Bridging the gap between payer and provider perspectives

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Evidence-Based Oncology

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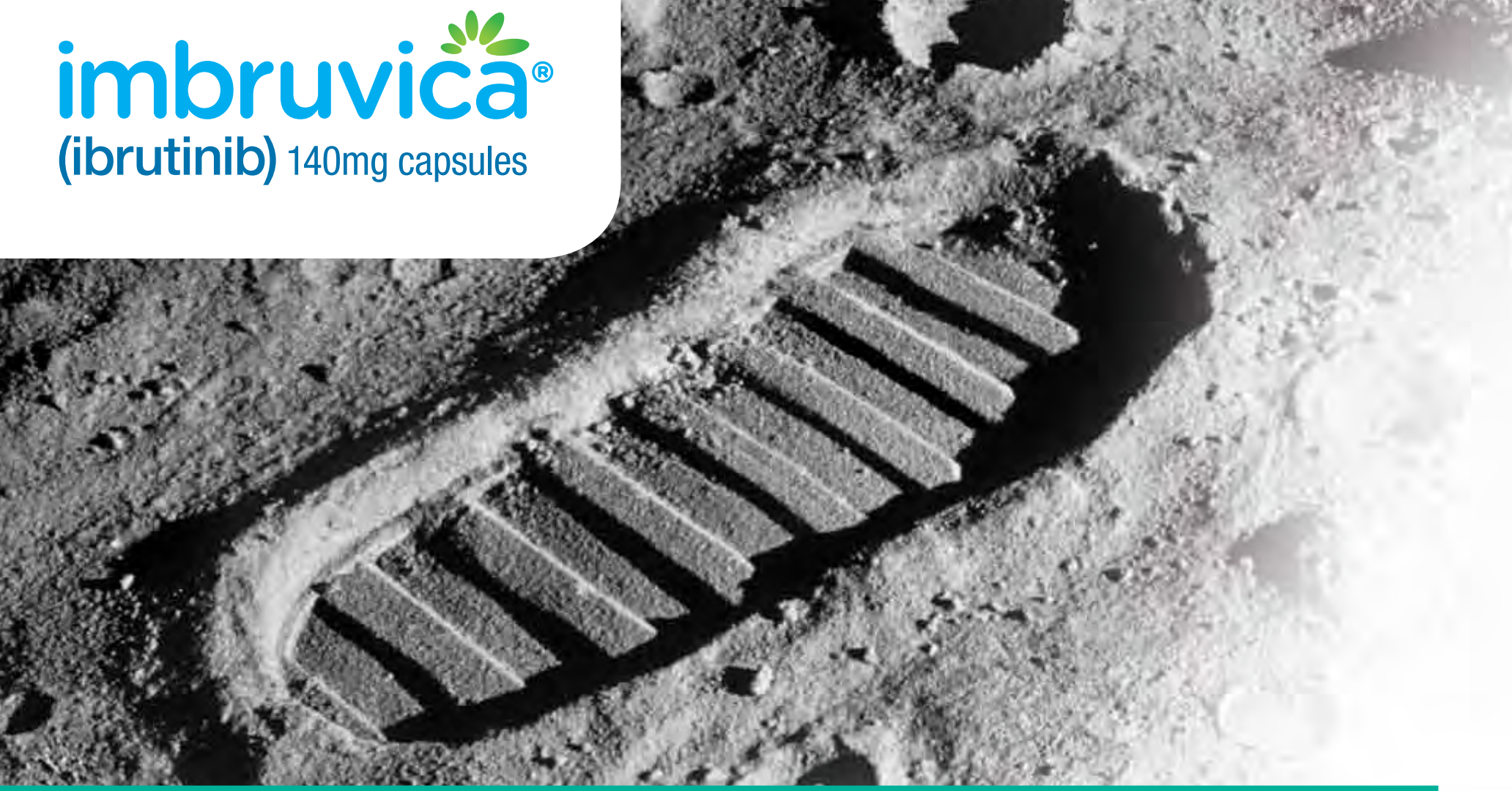
Highlights From Patient-Centered Oncology Care 2014

EXCLUSIVE CONFERENCE COVERAGE

Highlights Include:

- ASCO President Discusses Changing Value Proposition in Cancer Care
- Priority Health's VanderLaan on How ACA Is Changing Oncology Practice
- Payers Seek Cancer Quality Measures That Matter to Patients
- Oncology Medical Homes Deliver What Stakeholders Want
- As Cancer Patients Live Longer, Payers Shift to Survivorship Care
- The Rise of Molecular Diagnostics, and Challenges in Reimbursement

imbruvica®
(ibrutinib) 140mg capsules



DISCOVERING HOW FAR THERAPY CAN GO

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage - Fatal bleeding events have occurred in patients treated with IMBRUVICA®. Grade 3 or higher bleeding events (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. 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.

Infections - Fatal and non-fatal infections have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 14% to 26% of patients. Cases of progressive multifocal leukoencephalopathy (PML) have occurred in patients treated with IMBRUVICA®. Monitor patients for fever and infections and evaluate promptly.

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%) occurred in patients treated with 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, 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. If atrial fibrillation persists, consider the risks and benefits of IMBRUVICA® treatment and dose modification.

