needed processes and skills. Specific areas of focus include the Medicare Merit-based Incentive Payment System (MIPS), Medicare Advantage (MA) plans, Medicare Accountable Care Organizations (ACOs), and the new Medicare Oncology Care Model (OCM).

Palliative Care and MACRA's Merit-Based Incentive Payment System

The Medicare Access and CHIP Reauthorization Act (MACRA) expedites Medicare's transition to VBP by subjecting eligible clinicians to bonuses and penalties based on their quality performance relative to their peers. MACRA creates 2 payment tracks, and the vast majority of clinicians will participate in the MIPS in the first year. Under MIPS, CMS will calculate payment adjustments based on performance in 4 categories:

1. Quality
2. Cost
3. Advancing care information
4. Improvement activities

The eventual weighting of the Quality and Cost categories in the composite score used to adjust provider reimbursement creates a compelling rationale to involve palliative care specialists in the care of seriously ill patients:

- *Quality*
  Palliative care specialists manage symptoms and stress while patients undergo complex treatments, and they also support informed decisions as chronic illnesses progress. This improves the patients' experience of care as demonstrated in studies showing significant improvement in satisfaction scores.[14] Therefore, the inclusion of palliative care should improve results on the Consumer Assessment of Healthcare Providers and Systems (CAHPS) for MIPS surveys, which is expected to be one of the more popular "cross-cutting measures" under the quality category. Additionally, the provision of palliative care should help improve performance on a number of other proposed MIPS measures including advance care planning, pain assessment and follow-up, and medication reconciliation.

- *Cost*
  The significant impact of palliative care in reducing ED, hospital, and ICU utilization in seriously ill patients[4,10] will benefit treating clinicians in their resource use calculations. Efficient resource use is also a key factor determining provider payments in all of the advanced alternate payment models.

Palliative Care and Medicare Advantage

Palliative care can support MA plans in decreasing cost and increasing revenue. On the cost side, as noted, palliative care reduces utilization among the high-need, high-cost members of a population. Several leading MA plans have expanded access to palliative care for their seriously ill beneficiaries, generating significant savings. For example, Aetna's Compassionate Care Program, provided to the sickest 1% of the plan's MA members, achieved the following[15]:

- Reduced ICU days by 86%
- Decreased total acute care days by 82%
- Reduced ED use by 78%
- Maintained member satisfaction above 90%
- Savings of roughly $12,000 per participating member.

On the revenue side, palliative care positively impacts the measures on which MA plans are evaluated, appearing as publicly reported data and overall Star Ratings. These Star Ratings are calculated by using data from 3 sources:

1. A subset of the Healthcare Effectiveness Data and Information Set measures (HEDIS measures)
2. Results of the CAHPS surveys
3. Results of Health Outcomes surveys

Measures that are likely to be improved by palliative care include:

- All-cause readmissions
- ED utilization
- Hospitalization for potentially preventable complications
- Medication reconciliation post discharge
- Utilization of the Patient Health Questionnaire-9 to monitor depression symptoms
- Relative resource use (specific diagnoses)
- The level of pain that interferes with activity rating by members
- Member rating on how well doctor communicates[1]

Plans that perform better on their measures receive more stars, leading to higher premium payments and a greater ability to attract and retain members. Consumers consider the Medicare Star Ratings during the open enrollment period for MA[16] and 5-Star plans have the advantage of being able to enroll members switching from other MA plans at any time during the year.[17]

Palliative Care and Medicare Shared Savings Programs (MSSP)

Similar to MA plans, Medicare ACOs are evaluated on their performance on a set of quality measures and have financial incentives to manage resource utilization. The MSSP is the most common type of ACO and, here, too, palliative care can impact a number of quality measures, including:

- All-cause unplanned admissions (for specific diagnoses)
- Ambulatory-sensitive admissions (for specific diagnoses)
- Skilled nursing facility 30-day all-cause readmissions
- Depression remission at 12 months
- Provider communications rating by patients
- Shared decision making rating by patients

Palliative care can be particularly valuable in reducing readmissions. National data from CMS on hospital readmissions shows that since 2010, 43 states have reduced readmissions by more than 5%, and, in 2015, the national readmission rate fell below 18%.[18] However, 2015 data from the National Palliative Care Registry show that the average readmission rate for patients discharged alive from participating palliative care consultation services was only 13.8%.[19]

Perhaps more important than performance on specific quality measures is the role that palliative care can play in delivery redesign. Early analysis from a CAPC survey of MSSPs offering palliative care yielded 2 strategies that could have improved ACO results:

Home-Based Palliative Care for Highest-Risk Patients. Some of the more successful MSSPs stratify their population and connect the highest-risk patients with home-based palliative care services. These services involve an interdisciplinary team providing continuous comprehensive assessment, pain and symptom management, and expert conversations in the patients' homes, adjunctive to the care delivered by their treating providers. Published findings from home-based programs within ACOs show between 34% and 56% reduction in hospital utilization, resulting in average savings of $12,000 per case.[20,21]

Integration of Palliative Care Into Oncology Care. Several MSSPs have taken steps to integrate palliative care into oncology practices. At least 2 have conducted extensive training on advance care planning to ensure that patients' wishes are articulated and documented, and then ensure that those documents are easily accessible in the electronic health record. Other ACOs have embedded palliative care specialists into their practices to help meet the needs of the most complex patients. An ACO contract with Moffitt Cancer Center requires the participating oncology practices to screen all patients for palliative care needs and include a palliative care specialist in the management of patients with documented need.

Implications for Palliative Care and the Oncology Care Model (OCM)

Similar to the models and programs described above, the integration of palliative care can improve performance for practices participating in the OCM, as CMS will be evaluating them on the following:

- Pain assessment and management
- Patient experience of care
- ED visits and hospital admissions
- Proportion of Medicare beneficiaries receiving chemotherapy in the last 14 days of life
- Percentage of patients admitted to hospice for less than 3 days in the last 30 days of life.

Beyond quality measures, OCM practices should extract lessons learned on palliative care integration from those successfully participating in MSSP and other ACO contracts. These include training oncologists and other clinicians in core palliative care skills, or co-locating palliative care experts in the oncology practices. The latter, in particular, can facilitate collaboration, allowing the oncology team to treat the disease while the palliative care team provides an added layer of support during and after the episode. OCM practices can pay for these services by allocating a portion of the monthly enhanced oncology services payment and performance-based payment, thus ensuring that palliative care services are available to all patients according to their level of need.

Palliative Care and Value-Based Payment: Moving Forward

When done properly, VBP can improve quality of care for patients by creating greater flexibility in service delivery while holding clinicians accountable for resource utilization. This commentary provides examples from 4 significant value-based programs demonstrating how palliative care can simultaneously improve performance on quality measures while reducing costs. These examples suggest that oncologists can benefit under VBP by integrating core principles of palliative care into their standard practice and/or establishing formal relationships with palliative care specialists. ◆