Second Primary Malignancies - Other malignancies (range, 5 to 14%) including non-skin carcinomas (range, 1 to 3%) have occurred in patients treated with IMBRUVICA®. The most frequent second primary malignancy was non-melanoma skin cancer (range, 4 to 11%).

IMBRUVICA® (ibrutinib) is the first and only FDA-approved therapy for use in patients with Waldenström's macroglobulinemia (WM)

IMBRUVICA® is approved for use in 4 indications

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.

Chronic lymphocytic leukemia (CLL) who have received at least one prior therapy.

Chronic lymphocytic leukemia with 17p deletion.

Waldenström's macroglobulinemia (WM).

Tumor Lysis Syndrome - Tumor lysis syndrome has been reported with IMBRUVICA® therapy. Monitor patients closely and take appropriate precautions in patients at risk for tumor lysis syndrome (e.g. high tumor burden).

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®. 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.

ADVERSE REACTIONS

The most common adverse reactions (≥25%) in patients with B-cell malignancies (MCL, CLL, WM) were thrombocytopenia, neutropenia, diarrhea, anemia, fatigue, musculoskeletal pain, bruising, nausea, upper respiratory tract infection, and rash. Seven percent of patients receiving IMBRUVICA® discontinued treatment due to adverse events.

DRUG INTERACTIONS

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

CYP3A Inducers - Avoid co-administration 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 review the Brief Summary of full Prescribing Information on the following page.

To learn more, visit
www.IMBRUVICA.com

1/15 PRC-00811

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Brief Summary of Prescribing Information for IMBRUVICA® (ibrutinib)

IMBRUVICA® (ibrutinib) capsules, for oral use

See package insert for Full Prescribing Information

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: IMBRUVICA is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy *[see Clinical Studies (14.2) in Full Prescribing Information].*

Chronic Lymphocytic Leukemia with 17p deletion: IMBRUVICA is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL) 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 (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.

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 26% of patients. *[See Adverse Reactions].* Cases of progressive multifocal leukoencephalopathy (PML) have occurred in patients treated with IMBRUVICA. Monitor patients for fever and infections and evaluate promptly.

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%) occurred in patients treated with 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, 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. If atrial fibrillation persists, consider the risks and benefits of IMBRUVICA treatment and dose modification *[see Dosage and Administration (2.3) in Full Prescribing Information].*

Second Primary Malignancies: Other malignancies (range, 5 to 14%) including non-skin carcinomas (range, 1 to 3%) have occurred in patients treated with IMBRUVICA. The most frequent second primary malignancy was non-melanoma skin cancer (range, 4 to 11 %).

Tumor Lysis Syndrome: Tumor lysis syndrome has been reported with IMBRUVICA therapy. Monitor patients closely and take appropriate precautions in patients at risk for tumor lysis syndrome (e.g. high tumor burden).

Embryo-Fetal Toxicity: Based on findings in animals, IMBRUVICA can cause fetal harm when administered to a pregnant woman. Ibrutinib caused malformations in rats at exposures 14 times those reported in patients with MCL and 20 times those reported in patients with CLL or WM, receiving the ibrutinib dose of 560 mg per day and 420 mg per day, respectively. Reduced fetal weights were observed at lower exposures. Advise women to avoid becoming pregnant while taking IMBRUVICA. 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]*
- Second Primary Malignancies *[see Warnings and Precautions]*
- Tumor Lysis Syndrome *[see Warnings and Precautions]*

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.

Clinical Trials Experience: 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)

System Organ Class	Preferred Term	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
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 administrative site conditions	Fatigue	41	5
	Peripheral edema	35	3
	Pyrexia	18	1
	Asthenia	14	3

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

System Organ Class	Preferred Term	All Grades (%)	Grade 3 or 4 (%)
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: The data described below reflect exposure to IMBRUVICA in an open label clinical trial (Study 1) that included 48 patients with previously treated CLL and a randomized clinical trial (Study 2) that included 391 randomized patients with previously treated CLL or SLL.

The most commonly occurring adverse reactions in Study 1 and Study 2 (≥ 20%) were thrombocytopenia, neutropenia, diarrhea, anemia, fatigue, musculoskeletal pain, upper respiratory tract infection, rash, nausea, and pyrexia.

Approximately five percent of patients receiving IMBRUVICA in Study 1 and Study 2 discontinued treatment due to adverse events. These included infections, subdural hematomas and diarrhea. Adverse events leading to dose reduction occurred in approximately 6% of patients.

Study 1: Adverse reactions and laboratory abnormalities from the CLL trial (N=48) using single agent IMBRUVICA 420 mg daily occurring at a rate of ≥ 10% are presented in Tables 3 and 4.

Table 3: Non-Hematologic Adverse Reactions in ≥ 10% of Patients with CLL (N=48) in Study 1

System Organ Class	Preferred Term	All Grades (%)	Grade 3 or 4 (%)
Gastrointestinal disorders	Diarrhea	63	4
	Constipation	23	2
	Nausea	21	2
	Stomatitis	21	0
	Vomiting	19	2
	Abdominal pain	15	0
	Dyspepsia	13	0
Infections and infestations	Upper respiratory tract infection	48	2
	Sinusitis	21	6
	Skin infection	17	6
	Pneumonia	10	8
	Urinary tract infection	10	0
General disorders and administrative site conditions	Fatigue	31	4
	Pyrexia	25	2
	Peripheral edema	23	0
	Asthenia	13	4
	Chills	13	0
Skin and subcutaneous tissue disorders	Bruising	54	2
	Rash	27	0
	Petechiae	17	0
Respiratory, thoracic and mediastinal disorders	Cough	19	0
	Oropharyngeal pain	15	0
	Dyspnea	10	0
Musculoskeletal and connective tissue disorders	Musculoskeletal pain	27	6
	Arthralgia	23	0
	Muscle spasms	19	2
Nervous system disorders	Dizziness	21	0
	Headache	19	2
	Peripheral neuropathy	10	0
Metabolism and nutrition disorders	Decreased appetite	17	2
Neoplasms benign, malignant, unspecified	Second malignancies*	10*	0
Injury, poisoning and procedural complications	Laceration	10	2
Psychiatric disorders	Anxiety	10	0
	Insomnia	10	0
Vascular disorders	Hypertension	17	8

**One patient death due to histiocytic sarcoma.*

Table 4: Treatment-Emergent* Decrease of Hemoglobin, Platelets, or Neutrophils in Patients with CLL (N=48) in Study 1

	Percent of Patients (N=48)	
	All Grades (%)	Grade 3 or 4 (%)
Platelets Decreased	71	10
Neutrophils Decreased	54	27
Hemoglobin Decreased	44	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.

Table 5: Non-Hematologic Adverse Reactions ≥ 10% Reported in Study 2

System Organ Class ADR Term	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				
Fatigue	28	2	30	2
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

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 7 and 8 reflect exposure to IMBRUVICA with a median duration of 11.7 months in the WM trial.

Table 7: Non-Hematologic Adverse Reactions in ≥ 10% of Patients with Waldenström's Macroglobulinemia (N=63)

System Organ Class	Preferred Term	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

IMBRUVICA® (ibrutinib) capsules

Table 7: Non-Hematologic Adverse Reactions in ≥ 10% of Patients with Waldenström's Macroglobulinemia (N=63) (continued)

System Organ Class	Preferred Term	All Grades (%)	Grade 3 or 4 (%)
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 terms are sorted in descending frequency order.
* Includes multiple ADR terms.

Table 8: 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.

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.
Hypersensitivity reactions including anaphylactic shock (fatal), urticaria, and angioedema have been reported.

DRUG INTERACTIONS

Ibrutinib is primarily metabolized by cytochrome P450 enzyme 3A.

CYP3A Inhibitors: 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: Pregnancy Category D *[see Warnings and Precautions].*

Risk Summary: Based on findings in animals, IMBRUVICA can cause fetal harm when administered to a pregnant woman. 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.

Animal Data: Ibrutinib was administered orally to pregnant rats during the period of organogenesis at oral 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 post-implantation loss. The dose of 80 mg/kg/day in animals is approximately 14 times the exposure (AUC) in patients with MCL and 20 times the exposure in patients with CLL 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 animals is approximately 6 times the exposure (AUC) in patients with MCL administered the dose of 560 mg daily.

Nursing Mothers: It is not known whether ibrutinib is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from IMBRUVICA, a decision should be made whether 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 IMBRUVICA in pediatric patients has not been established.

Geriatric Use: Of the 111 patients treated for MCL, 63% were 65 years of age or older. No overall differences in effectiveness were observed between these patients and younger patients. Cardiac adverse events (atrial fibrillation and hypertension), infections (pneumonia and cellulitis) and gastrointestinal events (diarrhea and dehydration) occurred more frequently among elderly patients.

Of the 391 patients randomized in Study 2, 61% were ≥ 65 years of age. No overall differences in effectiveness were observed between age groups. Grade 3 or higher adverse events occurred more frequently among elderly patients treated with IMBRUVICA (61% of patients age ≥ 65 versus 51% of younger patients) *[see Clinical Studies (14.2) in Full Prescribing Information].*

Of the 63 patients treated for WM, 59% were 65 years of age or older. No overall differences in effectiveness were observed between these patients and younger patients. Cardiac adverse events (atrial fibrillation and hypertension), and infections (pneumonia and urinary tract infection) occurred more frequently among elderly patients.

Renal Impairment: Less than 1% of ibrutinib is excreted renally. Ibrutinib exposure is not altered in patients with Creatinine clearance (CLcr) > 25 mL/min. There are no data in patients with severe renal impairment (CLcr < 25 mL/min) or patients on dialysis *[see Clinical Pharmacology (12.3) 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 patients with hepatic impairment.

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 classes B and C) *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3) in Full Prescribing Information].*

Females and Males of Reproductive Potential: Advise women to avoid becoming pregnant while taking IMBRUVICA because IMBRUVICA can cause fetal harm *[see Use in Specific Populations].*

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

PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information).

- *Hemorrhage:*
  Inform patients of the possibility of bleeding, and to report any signs or symptoms (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].*
- *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 *[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 (2.5) 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.

Active ingredient made in China.