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REFERENCES

1. Smith G, Bernacki R, Block SD. The role of palliative care in population management and accountable care organizations. *J Palliat Med.* 2015;18(6):486-494. doi: 10.1089/jpm.2014.0231.
2. Cheville AL, Alberts SR, Rummans TA, et al. Improving adherence to cancer treatment by addressing quality of life in patients with advanced gastrointestinal cancers. *J Pain Symptom Manage.* 2015;50(3):321-327. doi: 10.1016/j.jpainsymman.2015.03.005.
3. Casarett D, Pickard A, Bailey FA, et al. Do palliative consultations improve patient outcomes? *J Am Geriatr Soc.* 2008;56(4):593-599. doi: 10.1111/j.1532-5415.2007.01610.x.
4. O'Connor NR, Moyer ME, Behta M, Casarett DJ. The impact of inpatient palliative care consultations on 30-day hospital readmissions. *J Palliat Med.* 2015;18(11):956-961. doi: 10.1089/jpm.2015.0138.
5. Scibetta C, Kerr K, Mcguire J, Rabow MW. The costs of waiting: implications of the timing of palliative care consultation among a cohort of decedents at a comprehensive cancer center. *J Palliat Med.* 2015;19(1):69-75. doi: 10.1089/jpm.2015.0119.
6. May P, Normand C, Morrison RS. Economic impact of hospital inpatient palliative care consultation: review of current evidence and directions for future research. *J Palliat Med.* 2014;17(9):1054-1063. doi: 10.1089/jpm.2013.0594
7. Whitford K, Shah ND, Moriarty J, Branda M, Thorsteinsdottir B. Impact of a palliative care consult service. *Am J Hosp Palliat Care.* 2014;31(2):175-182. doi: 10.1177/1049909113482746.
8. Adelson KB, Paris J, Smith CB, Horton J, Morrison RS. Standardized criteria for required palliative care consultation on the solid tumor oncology service [ASCO abstract 6623]. *J Clin Oncol.* 2014;32:5s (suppl).
9. Temel JD, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non–small-cell lung cancer. *N Engl J Med.* 2010;363(8):733-742. doi: 10.1056/NEJMoa1000678.
10. Scibetta C, Kerr K, Mcguire J, Rabow MW. The costs of waiting: implications of the timing of palliative care consultation among a cohort of decedents at a comprehensive cancer center. *J Palliat Med.* 2016;19(1):69-75. doi: 10.1089/jpm.2015.0119.
11. Price K, Dahl A. Achieving data driven success under the Oncology Care Model. *The American Journal of Managed Care* website. http://www.ajmc.com/contributor/kelly-price/2016/06/achieving-data-driven-success-under-the-oncology-care-model. Published June 30, 2016. Accessed October 19, 2016.
12. Breivik H, Cherny N, Collett B, et al. Cancer-related pain: a pan-European survey of prevalence, treatment and patient attitudes. *Ann Oncol.* 2009;20(8):1420-1433. doi: 10.1093/annonc/mdp001.
13. Smith TJ, Temin S, Alesi ER, et al. American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care. *J Clin Oncol.* 2012;30(8):880-887. doi: 10.1200/JCO.2011.38.5161.
14. Rabow M, Kvale E, Barbour L, et al. Moving upstream: a review of the evidence of the impact of outpatient palliative care. *J Palliat Med.* 2013;16(12):1540-1549. doi:10.1089/jpm.2013.0153.
15. Krakauer B, Agostini J, Krakauer R. Aetna's Compassionate Care Program and end-of-life decisions. *J Clinical Ethics.* 2014;25(2):131-134.
16. Pearson CF. Sixty percent of Medicare Advantage enrollees now in plans with four or more stars. Avalere Health website. http://avalere.com/expertise/managed-care/insights/sixty-percent-of-medicare-advantage-enrollees-now-in-plans-with-four-or-mor. Published March 18, 2015. Accessed October 19, 2016.
17. CMS. 5-star special enrollment period. Medicare.gov website. https://www.medicare.gov/sign-up-change-plans/when-can-i-join-a-health-or-drug-plan/five-star-enrollment/5-star-enrollment-period.html. Accessed October 19, 2016.
18. Conway P and Gronniger T. New data: 49 states plus DC reduce avoidable hospital readmissions. The CMS Blog website. https://blog.cms.gov/2016/09/13/new-data-49-states-plus-dc-reduce-avoidable-hospital-readmissions/. Published September 13, 2016. Accessed October 5, 2016.
19. National Palliative Care Registry. 2015 National Palliative Care Registry summary data table. National Palliative Care Registry website. https://registry.capc.org/metrics-resources/summary-data/. Published 2016. Accessed October 19, 2016.
20. Lustbader D, Mudra M, Romano C, et al. The impact of a home-based palliative care program in an Accountable Care Organization [published online August 30, 2016]. *J Palliat Med.* doi:10.1089/jpm.2016.0265.
21. Cassel JB, Kerr KM, McClish DK, et al. Effect of a home-based palliative care program on healthcare utilization and cost [published online September 2, 2016]. *J Am Geriatr Soc.* doi: 10.1111/jgs.14354.

#1 PRESCRIBED ORAL CLL THERAPY.*
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CLL
SLL

IMBRUVICA® is a once-daily oral therapy indicated for:

- Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)[2]
- CLL/SLL with 17p deletion[2]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage - Fatal bleeding events have occurred in patients treated with IMBRUVICA®. Grade 3 or higher bleeding events (intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post-procedural hemorrhage) have occurred in up to 6% of patients. Bleeding events of any grade, including bruising and petechiae, occurred in approximately half of patients treated with IMBRUVICA®.

The mechanism for the bleeding events is not well understood. IMBRUVICA® may increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies and patients should be monitored for signs of bleeding. Consider the benefit-risk of withholding IMBRUVICA® for at least 3 to 7 days pre- and postsurgery depending upon the type of surgery and the risk of bleeding.

Infections - Fatal and nonfatal infections have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 14% to 29% of patients. Cases of progressive multifocal leukoencephalopathy (PML) have occurred in patients treated with IMBRUVICA®. Evaluate patients for fever and infections and treat appropriately.

Cytopenias - Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 19% to 29%), thrombocytopenia (range, 5% to 17%), and anemia (range, 0% to 9%) based on laboratory measurements occurred in patients treated with single agent IMBRUVICA®. Monitor complete blood counts monthly.

Atrial Fibrillation - Atrial fibrillation and atrial flutter (range, 6% to 9%) have occurred in patients treated with IMBRUVICA®, particularly in patients with cardiac risk factors, hypertension, acute infections, and a previous history of atrial fibrillation. Periodically monitor patients clinically for atrial fibrillation. Patients who develop arrhythmic symptoms (eg, palpitations, lightheadedness) or new-onset dyspnea should have an ECG performed. Atrial fibrillation should be managed appropriately and if it persists, consider the risks and benefits of IMBRUVICA® treatment and follow dose modification guidelines.

Hypertension - Hypertension (range, 6% to 17%) has occurred in patients treated with IMBRUVICA® with a median time to onset of 4.6 months (range, 0.03 to 22 months). Monitor patients for new-onset hypertension or hypertension that is not adequately controlled after starting IMBRUVICA®. Adjust existing antihypertensive medications and/or initiate antihypertensive treatment as appropriate.

Second Primary Malignancies - Other malignancies (range, 5% to 16%) including non-skin carcinomas (range, 1% to 4%) have occurred in patients treated with IMBRUVICA®. The most frequent second primary malignancy was non-melanoma skin cancer (range, 4% to 13%).

Tumor Lysis Syndrome - Tumor lysis syndrome has been infrequently reported with IMBRUVICA® therapy. Assess the baseline risk (eg, high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

Embryo-Fetal Toxicity - Based on findings in animals, IMBRUVICA® can cause fetal harm when administered to a pregnant woman. Advise women to avoid becoming pregnant while taking IMBRUVICA® and for 1 month after cessation of therapy. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

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RESONATE™-2 FRONTLINE DATA

RESONATE™-2 was a multicenter, randomized 1:1, open-label, Phase 3 trial of IMBRUVICA® vs chlorambucil in frontline CLL/SLL patients ≥65 years (N=269)[2,3]
Patients with 17p deletion were not included in the RESONATE™-2 trial[3]

EXTENDED OVERALL SURVIVAL

IMBRUVICA® significantly extended OS vs chlorambucil[2]

Statistically significant reduction in risk of death[2]

56%

HR=0.44
(95% CI: 0.21, 0.92)

41% of patients crossed over to IMBRUVICA®

Estimated survival rates at 24 months

95% IMBRUVICA®
(95% CI: 89, 97)

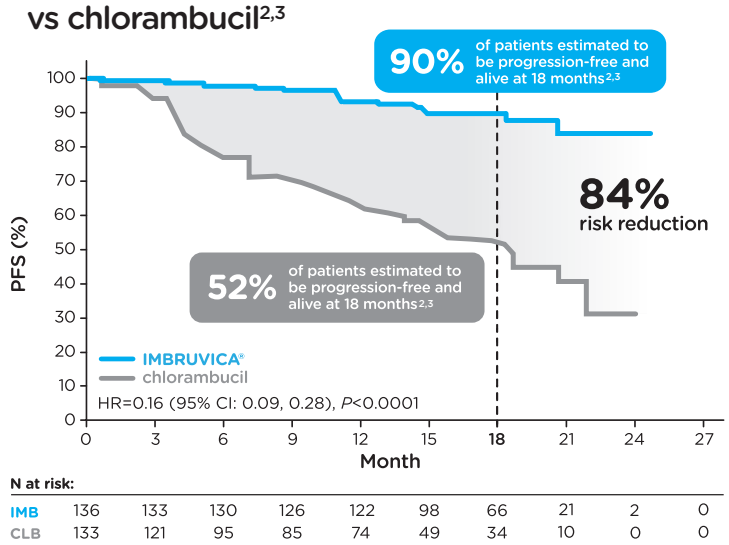
84% chlorambucil
(95% CI: 77, 90)

SECONDARY ENDPOINT: OS

- Median follow-up was 28 months[2]

PROLONGED PROGRESSION-FREE SURVIVAL

IMBRUVICA® significantly extended PFS vs chlorambucil[2,3]



PRIMARY ENDPOINT: PFS

- Median follow-up was 18 months[3]
- IMBRUVICA® median PFS not reached[2]
- Chlorambucil median PFS was 18.9 months (95% CI: 14.1, 22.0)[2]
- PFS was assessed by an IRC per revised IWCLL criteria[3]

Adverse reactions ≥20% across CLL/SLL registration studies[2]

- Neutropenia
- Thrombocytopenia
- Anemia
- Diarrhea
- Musculoskeletal pain
- Nausea
- Rash
- Bruising
- Fatigue
- Pyrexia
- Hemorrhage

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in patients with B-cell malignancies (MCL, CLL/SLL, and WM) were neutropenia‡ (64%), thrombocytopenia‡ (63%), diarrhea (43%), anemia‡ (41%), musculoskeletal pain (30%), rash (29%), nausea (29%), bruising (29%), fatigue (27%), hemorrhage (21%), and pyrexia (21%).