Distributed and Marketed by:
Pharmacyclics, Inc.
Sunnyvale, CA USA 94085
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A Panel Discussion During the 3rd Annual Patient-Centered Oncology Care Meeting in Baltimore, MD

Our Best Meeting Yet, With More in Store for 2015

This issue offers a review of our meeting, "*Patient-Centered Oncology Care 2014*." By all accounts, our third installment was our best to date. Both presenters and attendees marveled at the perfect mix of payers, providers, technology experts, patient advocates, clinical leaders, and policy thought leaders who came together for 24 hours. A special thanks goes to our keynote speakers: Dr Peter P. Yu, president of the American Society of Clinical Oncology, who enlightened us with the challenges of rising costs in oncology, and Dr Burton VanderLaan of Priority Health, who offered insights into how the Affordable Care Act is changing the payer mix among health insurance consumers. We also thank our moderators, Dr Ira Klein of Aetna, and Dr Jan Berger, editor-in-chief of *The American Journal of Pharmacy Benefits*, for engaging our panelists and encouraging thought-provoking discussions. At our reception, we were honored to once again welcome Amy Berman, who graciously provided us with an update to her remarkable cancer journey.

IRA M. KLEIN, MD, MBA

JAN BERGER, MD, MJ

Each year, we strive to make our meeting truly "patient-centered," and this year our program met that test from start to finish. Our Thursday evening sessions explored the importance of palliative care, highlighting evidence that taking care of a cancer patient's emotional and spiritual well-being, and giving patients and families a complete picture of their options, not only *improves* quality of life but also *extends* it. On Friday, our speakers and panelists asked whether today's focus on accountability is measuring *what matters to patients*, or simply recording what is easy to quantify. The hard part, our experts agreed, will be developing measures that reward outstanding cancer care providers who deliver what patients want. Finally, our technology sessions covered everything from how a cell phone can help patients schedule appointments to how molecular diagnostic testing not only lets oncologists better tailor treatments, but also can uncover risk for the rest of the family. Feedback from our meeting was outstanding. We received high marks on our program, the speakers, the networking opportunities—and even the food. With that in mind, the team at *The American Journal of Managed Care* and our steering committee are planning Patient-Centered Oncology Care 2015. We're returning to the same venue in Baltimore, and you can already register at http://www.ajmc.com/meetings/pcoc15. As much as there is to read in this issue, it's not the same as joining us. If you haven't been to our meeting, 2015 is the time to start.

As always, we appreciate your readership. Please look for updates on our live meetings and our conference coverage at www.ajmc.com.

Sincerely,

Brian Haug
President, *The American Journal of Managed Care*

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.

GRANIX®
(TBO-FILGRASTIM)
Injection

Take a bite out of G-CSF acquisition costs

Based on wholesale acquisition cost (WAC) of all short-acting G-CSF products as of November 11, 2013. WAC represents published catalogue or list prices and may not represent actual transactional prices. Please contact your supplier for actual prices.

GRANIX® is an option in short-acting G-CSF therapy

- A 71% reduction in duration of severe neutropenia vs placebo (1.1 days vs 3.8 days, $p<0.0001$)[1]
  - Efficacy was evaluated in a multinational, multicenter, randomized, controlled, Phase III study of chemotherapy-naïve patients with high-risk breast cancer receiving doxorubicin (60 mg/m^2 IV bolus)/docetaxel (75 mg/m^2)[1]
- The safety of GRANIX was established in 3 Phase III trials, with 680 patients receiving chemotherapy for either breast cancer, lung cancer, or non-Hodgkin lymphoma (NHL)[1]
- Now offering a new presentation for self-administration

Indication

- GRANIX is a leukocyte growth factor indicated for reduction in the duration of severe neutropenia in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

Important Safety Information

- **Splenic rupture:** Splenic rupture, including fatal cases, can occur following the administration of human granulocyte colony-stimulating factors (hG-CSFs). Discontinue GRANIX and evaluate for an enlarged spleen or splenic rupture in patients who report upper abdominal or shoulder pain after receiving GRANIX.
- **Acute respiratory distress syndrome (ARDS):** ARDS can occur in patients receiving hG-CSFs. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving GRANIX, for ARDS. Discontinue GRANIX in patients with ARDS.
- **Allergic reactions:** Serious allergic reactions, including anaphylaxis, can occur in patients receiving hG-CSFs. Reactions can occur on initial exposure. Permanently discontinue GRANIX in patients with serious allergic reactions. Do not administer GRANIX to patients with a history of serious allergic reactions to filgrastim or pegfilgrastim.
- **Use in patients with sickle cell disease:** Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disease receiving hG-CSFs. Consider the potential risks and benefits prior to the administration of GRANIX in patients with sickle cell disease. Discontinue GRANIX in patients undergoing a sickle cell crisis.
- **Capillary leak syndrome (CLS):** CLS can occur in patients receiving hG-CSFs and is characterized by hypotension, hypoalbuminemia, edema and hemoconcentration. Episodes vary in frequency, severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of CLS should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care.
- **Potential for tumor growth stimulatory effects on malignant cells:** The granulocyte colony-stimulating factor (G-CSF) receptor, through which GRANIX acts, has been found on tumor cell lines. The possibility that GRANIX acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which GRANIX is not approved, cannot be excluded.
- **Most common treatment-emergent adverse reaction:** The most common treatment-emergent adverse reaction that occurred in patients treated with GRANIX at the recommended dose with an incidence of at least 1% or greater and two times more frequent than in the placebo group was bone pain.

Please see brief summary of Full Prescribing Information on adjacent page.

For more information, visit GRANIXhcp.com.

Reference: 1. GRANIX® (tbo-filgrastim) Injection Prescribing Information. North Wales, PA: Teva Pharmaceuticals; 2014.

TEVA Oncology

GRANIX®
(TBO-FILGRASTIM)
Injection

BRIEF SUMMARY OF PRESCRIBING INFORMATION FOR
GRANIX® (tbo-filgrastim) injection, for subcutaneous use
SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

GRANIX is indicated to reduce the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Splenic Rupture

Splenic rupture, including fatal cases, can occur following administration of human granulocyte colony-stimulating factors. In patients who report upper abdominal or shoulder pain after receiving GRANIX, discontinue GRANIX and evaluate for an enlarged spleen or splenic rupture.

5.2 Acute Respiratory Distress Syndrome (ARDS)

Acute respiratory distress syndrome (ARDS) can occur in patients receiving human granulocyte colony-stimulating factors. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving GRANIX, for ARDS. Discontinue GRANIX in patients with ARDS.

5.3 Allergic Reactions

Serious allergic reactions including anaphylaxis can occur in patients receiving human granulocyte colony-stimulating factors. Reactions can occur on initial exposure. The administration of antihistamines, steroids, bronchodilators, and/or epinephrine may reduce the severity of the reactions. Permanently discontinue GRANIX in patients with serious allergic reactions. Do not administer GRANIX to patients with a history of serious allergic reactions to filgrastim or pegfilgrastim.

5.4 Use in Patients with Sickle Cell Disease

Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disease receiving human granulocyte colony-stimulating factors. Consider the potential risks and benefits prior to the administration of human granulocyte colony-stimulating factors in patients with sickle cell disease. Discontinue GRANIX in patients undergoing a sickle cell crisis.

5.5 Capillary Leak Syndrome

Capillary leak syndrome (CLS) can occur in patients receiving human granulocyte colony-stimulating factors and is characterized by hypotension, hypoalbuminemia, edema and hemoconcentration. Episodes vary in frequency, severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of capillary leak syndrome should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care.

5.6 Potential for Tumor Growth Stimulatory Effects on Malignant Cells

The granulocyte colony-stimulating factor (G-CSF) receptor through which GRANIX acts has been found on tumor cell lines. The possibility that GRANIX acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which GRANIX is not approved, cannot be excluded.

6 ADVERSE REACTIONS

The following potential serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Splenic Rupture [*see Warnings and Precautions (5.1)*]
- Acute Respiratory Distress Syndrome [*see Warnings and Precautions (5.2)*]
- Serious Allergic Reactions [*see Warnings and Precautions (5.3)*]
- Use in Patients with Sickle Cell Disease [*see Warnings and Precautions (5.4)*]
- Capillary Leak Syndrome *[see Warnings and Precautions (5.5)]*
- Potential for Tumor Growth Stimulatory Effects on Malignant Cells [*see Warnings and Precautions (5.6)*]

The most common treatment-emergent adverse reaction that occurred at an incidence of at least 1% or greater in patients treated with GRANIX at the recommended dose and was numerically two times more frequent than in the placebo group was bone pain.

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 clinical practice.

GRANIX clinical trials safety data are based upon the results of three randomized clinical trials in patients receiving myeloablative chemotherapy for breast cancer (N=348), lung cancer (N=240) and non-Hodgkin's lymphoma (N=92). In the breast cancer study, 99% of patients were female, the median age was 50 years, and 86% of patients were Caucasian. In the lung cancer study, 80% of patients were male, the median age was 58 years, and 95% of patients were Caucasian. In the non-Hodgkin's lymphoma study, 52% of patients were male, the median age was 55 years, and 88% of patients were Caucasian. In all three studies a placebo (Cycle 1 of the breast cancer study only) or a non-US-approved filgrastim product were used as controls. Both GRANIX and the non-US-approved filgrastim product were administered at 5 mcg/kg subcutaneously once daily beginning one day after chemotherapy for at least five days and continued to a maximum of 14 days or until an ANC of ≥10,000 x 10^6/L after nadir was reached.

Bone pain was the most frequent treatment-emergent adverse reaction that occurred in at least 1% or greater in patients treated with GRANIX at the recommended dose and was numerically two times more frequent than in the placebo group. The overall incidence of bone pain in Cycle 1 of treatment was 3.4% (3.4% GRANIX, 1.4% placebo, 7.5% non-US-approved filgrastim product).

Leukocytosis

In clinical studies, leukocytosis (WBC counts > 100,000 x 10^6/L) was observed in less than 1% patients with non-myeloid malignancies receiving GRANIX. No complications attributable to leukocytosis were reported in clinical studies.

Additional Adverse Reactions

Other adverse reactions known to occur following administration of human granulocyte colony-stimulating factors include myalgia, headache, vomiting, Sweet's syndrome (acute febrile neutrophilic dermatosis), cutaneous vasculitis and thrombocytopenia.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The incidence of antibody development in patients receiving GRANIX has not been adequately determined.

7 DRUG INTERACTIONS

No formal drug interaction studies between GRANIX and other drugs have been performed.