‡Based on adverse reactions and/or laboratory measurements (noted as platelets, neutrophils, or hemoglobin decreased).

The most common Grade 3 or 4 non-hematologic adverse reactions (≥5%) in MCL patients were pneumonia (7%), abdominal pain (5%), atrial fibrillation (5%), diarrhea (5%), fatigue (5%), and skin infections (5%).

Approximately 6% (CLL/SLL), 14% (MCL), and 11% (WM) of patients had a dose reduction due to adverse reactions.

Approximately 4%-10% (CLL/SLL), 9% (MCL), and 6% (WM) of patients discontinued due to adverse reactions. Most frequent adverse reactions leading to discontinuation were pneumonia, hemorrhage, atrial fibrillation, rash, and neutropenia (1% each) in CLL/SLL patients and subdural hematoma (1.8%) in MCL patients.

DRUG INTERACTIONS

CYP3A Inhibitors - Avoid coadministration with strong and moderate CYP3A inhibitors. If a moderate CYP3A inhibitor must be used, reduce the IMBRUVICA® dose.

CYP3A Inducers - Avoid coadministration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Hepatic Impairment - Avoid use in patients with moderate or severe baseline hepatic impairment. In patients with mild impairment, reduce IMBRUVICA® dose.

Please see the Brief Summary on the following pages.

*Based on market share 2016 July YTD data from IMS.
†Based on IMS data February 2014 to date.

CI=confidence interval, CLL=chronic lymphocytic leukemia, HR=hazard ratio, IRC=Independent Review Committee, IWCLL=International Workshop on CLL, OS=overall survival, PFS=progression-free survival, SLL=small lymphocytic leukemia.

References: 1. Data on file. Pharmacyclics LLC. **2.** IMBRUVICA® (ibrutinib) Prescribing Information. Pharmacyclics LLC 2016. **3.** Burger JA, Tedeschi A, Barr PM, et al; for the RESONATE-2 Investigators. Ibrutinib as initial therapy for patients with chronic lymphocytic leukemia. *N Engl J Med.* 2015;373(25):2425-2437.

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Brief Summary of Prescribing Information for IMBRUVICA® (ibrutinib)

IMBRUVICA® (ibrutinib) capsules, for oral use

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INDICATIONS AND USAGE

Mantle Cell Lymphoma: IMBRUVICA is indicated for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

Accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials *[see Clinical Studies (14.1) in Full Prescribing Information].*

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: IMBRUVICA is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) *[see Clinical Studies (14.2) in Full Prescribing Information].*

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma with 17p deletion: IMBRUVICA is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) with 17p deletion *[see Clinical Studies (14.2) in Full Prescribing Information].*

Waldenström's Macroglobulinemia: IMBRUVICA is indicated for the treatment of patients with Waldenström's macroglobulinemia (WM) *[see Clinical Studies (14.3) in Full Prescribing Information].*

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Hemorrhage: Fatal bleeding events have occurred in patients treated with IMBRUVICA. Grade 3 or higher bleeding events (intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post procedural hemorrhage) have occurred in up to 6% of patients. Bleeding events of any grade, including bruising and petechiae, occurred in approximately half of patients treated with IMBRUVICA.

The mechanism for the bleeding events is not well understood.

IMBRUVICA may increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies and patients should be monitored for signs of bleeding.

Consider the benefit-risk of withholding IMBRUVICA for at least 3 to 7 days pre and post-surgery depending upon the type of surgery and the risk of bleeding *[see Clinical Studies (14) in Full Prescribing Information].*

Infections: Fatal and non-fatal infections have occurred with IMBRUVICA therapy. Grade 3 or greater infections occurred in 14% to 29% of patients *[see Adverse Reactions].* Cases of progressive multifocal leukoencephalopathy (PML) have occurred in patients treated with IMBRUVICA. Evaluate patients for fever and infections and treat appropriately.

Cytopenias: Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 19 to 29%), thrombocytopenia (range, 5 to 17%), and anemia (range, 0 to 9%) based on laboratory measurements occurred in patients treated with single agent IMBRUVICA.

Monitor complete blood counts monthly.

Atrial Fibrillation: Atrial fibrillation and atrial flutter (range, 6 to 9%) have occurred in patients treated with IMBRUVICA, particularly in patients with cardiac risk factors, hypertension, acute infections, and a previous history of atrial fibrillation. Periodically monitor patients clinically for atrial fibrillation. Patients who develop arrhythmic symptoms (e.g., palpitations, lightheadedness) or new onset dyspnea should have an ECG performed. Atrial fibrillation should be managed appropriately, and if it persists, consider the risks and benefits of IMBRUVICA treatment and follow dose modification guidelines *[see Dosage and Administration (2.3) in Full Prescribing Information].*

Hypertension: Hypertension (range, 6 to 17%) has occurred in patients treated with IMBRUVICA with a median time to onset of 4.6 months (range, 0.03 to 22 months). Monitor patients for new onset hypertension or hypertension that is not adequately controlled after starting IMBRUVICA. Adjust existing anti-hypertensive medications and/or initiate anti-hypertensive treatment as appropriate.

Second Primary Malignancies: Other malignancies (range, 5 to 16%) including non-skin carcinomas (range, 1 to 4%) have occurred in patients treated with IMBRUVICA. The most frequent second primary malignancy was non-melanoma skin cancer (range, 4 to 13%).

Tumor Lysis Syndrome: Tumor lysis syndrome has been infrequently reported with IMBRUVICA therapy. Assess the baseline risk (e.g., high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

Embryo-Fetal Toxicity: Based on findings in animals, IMBRUVICA can cause fetal harm when administered to a pregnant woman. Administration of ibrutinib to pregnant rats and rabbits during the period of organogenesis caused embryofetal toxicity including malformations at exposures that were 2-20 times higher than those reported in patients with MCL, CLL/SLL or WM. Advise women to avoid becoming pregnant while taking IMBRUVICA and for 1 month after cessation of therapy. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus *[see Use in Specific Populations].*

ADVERSE REACTIONS

The following adverse reactions are discussed in more detail in other sections of the labeling:

- Hemorrhage *[see Warnings and Precautions]*
- Infections *[see Warnings and Precautions]*
- Cytopenias *[see Warnings and Precautions]*
- Atrial Fibrillation *[see Warnings and Precautions]*
- Hypertension *[see Warnings and Precautions]*
- Second Primary Malignancies *[see Warnings and Precautions]*
- Tumor Lysis Syndrome *[see Warnings and Precautions]*

Clinical Trials Experience: Because clinical trials are conducted under widely variable conditions, adverse event rates observed in clinical trials of a drug cannot be directly compared with rates of clinical trials of another drug and may not reflect the rates observed in practice.

Mantle Cell Lymphoma: The data described below reflect exposure to IMBRUVICA in a clinical trial that included 111 patients with previously treated MCL treated with 560 mg daily with a median treatment duration of 8.3 months.

The most commonly occurring adverse reactions (≥ 20%) were thrombocytopenia, diarrhea, neutropenia, anemia, fatigue, musculoskeletal pain, peripheral edema, upper respiratory tract infection, nausea, bruising, dyspnea, constipation, rash, abdominal pain, vomiting and decreased appetite (see Tables 1 and 2).

The most common Grade 3 or 4 non-hematological adverse reactions (≥ 5%) were pneumonia, abdominal pain, atrial fibrillation, diarrhea, fatigue, and skin infections.

Fatal and serious cases of renal failure have occurred with IMBRUVICA therapy. Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 9% of patients.

Adverse reactions from the MCL trial (N=111) using single agent IMBRUVICA 560 mg daily occurring at a rate of ≥ 10% are presented in Table 1.