Drugs which may potentiate the release of neutrophils, such as lithium, should be used with caution.

Increased hematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone imaging changes. This should be considered when interpreting bone-imaging results.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Risk Summary

There are no adequate and well-controlled studies of GRANIX in pregnant women. In animal reproduction studies, treatment of pregnant rabbits with tbo-filgrastim resulted in increased spontaneous abortion and fetal malformations at systemic exposures substantially higher than the human exposure. GRANIX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data

In an embryofetal developmental study, pregnant rabbits were administered subcutaneous doses of tbo-filgrastim during the period of organogenesis at 1, 10 and 100 mcg/kg/day. Increased abortions were evident in rabbits treated with tbo-filgrastim at 100 mcg/kg/day. This dose was maternally toxic as demonstrated by reduced body weight. Other embryofetal findings at this dose level consisted of post-implantation loss, decrease in mean live litter size and fetal weight, and fetal malformations such as malformed hindlimbs and cleft palate. The dose of 100 mcg/kg/day corresponds to a systemic exposure (AUC) of approximately 50-90 times the exposures observed in patients treated with the clinical tbo-filgrastim dose of 5 mcg/kg/day.

8.3 Nursing Mothers

It is not known whether tbo-filgrastim is secreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when GRANIX is administered to a nursing woman. Other recombinant G-CSF products are poorly secreted in breast milk and G-CSF is not orally absorbed by neonates.

8.4 Pediatric Use

The safety and effectiveness of GRANIX in pediatric patients have not been established.

8.5 Geriatric Use

Among 677 cancer patients enrolled in clinical trials of GRANIX, a total of 111 patients were 65 years of age and older. No overall differences in safety or effectiveness were observed between patients age 65 and older and younger patients.

8.6 Renal Impairment

The safety and efficacy of GRANIX have not been studied in patients with moderate or severe renal impairment. No dose adjustment is recommended for patients with mild renal impairment.

8.7 Hepatic Impairment

The safety and efficacy of GRANIX have not been studied in patients with hepatic impairment.

10 OVERDOSAGE

No case of overdose has been reported.

TEVA Oncology

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Teva Pharmaceuticals USA, Inc.
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Product of Israel

GRX-40502 December 2014

This brief summary is based on TBO-004 GRANIX full Prescribing Information.

PETER B. BACH, MD, MAPP

Director, Center for Health Policy and Outcomes
Memorial Sloan Kettering Cancer Center

Dr Bach's main research interests cover healthcare policy, particularly as it relates to Medicare, racial disparities in cancer care quality, and lung cancer epidemiology. His research examining quality of care for Medicare beneficiaries has demonstrated that blacks do not receive as high quality care as whites when diagnosed with lung cancer, and that the aptitude and resources of primary care physicians who primarily treat blacks are inferior compared with those of primary care physicians who primarily treat whites. In 2007, he was the senior author on a study demonstrating that care in Medicare is highly fragmented, with the average beneficiary seeing multiple primary care physicians and specialists. He is funded by grants from the National Institute of Aging, a contract from the National Cancer Institute, and philanthropic sources. He formerly served as a senior advisor to the administrator of CMS. He serves on several national committees, including the Institute of Medicine's National Cancer Policy Forum and the Committee on Performance Measurement of the National Committee on Quality Assurance. He chairs the Technical Expert Panel that is developing measures of cancer care quality for CMS. Along with publishing in the medical literature, Dr Bach's opinion pieces have appeared in numerous lay news outlets, including *The New York Times*, *The Wall Street Journal*, *Forbes Online*, and National Public Radio.

JAN BERGER, MD, MJ

President
Health Intelligence Partners

Dr Berger founded Health Intelligence Partners 6 years ago as a healthcare consultancy that blends more than 25 years of both business and clinical experience. Much of Dr Berger's focus is on consumer engagement and behavior change, and how both affect the decisions that consumers make and the actions they take. Prior to founding Health Intelligence Partners, Dr Berger served as senior vice president and chief clinical officer for CVS Caremark. During that time, she had executive management, P&L, operations, and strategy responsibilities. Before going to CVS Caremark, Dr Berger had 15 years' experience in healthcare administration within the health plan and academic arenas. She sits on the boards of Care Core National, Meals to Heal, The University of Arizona School of Pharmacy, RxAnte, and Midwest Business Group on Health. She also sits on numerous business and healthcare committees. Dr Berger is the author of the books *Leveraging Health* and *Thirteen Common Pitfalls in Consumer Engagement*, the editor-in-chief of *The American Journal of Pharmacy Benefits*, and a member of the editorial boards of a number of healthcare journals. Dr Berger holds a doctor of medicine degree, a master's degree in jurisprudence from Loyola University in Chicago, and a certificate in healthcare business administration from the University of South Florida. She also holds a black belt in Six Sigma. She is an assistant professor at Northwestern University School of Medicine in Chicago, Illinois.

AMY BERMAN, BS, RN

Senior Program Officer
The Hartford Foundation

Ms Berman is a senior program officer with the John A. Hartford Foundation. She heads the Foundation's development and dissemination of innovative, cost-effective models of care that improve health outcomes for older adults. Her work includes efforts to advance palliative care and reduce avoidable readmissions. She also works on collaborations with CMS, the Centers for Medicare and Medicaid Innovation, the Office of the National Coordinator for Health Information Technology (HIT), and the Administration for Community Living. Ms Berman openly shares her experiences living with Stage 4 breast cancer. She has presented to the Institute of Medicine and has authored numerous pieces about her healthcare choices, palliative care, and implications for patients, practice, and policy. Her piece in *Health Affairs*, "Living Life in My Own Way—And Dying That Way as Well," was among the journal's most read in 2012. Previously, Ms Berman served as nursing education initiatives director for the Hartford Institute for Geriatric Nursing at New York University College of Nursing. In that capacity, she developed resources and programs to improve the geriatric expertise of nursing educators and clinicians. Before NYU, she had spent 20 years working on quality improvement, HIT, and regulatory compliance issues. Ms Berman has received many honors for her advocacy for older adults and those facing serious illnesses. In 2012, the international honor society of nursing, Sigma Theta Tau, established the Amy J. Berman Geriatric Nurse Leadership Award, given at their biennial meeting. Her BS in nursing is from NYU College of Nursing, and her BS in healthcare administration is from the University of Massachusetts at Amherst.

MELISSA COHEN, JD, MPA

Health Insurance Specialist
Centers for Medicare & Medicaid Services

Ms Cohen is currently the project lead for the Pioneer ACO Model in the Seamless Care Models Group at the Center for Medicare and Medicaid Innovation (the Innovation Center), a component of CMS. After completing her law degree at Fordham University School of Law, Ms Cohen practiced medical malpractice defense law for 6 years at 2 litigation firms in Manhattan, most recently as a senior associate at Garson, DeCorato & Cohen, LLP, where she represented physicians as well as major metropolitan health systems in the New York City area. In 2011, she earned an MPA with a concentration in health policy from the Harvard Kennedy School of Government. At the CMS Innovation Center, Ms Cohen has been involved in the design and implementation of the Bundled Payments for Care Improvement Initiative, the Comprehensive ESRD Care Initiative, and the Pioneer Accountable Care Organization Initiative, and has other health initiatives under consideration or in development. Prior to CMS, she also worked with nonprofits seeking passage of health reform. Ms Cohen's undergraduate degree is from the University of Pennsylvania, where she was a University Scholar.

ELIZABETH (LIZ) DANIELSON, MHA

Director of Payer & Employer Initiatives
National Comprehensive Cancer Network

Ms Danielson is the director of payer and employer initiatives at National Comprehensive Cancer Network (NCCN). She is responsible for developing, maintaining, and expanding working relationships between NCCN and managed care organizations, employers, and other payer organizations nationwide. Her responsibilities include providing consulting services to employers, health plans, and other organizations related to product development, benefit design, and implementation. She is also responsible for the development and implementation of clinical training programs for payer case managers, medical directors, and related staff. From 1997 to 2008, Ms Danielson was director of cancer programs at OptumHealth, a UnitedHealth Group Company, responsible for developing, launching, and selling Cancer Resource Services, the first-ever cancer "centers of excellence" program, and was a key contributor in developing

and launching the Cancer Support Program, Optum's cancer case management program. Prior to that, she was administrative director of the Blood and Marrow Transplant Program at the University of Minnesota from 1990 to 1997. She earned a BA in sociology and an MHA from the University of Minnesota.

JESSICA DEMARTINO, PHD

Manager, Health Policy Programs
National Comprehensive Cancer Network

Dr DeMartino joined the National Comprehensive Cancer Network (NCCN) in 2008 as a policy fellow focused on understanding payers' use of the NCCN Guidelines and Compendium. After 2 years, she advanced to the role of manager of health policy programs. Dr DeMartino is responsible for developing and executing the NCCN Policy Summit series as well as the NCCN Patient Advocacy Summits. Past topics for summits have included comparative effectiveness research, biosimilars, molecular testing, quality measures, data needs, clinical trials, and healthcare reform. Dr DeMartino has published several white papers and articles on healthcare policy issues. She is responsible for any policy issues that arise that may require NCCN's attention and response. Prior to joining NCCN, Dr DeMartino earned a doctor of philosophy in organic chemistry at The Scripps Research Institute in La Jolla, California. She also received a bachelor of science in biochemistry from the University of Delaware.

STACIE B. DUSETZINA, PHD

Assistant Professor
University of North Carolina at Chapel Hill

Dr Dusetzina is a pharmacoepidemiologist and health services researcher by training and has expertise in the design and conduct of secondary database analyses. She is an assistant professor in the Division of Pharmaceutical Outcomes and Policy in the UNC Eshelman School of Pharmacy and is jointly appointed in the Department of Health Policy and Management in the UNC Gillings School of Global Public Health. Dr Dusetzina has worked extensively with large claims data sources, public use data files, and registry-linked claims databases. Her work to date has focused on estimating changes in the utilization and costs of medication in large secondary data sources and on assessing the quality of medication prescribing and use in US-based samples. Her research seeks to assess the role of health system policies and costs on prescription drug utilization and the subsequent health outcomes for patients, particularly among individuals with cancer.