Table 1: Non-Hematologic Adverse Reactions in ≥ 10% of Patients with MCL (N=111)

Body System	Adverse Reaction	All Grades (%)	Grade 3 or 4 (%)
Gastrointestinal disorders	Diarrhea	51	5
	Nausea	31	0
	Constipation	25	0
	Abdominal pain	24	5
	Vomiting	23	0
	Stomatitis	17	1
	Dyspepsia	11	0

Table 1: Non-Hematologic Adverse Reactions in ≥ 10% of Patients with MCL (N=111) (continued)

Body System	Adverse Reaction	All Grades (%)	Grade 3 or 4 (%)
Infections and infestations	Upper respiratory tract infection	34	0
	Urinary tract infection	14	3
	Pneumonia	14	7
	Skin infections	14	5
	Sinusitis	13	1
General disorders and administration site conditions	Fatigue	41	5
	Peripheral edema	35	3
	Pyrexia	18	1
	Asthenia	14	3
Skin and subcutaneous tissue disorders	Bruising	30	0
	Rash	25	3
	Petechiae	11	0
Musculoskeletal and connective tissue disorders	Musculoskeletal pain	37	1
	Muscle spasms	14	0
	Arthralgia	11	0
Respiratory, thoracic and mediastinal disorders	Dyspnea	27	4
	Cough	19	0
	Epistaxis	11	0
Metabolism and nutrition disorders	Decreased appetite	21	2
	Dehydration	12	4
Nervous system disorders	Dizziness	14	0
	Headache	13	0

Table 2: Treatment-Emergent* Decrease of Hemoglobin, Platelets, or Neutrophils in Patients with MCL (N=111)

	Percent of Patients (N=111)	
	All Grades (%)	Grade 3 or 4 (%)
Platelets Decreased	57	17
Neutrophils Decreased	47	29
Hemoglobin Decreased	41	9

* Based on laboratory measurements and adverse reactions

Ten patients (9%) discontinued treatment due to adverse reactions in the trial (N=111). The most frequent adverse reaction leading to treatment discontinuation was subdural hematoma (1.8%). Adverse reactions leading to dose reduction occurred in 14% of patients.

Patients with MCL who develop lymphocytosis greater than 400,000/mcL have developed intracranial hemorrhage, lethargy, gait instability, and headache. However, some of these cases were in the setting of disease progression.

Forty percent of patients had elevated uric acid levels on study including 13% with values above 10 mg/dL. Adverse reaction of hyperuricemia was reported for 15% of patients.

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: The data described below reflect exposure in one single-arm, open-label clinical trial and three randomized controlled clinical trials in patients with CLL/SLL (n=1278 total and n=668 patients exposed to IMBRUVICA). Study 1 included 51 patients with previously treated CLL/SLL, Study 2 included 391 randomized patients with previously treated CLL or SLL who received single agent IMBRUVICA or ofatumumab, Study 3 included 269 randomized patients 65 years or older with treatment naïve-CLL or SLL who received single agent IMBRUVICA or chlorambucil and Study 4 included 578 randomized patients with previously treated CLL or SLL who received IMBRUVICA in combination with bendamustine and rituximab or placebo in combination with bendamustine and rituximab.

The most commonly occurring adverse reactions in Studies 1, 2, 3 and 4 in patients with CLL/SLL receiving IMBRUVICA (≥ 20%) were neutropenia, thrombocytopenia, anemia, diarrhea, musculoskeletal pain, nausea, rash, bruising, fatigue, pyrexia and hemorrhage. Four to 10 percent of patients receiving IMBRUVICA in Studies 1, 2, 3 and 4 discontinued treatment due to adverse reactions. These included pneumonia, hemorrhage, atrial fibrillation, rash and neutropenia (1% each). Adverse reactions leading to dose reduction occurred in approximately 6% of patients.

Study 1: Adverse reactions and laboratory abnormalities from the CLL/SLL trial (N=51) using single agent IMBRUVICA 420 mg daily in patients with previously treated CLL/SLL occurring at a rate of ≥ 10% with a median duration of treatment of 15.6 months are presented in Tables 3 and 4.

Table 3: Non-Hematologic Adverse Reactions in ≥ 10% of Patients with CLL/SLL (N=51) in Study 1

Body System	Adverse Reaction	All Grades (%)	Grade 3 or 4 (%)
Gastrointestinal disorders	Diarrhea	59	4
	Constipation	22	2
	Nausea	20	2
	Stomatitis	20	0
	Vomiting	18	2
	Abdominal pain	14	0
	Dyspepsia	12	0
Infections and infestations	Upper respiratory tract infection	47	2
	Sinusitis	22	6
	Skin infection	16	6
	Pneumonia	12	10
	Urinary tract infection	12	2
General disorders and administration site conditions	Fatigue	33	6
	Pyrexia	24	2
	Peripheral edema	22	0
	Asthenia	14	6
	Chills	12	0
Skin and subcutaneous tissue disorders	Bruising	51	2
	Rash	25	0
	Petechiae	16	0
Respiratory, thoracic and mediastinal disorders	Cough	22	0
	Oropharyngeal pain	14	0
	Dyspnea	12	0
Musculoskeletal and connective tissue disorders	Musculoskeletal pain	25	6
	Arthralgia	24	0
	Muscle spasms	18	2
Nervous system disorders	Dizziness	20	0
	Headache	18	2

Table 3: Non-Hematologic Adverse Reactions in ≥ 10% of Patients with CLL/SLL (N=51) in Study 1 (continued)

Body System	Adverse Reaction	All Grades (%)	Grade 3 or 4 (%)
Metabolism and nutrition disorders	Decreased appetite	16	2
Neoplasms benign, malignant, unspecified	Second malignancies*	12*	0
Vascular disorders	Hypertension	16	8

* One patient death due to histiocytic sarcoma.

Table 4: Treatment-Emergent* Decrease of Hemoglobin, Platelets, or Neutrophils in Patients with CLL/SLL (N=51) in Study 1

	Percent of Patients (N=51)	
	All Grades (%)	Grade 3 or 4 (%)
Platelets Decreased	69	12
Neutrophils Decreased	53	26
Hemoglobin Decreased	43	0

* Based on laboratory measurements per IWCLL criteria and adverse reactions.

Study 2: Adverse reactions and laboratory abnormalities described below in Tables 5 and 6 reflect exposure to IMBRUVICA with a median duration of 8.6 months and exposure to ofatumumab with a median of 5.3 months in Study 2 in patients with previously treated CLL/SLL.

Table 5: Adverse Reactions Reported in ≥ 10% of Patients and at Least 2% Greater in the IMBRUVICA Treated Arm in Patients in Study 2

Body System Adverse Reaction	IMBRUVICA (N=195)		Ofatumumab (N=191)	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Gastrointestinal disorders				
Diarrhea	48	4	18	2
Nausea	26	2	18	0
Stomatitis*	17	1	6	1
Constipation	15	0	9	0
Vomiting	14	0	6	1
General disorders and administration site conditions				
Pyrexia	24	2	15	1
Infections and infestations				
Upper respiratory tract infection	16	1	11	2
Pneumonia*	15	10	13	9
Sinusitis*	11	1	6	0
Urinary tract infection	10	4	5	1
Skin and subcutaneous tissue disorders				
Rash*	24	3	13	0
Petechiae	14	0	1	0
Bruising*	12	0	1	0
Musculoskeletal and connective tissue disorders				
Musculoskeletal Pain*	28	2	18	1
Arthralgia	17	1	7	0
Nervous system disorders				
Headache	14	1	6	0
Dizziness	11	0	5	0
Injury, poisoning and procedural complications				
Contusion	11	0	3	0
Eye disorders				
Vision blurred	10	0	3	0

Subjects with multiple events for a given ADR term are counted once only for each ADR term.
The system organ class and individual ADR terms are sorted in descending frequency order in the IMBRUVICA arm.
* Includes multiple ADR terms

Table 6: Treatment-Emergent* Decrease of Hemoglobin, Platelets, or Neutrophils in Study 2

	IMBRUVICA (N=195)		Ofatumumab (N=191)	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Neutrophils Decreased	51	23	57	26
Platelets Decreased	52	5	45	10
Hemoglobin Decreased	36	0	21	0

* Based on laboratory measurements per IWCLL criteria.

Study 3: Adverse reactions described below in Table 7 reflect exposure to IMBRUVICA with a median duration of 17.4 months. The median exposure to chlorambucil was 7.1 months in Study 3.

IMBRUVICA® (ibrutinib) capsules

Table 7: Adverse Reactions Reported in ≥ 10% of Patients and at Least 2% Greater in the IMBRUVICA Treated Arm in Patients in Study 3

Body System Adverse Reaction	IMBRUVICA (N=135)		Chlorambucil (N=132)	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Gastrointestinal disorders				
Diarrhea	42	4	17	0
Stomatitis*	14	1	4	1
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain*	36	4	20	0
Arthralgia	16	1	7	1
Muscle spasms	11	0	5	0
Eye Disorders				
Dry eye	17	0	5	0
Lacrimation increased	13	0	6	0
Vision blurred	13	0	8	0
Visual acuity reduced	11	0	2	0
Skin and subcutaneous tissue disorders				
Rash*	21	4	12	2
Bruising*	19	0	7	0
Infections and infestations				
Skin infection*	15	2	3	1
Pneumonia*	14	8	7	4
Urinary tract infections	10	1	8	1
Respiratory, thoracic and mediastinal disorders				
Cough	22	0	15	0
General disorders and administration site conditions				
Peripheral edema	19	1	9	0
Pyrexia	17	0	14	2
Vascular Disorders				
Hypertension*	14	4	1	0
Nervous System Disorders				
Headache	12	1	10	2

Subjects with multiple events for a given ADR term are counted once only for each ADR term.
The system organ class and individual ADR terms are sorted in descending frequency order in the IMBRUVICA arm.
* Includes multiple ADR terms

Study 4: Adverse reactions described below in Table 8 reflect exposure to IMBRUVICA + BR with a median duration of 14.7 months and exposure to placebo + BR with a median of 12.8 months in Study 4 in patients with previously treated CLL/SLL.

Table 8: Adverse Reactions Reported in at Least 10% of Patients and at Least 2% Greater in the IMBRUVICA Arm in Patients in Study 4

Body System Adverse Reaction	Ibrutinib + BR (N=287)		Placebo + BR (N=287)	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Blood and lymphatic system disorders				
Neutropenia*	66	61	60	55
Thrombocytopenia*	34	16	26	16
Skin and subcutaneous tissue disorders				
Rash*	32	4	25	1
Bruising*	20	<1	8	<1
Gastrointestinal disorders				
Diarrhea	36	2	23	1
Abdominal Pain	12	1	8	<1
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain*	29	2	20	0
Muscle spasms	12	<1	5	0
General disorders and administration site conditions				
Pyrexia	25	4	22	2
Vascular Disorders				
Hemorrhage*	19	2	9	1
Hypertension*	11	5	5	2
Infections and infestations				
Bronchitis	13	2	10	3
Skin infection*	10	3	6	2
Metabolism and nutrition disorders				
Hyperuricemia	10	2	6	0

The system organ class and individual ADR terms are sorted in descending frequency order in the IMBRUVICA arm.
* Includes multiple ADR terms
<1 used for frequency above 0 and below 0.5%

Atrial fibrillation of any grade occurred in 7% of patients treated with IMBRUVICA + BR and 2% of patients treated with placebo + BR. The frequency of Grade 3 and 4 atrial fibrillation was 3% in patients treated with IMBRUVICA + BR and 1% in patients treated with placebo + BR.

Waldenström's Macroglobulinemia: The data described below reflect exposure to IMBRUVICA in an open-label clinical trial that included 63 patients with previously treated WM.

The most commonly occurring adverse reactions in the WM trial (≥ 20%) were neutropenia, thrombocytopenia, diarrhea, rash, nausea, muscle spasms, and fatigue.

Six percent of patients receiving IMBRUVICA in the WM trial discontinued treatment due to adverse events. Adverse events leading to dose reduction occurred in 11% of patients.

Adverse reactions and laboratory abnormalities described below in Tables 9 and 10 reflect exposure to IMBRUVICA with a median duration of 11.7 months in the WM trial.

Table 9: Non-Hematologic Adverse Reactions in ≥ 10% of Patients with Waldenström's Macroglobulinemia (N=63)

Body System	Adverse Reaction	All Grades (%)	Grade 3 or 4 (%)
Gastrointestinal disorders	Diarrhea	37	0
	Nausea	21	0
	Stomatitis*	16	0
	Gastroesophageal reflux disease	13	0
Skin and subcutaneous tissue disorders	Rash*	22	0
	Bruising*	16	0
	Pruritus	11	0
General disorders and administrative site conditions	Fatigue	21	0
Musculoskeletal and connective tissue disorders	Muscle spasms	21	0
	Arthropathy	13	0
Infections and infestations	Upper respiratory tract infection	19	0
	Sinusitis	19	0
	Pneumonia*	14	6
	Skin infection*	14	2
Respiratory, thoracic and mediastinal disorders	Epistaxis	19	0
	Cough	13	0
Nervous system disorders	Dizziness	14	0
	Headache	13	0
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	Skin cancer*	11	0

The system organ class and individual ADR preferred terms are sorted in descending frequency order.
* Includes multiple ADR terms.

Table 10: Treatment-Emergent* Decrease of Hemoglobin, Platelets, or Neutrophils in Patients with WM (N=63)

	Percent of Patients (N=63)	
	All Grades (%)	Grade 3 or 4 (%)
Platelets Decreased	43	13
Neutrophils Decreased	44	19
Hemoglobin Decreased	13	8

* Based on laboratory measurements.

Additional Important Adverse Reactions: *Diarrhea:* Diarrhea of any grade occurred at a rate of 43% (range, 36% to 63%) of patients treated with IMBRUVICA. Grade 2 diarrhea occurred in 9% (range, 3% to 15%) and Grade 3 in 3% (range, 0 to 5%) of patients treated with IMBRUVICA. The median time to first onset of any grade diarrhea was 12 days (range, 0 to 627), of Grade 2 was 37 days (range, 1 to 667) and of Grade 3 was 71 days (range, 3 to 627). Of the patients who reported diarrhea, 83% had complete resolution, 1% had partial improvement and 16% had no reported improvement at time of analysis. The median time from onset to resolution or improvement of any grade diarrhea was 5 days (range, 1 to 418), and was similar for Grades 2 and 3. Less than 1% of patients discontinued IMBRUVICA due to diarrhea.

Visual Disturbance: Blurred vision and decreased visual acuity of any grade occurred in 10% of patients treated with IMBRUVICA (9% Grade 1, 2% Grade 2). The median time to first onset was 88 days (range, 1 to 414 days). Of the patients with visual disturbance, 64% had complete resolution and 36% had no reported improvement at time of analysis. The median time from onset to resolution or improvement was 29 days (range, 1 to 281 days).

Postmarketing Experience: The following adverse reactions have been identified during post-approval use of IMBRUVICA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Hepatobiliary disorders: hepatic failure (includes multiple terms)

Respiratory disorders: interstitial lung disease (includes multiple terms)

Metabolic and nutrition disorders: tumor lysis syndrome *[see Warnings & Precautions]*

Skin and subcutaneous tissue disorders: anaphylactic shock, angioedema, urticaria

DRUG INTERACTIONS

CYP3A Inhibitors: Ibrutinib is primarily metabolized by cytochrome P450 enzyme 3A (CYP3A). In healthy volunteers, co-administration of ketoconazole, a strong CYP3A inhibitor, increased C_{max} and AUC of ibrutinib by 29- and 24-fold, respectively. The highest ibrutinib dose evaluated in clinical trials was 12.5 mg/kg (actual doses of 840 – 1400 mg) given for 28 days with single dose AUC values of 1445 ± 869 ng • hr/mL which is approximately 50% greater than steady state exposures seen at the highest indicated dose (560 mg).

Avoid concomitant administration of IMBRUVICA with strong or moderate inhibitors of CYP3A. For strong CYP3A inhibitors used short-term (e.g., antifungals and antibiotics for 7 days or less, e.g., ketoconazole, itraconazole, voriconazole, posaconazole, clarithromycin, telithromycin) consider interrupting IMBRUVICA therapy during the duration of inhibitor use. Avoid strong CYP3A inhibitors that are needed chronically. If a moderate CYP3A inhibitor must be used, reduce the IMBRUVICA dose. Patients taking concomitant strong or moderate CYP3A4 inhibitors should be monitored more closely for signs of IMBRUVICA toxicity *[see Dosage and Administration (2.4) in Full Prescribing Information].*

Avoid grapefruit and Seville oranges during IMBRUVICA treatment, as these contain moderate inhibitors of CYP3A *[see Dosage and Administration (2.4), and Clinical Pharmacology (12.3) in Full Prescribing Information].*

CYP3A Inducers: Administration of IMBRUVICA with rifampin, a strong CYP3A inducer, decreased ibrutinib C_{max} and AUC by approximately 13- and 10-fold, respectively.

Avoid concomitant use of strong CYP3A inducers (e.g., carbamazepine, rifampin, phenytoin, and St. John's Wort). Consider alternative agents with less CYP3A induction *[see Clinical Pharmacology (12.3) in Full Prescribing Information].*

USE IN SPECIFIC POPULATIONS

Pregnancy: *Risk Summary:* IMBRUVICA, a kinase inhibitor, can cause fetal harm based on findings from animal studies. In animal reproduction studies, administration of ibrutinib to pregnant rats and rabbits during the period of organogenesis at exposures up to 2-20 times the clinical doses of 420-560 mg daily produced embryofetal toxicity including malformations *[see Data].* If IMBRUVICA is used during pregnancy or if the patient becomes pregnant while taking IMBRUVICA, the patient should be apprised of the potential hazard to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Animal Data: Ibrutinib was administered orally to pregnant rats during the period of organogenesis at doses of 10, 40 and 80 mg/kg/day. Ibrutinib at a dose of 80 mg/kg/day was associated with visceral malformations (heart and major vessels) and increased resorptions and post-implantation loss. The dose of 80 mg/kg/day in rats is approximately 14 times the exposure (AUC) in patients with MCL and 20 times the exposure in patients with CLL/SLL or WM administered the dose of 560 mg daily and 420 mg daily, respectively. Ibrutinib at doses of 40 mg/kg/day or greater was associated with decreased fetal weights. The dose of 40 mg/kg/day in rats is approximately 6 times the exposure (AUC) in patients with MCL administered the dose of 560 mg daily.

Ibrutinib was also administered orally to pregnant rabbits during the period of organogenesis at doses of 5, 15, and 45 mg/kg/day. Ibrutinib at a dose of 15 mg/kg/day or greater was associated with skeletal variations (fused sternebrae) and ibrutinib at a dose of 45 mg/kg/day was associated with increased resorptions and post-implantation loss. The dose of 15 mg/kg/day in rabbits is approximately 2.0 times the exposure (AUC) in patients with MCL and 2.8 times the exposure in patients with CLL/SLL or WM administered the dose of 560 and 420 mg daily, respectively.

Lactation: *Risk Summary:* There is no information regarding the presence of ibrutinib or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production.

The development and health benefits of breastfeeding should be considered along with the mother's clinical need for IMBRUVICA and any potential adverse effects on the breastfed child from IMBRUVICA or from the underlying maternal condition.

Females and Males of Reproductive Potential: *Pregnancy Testing:* Verify the pregnancy status of females of reproductive potential prior to initiating IMBRUVICA therapy.

Contraception:

Females: Advise females of reproductive potential to avoid pregnancy while taking IMBRUVICA and for up to 1 month after ending treatment. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus.

Males: Advise men to avoid fathering a child while receiving IMBRUVICA, and for 1 month following the last dose of IMBRUVICA.

Pediatric Use: The safety and effectiveness of IMBRUVICA in pediatric patients has not been established.

Geriatric Use: Of the 839 patients in clinical studies of IMBRUVICA, 62% were ≥ 65 years of age, while 21% were ≥75 years of age. No overall differences in effectiveness were observed between younger and older patients. Grade 3 or higher pneumonia occurred more frequently among older patients treated with IMBRUVICA *[see Clinical Studies (14.2) in Full Prescribing Information].*

Hepatic Impairment: Ibrutinib is metabolized in the liver. In a hepatic impairment study, data showed an increase in ibrutinib exposure. Following single dose administration, the AUC of ibrutinib increased 2.7-, 8.2- and 9.8-fold in subjects with mild (Child-Pugh class A), moderate (Child-Pugh class B), and severe (Child-Pugh class C) hepatic impairment compared to subjects with normal liver function.

The safety of IMBRUVICA has not been evaluated in cancer patients with mild to severe hepatic impairment by Child-Pugh criteria.

Monitor patients for signs of IMBRUVICA toxicity and follow dose modification guidance as needed. It is not recommended to administer IMBRUVICA to patients with moderate or severe hepatic impairment (Child-Pugh class B and C) *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3) in Full Prescribing Information].*

Plasmapheresis: Management of hyperviscosity in WM patients may include plasmapheresis before and during treatment with IMBRUVICA. Modifications to IMBRUVICA dosing are not required.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

- *Hemorrhage:* Inform patients of the possibility of bleeding, and to report any signs or symptoms (severe headache, blood in stools or urine, prolonged or uncontrolled bleeding). Inform the patient that IMBRUVICA may need to be interrupted for medical or dental procedures *[see Warnings and Precautions].*
- *Infections:* Inform patients of the possibility of serious infection, and to report any signs or symptoms (fever, chills, weakness, confusion) suggestive of infection *[see Warnings and Precautions].*
- *Atrial fibrillation:* Counsel patients to report any signs of palpitations, lightheadedness, dizziness, fainting, shortness of breath, and chest discomfort *[see Warnings and Precautions].*
- *Hypertension:* Inform patients that high blood pressure has occurred in patients taking IMBRUVICA, which may require treatment with anti-hypertensive therapy *[see Warnings and Precautions].*
- *Second primary malignancies:* Inform patients that other malignancies have occurred in patients who have been treated with IMBRUVICA, including skin cancers and other carcinomas *[see Warnings and Precautions].*
- *Tumor lysis syndrome:* Inform patients of the potential risk of tumor lysis syndrome and report any signs and symptoms associated with this event to their healthcare provider for evaluation *[see Warnings and Precautions].*
- *Embryo-fetal toxicity:* Advise women of the potential hazard to a fetus and to avoid becoming pregnant during treatment and for 1 month after the last dose of IMBRUVICA *[see Warnings and Precautions].*
- Inform patients to take IMBRUVICA orally once daily according to their physician's instructions and that the capsules should be swallowed whole with a glass of water without being opened, broken, or chewed at approximately the same time each day *[see Dosage and Administration (2.1) in Full Prescribing Information].*
- Advise patients that in the event of a missed daily dose of IMBRUVICA, it should be taken as soon as possible on the same day with a return to the normal schedule the following day. Patients should not take extra capsules to make up the missed dose *[see Dosage and Administration (2.6) in Full Prescribing Information].*
- Advise patients of the common side effects associated with IMBRUVICA *[see Adverse Reactions].* Direct the patient to a complete list of adverse drug reactions in PATIENT INFORMATION.
- Advise patients to inform their health care providers of all concomitant medications, including prescription medicines, over-the-counter drugs, vitamins, and herbal products *[see Drug Interactions].*
- Advise patients that they may experience loose stools or diarrhea, and should contact their doctor if their diarrhea persists. Advise patients to maintain adequate hydration.

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POLICY

National Hospice and Palliative Care Organization

Palliative Care for Patients With Advanced Illness: A Changing Policy Landscape

Sharon Pearce

continued from cover

with new cancer diagnoses were Medicare beneficiaries, with that figure expected to rise over 10 years.[3] Additionally, $1 in every $12 of Medicare fee-for-service spending was spent on cancer care in 2015.[4]

With the demographic shift underway, policy makers, payers, and providers have been exploring models of care that can offer better quality, improve the overall patient experience, and also reduce costs. In the 6 years since passage of the landmark and controversial Affordable Care Act (ACA), a variety of new approaches have emerged with this goal in mind, and a significant change has been the integration of palliative care.

Palliative care is patient- and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. Unlike the Medicare hospice benefit—which is available only to individuals who have a terminal prognosis of 6 months or less to live and who agree to forego more conventional, aggressive therapies—palliative care is provided throughout the continuum of illness, irrespective of whether the patient has a terminal prognosis, and can be provided concurrent with care aimed at cure or disease modification.

Palliative care addresses the physical, intellectual, emotional, social, and spiritual needs in order to facilitate patient autonomy, access to information, and treatment choice. The following features characterize palliative care philosophy and delivery:

- Care is provided and services are coordinated by an interdisciplinary team (IDT) that includes, but is not limited to, physicians, advance practice nurses, social workers, and spiritual counselors/chaplains.
- Patients, families, and palliative and non-palliative healthcare providers collaborate and communicate about care needs, and patient family preferences are incorporated into the care.
- Services are available concurrent with, or independent of, curative or life-prolonging care.
- Patient and family hopes for peace and dignity are supported throughout the course of illness, during the dying process, and after death.

Need for an Interdisciplinary Team

An interdisciplinary palliative care team typically includes a physician, registered nurse, social worker, and pastoral or spiritual counselor. Other disciplines such as nutritionists, physical or occupational therapists, and home care aides may be added to the team depending on the patient's individual needs. Working with the patient, his or her family and caregivers, and in partnership with the patient's primary care and specialty care teams, the palliative IDT develops a plan of care to help the patient manage the side effects of treatment, minimize pain and symptoms, preserve existing function, and address the psychosocial and spiritual effects of advanced illness.

Among the diagnoses where palliative care is often involved, patients with cancer may greatly benefit from palliative care, as curative therapies such as surgery, chemotherapies, and radiation can create an even greater symptom burden in these patients than the underlying cancer. For example, nutritional counseling can help patients maintain their weight and minimize the loss of appetite associated with chemotherapy.

A 2016 study from the American Society of Clinical Oncology (ASCO) found that introducing palliative care shortly after a diagnosis of certain metastatic cancers greatly increases a patient's coping abilities, as well as overall quality of life. Researchers also found that early integration of palliative care results in an increase in discussions about patient EOL care preferences.[5]

Not only do these interventions improve patient comfort and quality of life, they can significantly reduce costs. A 2009 study found that patients receiving concurrent palliative and curative treatments were half as likely to visit the emergency department, and had hospitalizations and days in the intensive care unit at one-third the rate of the comparator population.[6]

PEARCE

Sharon Pearce is vice president for public policy, The National Hospice and Palliative Care Organization.

How Can Policy Changes Catch Up?

Despite the growing body of evidence supporting the integration of palliative care into treatment plans for individuals with advanced illness, public policy has lagged behind. Currently, most palliative services are delivered in an inpatient or hospital-based setting, and focus more on the medical/clinical elements of palliative care. Palliative medicine—in the form of consults from doctors, nurse practitioners, and some social workers—may be covered by the Medicare program; however, many important services, including spiritual counseling, caregiver support, and other essential services, must be financed separately, often through charitable giving. There are similar and even more sizeable policy and financial gaps when it comes to community based palliative care.

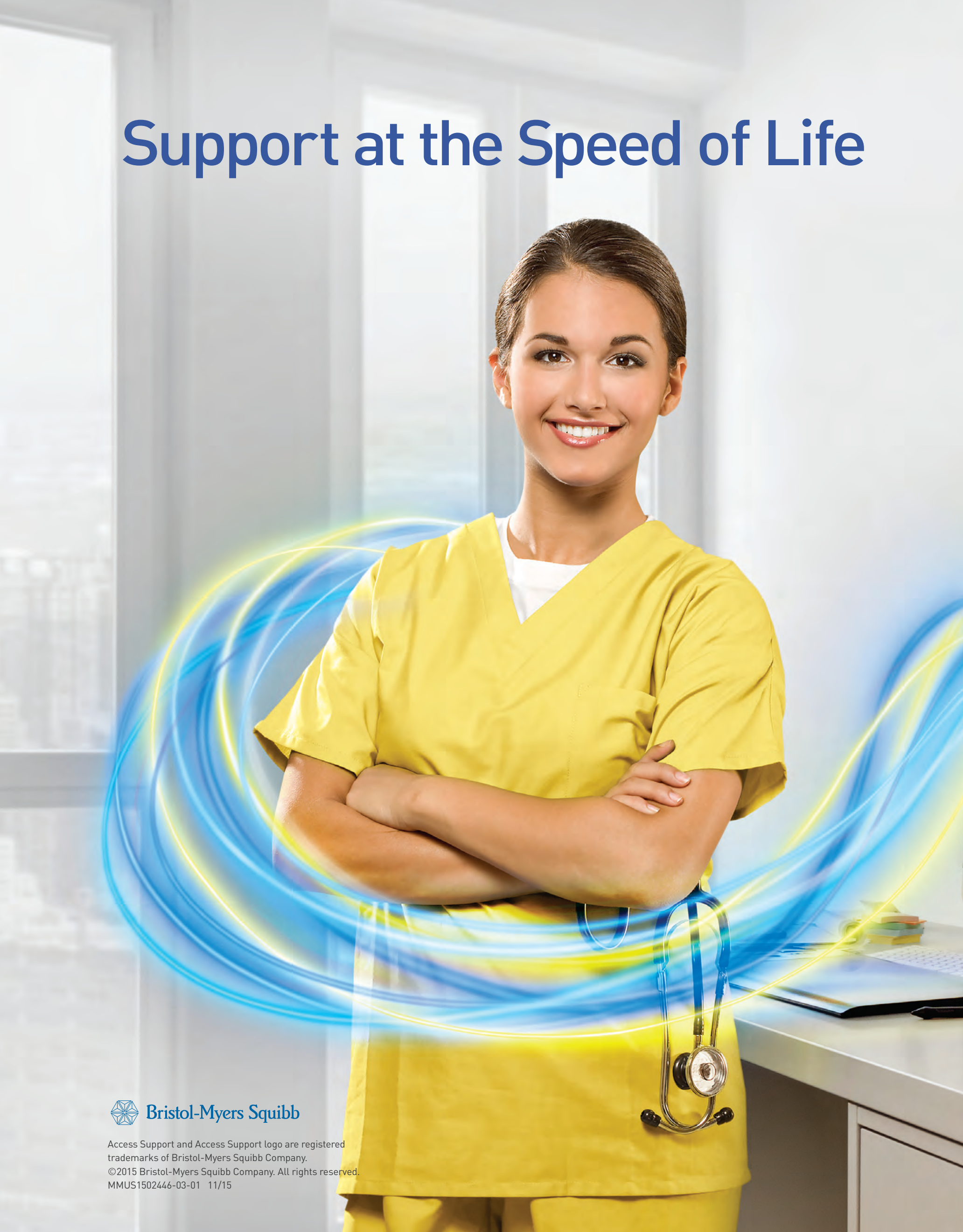
Although the National Consensus Project for Quality Palliative Care has laid out a clinical practice guidance,[7] there is no federal policy or regulatory framework. Accrediting bodies, such as the Joint Commission for the Accreditation of Healthcare Organizations and others, have adopted standards and quality measures for community based palliative care, but these are voluntary measures and not uniformly applied across programs. This results in significant variation across palliative care programs, and hinders access to consistent, standardized, and measurable palliative care services.

Policy progress has been further thwarted by the highly charged political climate of the day. When it was first raised during debate over the ACA, Medicare coverage for advance care planning services—a central component of palliative care—morphed into the infamous "death panel." Even as that rhetoric has died down in recent years, the rancorous political climate in Washington has inhibited the type of wholesale policy changes necessary for more widespread access to community based palliative care.

In lieu of sweeping policy changes, palliative care advocates have adopted a more incremental approach. Recent policy changes, primarily in the ACA, are allowing small-scale testing of community-based palliative care delivery, and for some innovations in other delivery systems. Other administrative changes are slowly

(continued on SP638)

Support at the Speed of Life



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(continued from SP635)

increasing access to Advance Care Planning. While many of these demonstrations are still playing out, some models, including the Medicare Care Choices Model (MCCM), accountable care organizations (ACOs), and the Independence at Home Demonstration, are showing early promise.

Medicare Care Choices Model

MCCM is one of the demonstration initiatives under the Centers for Medicare & Medicaid Innovation (CMMI) to allow patients, who are eligible but not enrolled in the Medicare hospice benefit, to receive supportive palliative care services while concurrently receiving "curative" or conventional care. The demonstration is limited to hospice providers as awardees and is intended to test whether these patients benefit from additional care coordination, enjoy a higher quality of life, experience fewer hospitalizations and other preventable health expenditures, and, if their health deteriorates, are able to transition to hospice in a more-timely fashion.

It is also limited to patients with advanced cancer, congestive heart failure, HIV, and chronic obstructive pulmonary disease. More than 141 hospices are participating in the demonstration, which began in January 2016.

While the demonstration is still in its early days, the initial response has been mixed. At first, eligibility criteria were so tightly managed that few patients were able to participate—a patient had to meet a total of 14 individual requirements before he or she could be enrolled. Noting the enrollment challenges in the first few months, CMMI modified the eligibility criteria in April 2016. While that modification allowed for some increased participation in the demonstration project, additional refinement is needed to further relax the eligibility requirements for enrollment. In addition, modifying the financial structure will be necessary to construct a more sustainable model.

Accountable Care Organizations and Independence at Home Demonstration

The ACA led to the creation of a variety of delivery and payment system reforms that are creating new challenges and opportunities for hospitals, health systems, health plans, and others. Hospital reimbursement is more at risk than ever before, placing greater emphasis on the ability to manage patient care and patient costs.

ACOs and the Independence at Home Demonstration are both models that, through a variety of approaches, encourage providers to collaborate on care delivery and to assume greater financial risk for their patient populations. Palliative care can help achieve those objectives, and hospice and palliative care organizations are increasingly aligning with these care models to provide concurrent palliative care for individuals with advanced illness, and to facilitate transition to hospice at the appropriate time. ACOs recognize the value in establishing or partnering with palliative care programs. In fact, over 70% of all ACO hospitals and 82% of ACO hospitals with 50 or more beds had active palliative care programs in 2015.[8]

Independence at Home is testing the effectiveness of in-home primary care services with the aim of improving care for Medicare beneficiaries with multiple chronic conditions. Fifteen sites, serving more than 10,000 beneficiaries, are currently participating in Independence at Home. In 2015, Independence at Home practices saved Medicare an average of $1010 per beneficiary across a 2-year demonstration period.[9] Some hospice and palliative care programs are coordinating with Independence at Home providers, both to subcontract for palliative care, as well as to coordinate with and transition to hospice when appropriate.

Medicare Access and CHIP Reauthorization Act

The Medicare Access and CHIP Reauthorization Act (MACRA) fundamentally changed the way that physicians are paid under Medicare. Specifically, MACRA repealed the troubled Sustainable Growth Rate formula and replaced it with a Quality Payment Program that emphasizes the overall value of care, rather than the volume of procedures provided, using 2 different approaches:

- The new Merit-based Incentive Payment System
- Adoption of alternative payment models (APMs)

Under MIPS, physicians are assessed and incentivized to offer care that emphasizes quality, minimizes ineffective resource utilization, integrates clinical practice improvements, and advances the use of information technology. APMs include ACOs and other payment models that shift additional risk onto providers.

Given the greater emphasis on value and the corresponding financial incentives, the MACRA payment reforms could allow for even more widespread access to palliative care.

Advance Care Planning

In its 2016 Physician Fee Schedule Final Rule, adopted in October 2015, CMS included 2 Current Procedural Terminology codes for advance care planning conversations. Under this change, any physician or nonphysician practitioner who bills Medicare Part B for their services can document and bill for conversations that cover patient goals of care, discussions of advance care planning, and help with understanding advance directives, which are a helpful tool for patients, their family caregivers, and the professionals caring for them during the course of a serious illness.[10]

While payment for these services is a good first step to promote broader, earlier discussion of EOL care, significant work must be done to ensure that patients can access comprehensive advance care planning services. A recent survey from the John A. Hartford Foundation found that physicians are largely unprepared to lead advance care planning discussions—only 14% of physicians have billed under the new codes, and only 29% felt they were appropriately trained to have discussions about EOL care.[11] Several pieces of legislation have been introduced to address these shortcomings and allow for more robust, effective advance care planning conversations.

Policy on the Horizon

In addition to the demonstrations and administrative actions already in place, several pieces of federal legislation have been introduced that would facilitate greater growth and availability of community based palliative care.

The Care Planning Act (S. 1549) was introduced by Senator Mark Warner (D-VA) and Senator Johnny Isakson (R-GA) to improve individual care planning and coordination of services for individuals facing advanced and terminal illness.[12] The legislation creates a Medicare benefit, called Planning Services, for those with serious or life-threatening illness, including team-based discussion of goals of care and values, explanation of disease progression, exploration of a relevant range of treatment options, and a documented care plan that reflects the individual's goals, values, and preferences. The bill would also direct CMMI to conduct an Advanced Illness Coordination Services demonstration, which will deliver wrap-around, home-based services to beneficiaries who need assistance with 2 or more progressive disease-related activities of daily living. This demonstration would build upon the MCCM already underway, and expand palliative care services to individuals who are poorly served by the current delivery system.

The legislation includes other provisions to support quality measurement; increase awareness of care planning; provide information about advance care planning, portable treatment orders, palliative care, hospice, and planning services, and other activities.

In the US House of Representatives, Congressman Earl Blumenauer (D-OR) and Congressman Phil Roe (R-TN) introduced

the Personalize Your Care Act (H.R. 5555).[13] Similar to the Care Planning Act, the Personalize Your Care Act would establish a new Medicare model that allows individuals receiving conventional therapies to receive concurrent care choices such as hospice care, a functional assessment of the individual, in-home services and supports, 24/7 emergency support, and other palliative care services. H.R. 5555 also provides grants to establish or expand Physician Orders for Life Sustaining Treatment (POLST programs) and would require that certified electronic health records display current advance directives and physician orders for life sustaining treatment. Other provisions would require for portability of advance directives, public education and awareness for advance care planning, and training for clinicians.

Palliative Care Training and Education

Even if the policy landscape allowed for more widespread access to palliative care, significant workforce shortages continue to inhibit the growth and availability of these much needed services. Hospice and palliative care professionals require a multi-dimensional set of skills, attitudes, and competencies, including the ability to manage the myriad symptoms associated with advanced and comorbid illnesses; the ability to facilitate communication and problem solving between patients, their families, and their care teams; and the ability to coordinate and provide team-based care across a range of settings.

A 2010 study published in the *Journal of Pain and Symptom Management* found a significant shortage in the number of adequately trained hospice and palliative care physicians and recommended additional 6000-18,000 physicians to meet existing hospice and palliative care needs.[14] In the 6 years that have followed, that need has likely increased significantly. Further, palliative and EOL care must be better integrated into other specialties. About 65% of those responding to an ASCO survey felt that they had received inadequate education in controlling symptoms associated with cancer, and 81% felt they had inadequate mentoring in discussing a poor prognosis with their patients and families.[15]

The Palliative Care and Hospice Education and Training Act[16] (H.R. 3119/S. 2748) would address these gaps by supporting programs that provide clinical palliative medicine training in a variety of settings, including hospice, and developing specific measures to evaluate the competency of trainees. The Palliative Medicine and Hospice Academic Career Award program will enable hospice and palliative physicians to train members of interdisciplinary teams of healthcare professionals in palliative and hospice care techniques.

Where to Next?

As this article goes to press, Donald J. Trump has been elected President of the United States. Given his campaign's emphasis on repealing and replacing the ACA, the future of many of these initiatives is unclear. Congressional Republicans are beginning to outline how they would go about repealing the law, and how they would replace it, but narrow Republican margins in the Senate will likely complicate wholesale repeal. Further, many of these initiatives —including the Independence at Home program and value-based purchasing under MACRA—enjoy bipartisan support, so work in these areas will most certainly continue.

As this new policy environment unfolds, the National Hospice and Palliative Care Organization, along with other hospice and palliative care organizations, will endorse policies that promote and protect the Medicare hospice benefit, and will support policies that allow hospice and palliative care providers to innovate and refine patient care services and ensure that all patients with advanced and terminal illness have access to the pain and symptom relief, psychosocial services and support, and spiritual care that they need. ◆

DISCLOSURE

The National Hospice and Palliative Care Organization is the largest nonprofit membership organization representing hospice and palliative care programs and professionals in the United States. Founded in 1978 as the National Hospice Organization, the organization changed its name in February 2000 to include palliative care, recognizing that hospice care and palliative care share the same core values and philosophies.

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REFERENCES

1. The demographics of aging. Transgenerational Design Matters website. http://transgenerational.org/aging/demographics.htm. Accessed October 24, 2016.
2. Neuman T, Cubanski J, Huang J, Damico A. The rising cost of living longer: analysis of Medicare spending by age for beneficiaries in traditional Medicare." Kaiser Family Foundation website. http://kff.org/medicare/report/the-rising-cost-of-living-longer-analysis-of-medicare-spending-by-age-for-beneficiaries-in-traditional-medicare/. Published January 14, 2015. Accessed October 24, 2016.
3. Stockdale H, Guillory K; American Cancer Society Cancer Action Network. Lifeline: Why cancer patients depend on Medicare for critical coverage. CMS website. https://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2016-Fact-sheets-items/2016-08-09.html. Published 2013. Accessed October 24, 2016.
4. Maroongroge S, Kim SP, Mougalian S, et al. The cost of cancer-related physician services to Medicare. *Yale J Biol Med.* 2015;88(2):107-114.
5. Greer JA, El-Jawahri A, Pirl, WF, et al. Randomized trial of early integrated palliative and oncology care. *J Clin Oncol.* 2016;34(suppl; abstract 10003).
6. Spettel CM, Rawlins WS, Krakauer R, et al. A comprehensive case management program to improve palliative care. *J Palliat Med.* 2009;12(9):827-832. doi: 10.1089/jpm.2009.0089.
7. National Consensus Project for Quality Palliative Care. Clinical practice guidelines for quality palliative care. HPNA website. https://www.hpna.org/multimedia/NCP_Clinical_Practice_Guidelines_3rd_Edition.pdf. Published 2013. Accessed November 1, 2016.
8. Kelley AS, Meier DE. The role of palliative care in accountable care organizations. *Am J Manag Care.* 2015;21(6);(suppl):S212-S214.
9. Independence at Home Demonstration performance year 2 results [press release]. Baltimore, MD: CMS; August 9, 2016. https://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2016-Fact-sheets-items/2016-08-09.html. Accessed October 24, 2016.
10. Center for Medicare and Medicaid Services. Medicare program; revisions to payment policies under the Physician Fee Schedule and other revisions to Part B for CY 2016. CMS website http://www.federalregister.gov/documents/2015/11/16/2015-28005/medicare-program-revisions-to-payment-policies-under-the-physician-fee-schedule-and-other-revisions. Published November 16, 2015. Accessed November 1, 2016.
11. Conversation stopper: what's preventing physicians from talking with patients about end-of-life and advance care planning? John A. Hartford Foundation website. http://johnahartford.org/newsroom/view/advance-care-planning-poll. Published April 7, 2016. Accessed November 1, 2016.
12. S. 1549 - Care Planning Act of 2015. Congress.gov website. https://www.congress.gov/bill/114th-congress/senate-bill/1549. Published June 10, 2015. Accessed November 1, 2016.
13. H.R. 5555 - Personalize Your Care Act 2.0. Congress.gov website. https://www.congress.gov/bill/114th-congress/house-bill/5555. Published June 22, 2016. Accessed November 1, 2016.
14. Lupu D; American Academy of Hospice and Palliative Medicine Workforce Task Force. Estimate of current hospice and palliative medicine physician workforce shortage. *J Pain Symptom Manage.* 2010;40(6):899-911. doi: 10.1016/j.jpainsymman.2010.07.004.
15. Ferris FD, Bruera E, Cherny N, et al. Palliative cancer care a decade later: accomplishments, the need, next steps—from the American Society of Clinical Oncology. *J Clin Oncol.* 2009;27(8):3052-3058. doi: 10.1200/jco.2008.20.1558.
16. H.R. 3119 - Palliative Care and Hospice Education and Training Act. https://www.congress.gov/bill/114th-congress/house-bill/3119. Published July 21, 2015 and April 5, 2016. Accessed November 1, 2016.

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