BRUCE A. FEINBERG, DO

Vice President and Chief Medical Officer
Cardinal Health Specialty Solutions, Clinical Pathways

Dr Feinberg is a leading oncologist recognized for his expertise in oncology and the business of specialty healthcare. He serves as vice president and chief medical officer for the Clinical Pathways business of Cardinal Health Specialty Solutions. Clinical Pathways aims to control costs, improve the quality of care, and increase predictability—which are critical goals for payers and providers who drive the pathways process. Prior to joining the Cardinal Health team, Dr Feinberg was instrumental in establishing Georgia Cancer Specialists (GCS), the largest and first integrated oncologic specialty practice in the Southeast. As CEO and president of GCS, he expanded community access to oncology care by bringing the latest cancer treatments, technologies, and clinical trials closer to the patient. In 2012, Specialty Solutions launched PathWare™ Decision Transaction Solutions, a software technology Dr Feinberg was instrumental in designing to improve the work flow process for payers and physicians. He is the author of the best-selling *Breast Cancer Answers* and its follow-up book, *Colon Cancer Answers*. Dr Feinberg was an early adopter of HIT, incorporated electronic medical records (EMRs) at GCS in 1999, and subsequently developed OASIS, a proprietary EMRs software application that incorporates artificial intelligence logic into common EMR functions. Dr Feinberg is the innovator behind ChemoOrders.com, a free online disease management system for healthcare providers.

PATTI FOREST, MD, MBA

Senior Medical Director, Health Delivery Redesign
Blue Cross Blue Shield of North Carolina

Dr Forest is a senior medical director at Blue Cross Blue Shield of North Carolina (BCBSNC). She collaborates with providers to develop and implement value-based initiatives to improve quality and lower the cost of healthcare. Dr Forest received her doctor of medicine and masters of business administration degrees from the University of Tennessee, completed a residency in family medicine in the United States Navy, and joined the family medicine faculty at the Naval Hospital Pensacola residency program. After serving 7 years in the Navy, Dr Forest accepted a position as program director for St. Luke's Family Medicine Residency in Bethlehem, Pennsylvania, and was later appointed director of quality for St. Luke's Hospital and Health Network. She relocated to North Carolina and served as medical director for the North Carolina Division of Medical Assistance from 2007 until she joined BCBSNC in January 2010.

JOHN L. FOX, MD, MHA

Senior Medical Director
Priority Health

Dr Fox is the senior medical director and associate vice president of medical affairs for Priority Health, a provider-sponsored health plan with 640,000 members headquartered in Grand Rapids, Michigan. He is responsible for technology assessment (medical and pharmaceutical), utilization, and case management. He is engaged in new program development including physician profiling, pay-for-performance (PFP) programs, integrated specialty pharmacy, and value-based benefit designs. He is currently involved in the development of payment reform strategies, including the oncology medical home. In addition, he works with a talented group of clinicians and programmers to develop Web-based cost and quality comparison tools, personal health records, and patient registries. Dr Fox received his doctor of medicine degree from Johns Hopkins University School of Medicine and completed a pediatric internship and residency at the Johns Hopkins Hospital. He also earned his MHA from the University of Wisconsin. Prior to joining Priority Health, he was the senior medical director at Physicians Plus Insurance in Madison, Wisconsin. He has also worked for the Indian Health Service and with the Epidemic Intelligence Service in the CDC. Widely published on a variety of subjects, his current interests include the use of cost-effectiveness and number-needed-to-treat analyses in coverage determinations, specialty pharmacy management, the effect of PFP programs on health outcomes, and implementation of bundled payment models.

MARIAN GRANT, DNP, RN, CRNP

Assistant Professor, OSAH
University of Maryland School of Nursing

Dr Grant is a nurse practitioner dually certified in acute care and palliative care/hospice and an assistant professor at the University of Maryland School of Nursing where she teaches courses on communication, evidence-based practice, acute care, and end-of-life nursing. She practices at the University of Maryland Medical Center on their Palliative Care Service. Dr Grant is on the board of the National Hospice and Palliative Nurses Association, is co-chair of the Public Engagement Workgroup for the national Coalition to Transform Advanced Care, and blogs monthly for the *Journal of Palliative Medicine*. Her focus is on how to raise clinician and public awareness of palliative care and advocating to make these services more widely available. Before becoming a nurse, Dr Grant studied mass communication and worked in advertising and marketing for the Procter & Gamble Company, where her last job was on the Max Factor and Cover Girl brands.

HOWARD L. KAUFMAN, MD, FACS

Chief Surgical Officer, Associate Director for Clinical Science
Rutgers Cancer Institute of New Jersey

Dr Kaufman is a leading authority on tumor immunotherapy for the treatment of melanoma. He pioneered the development of recombinant viral vectors encoding eukaryotic tumor antigens and immune modulatory genes for cancer therapy and has conducted over 50 cancer vaccine and immunotherapy clinical trials. Dr Kaufman has maintained an NIH-funded laboratory in tumor immunology for nearly 15 years. He was born in Chicago, Illinois, and received his doctor of medicine degree from Loyola University, did a residency in general surgery at Boston University, and completed fellowship training in tumor immunology and surgical oncology at the National Cancer Institute. He has previously held appointments as chief of the Division of Surgical Oncology and associate director of the Herbert Irving Comprehensive Cancer Center at Columbia University in New York City. In 2009, he was recruited to be the first director of the Rush University Cancer Center in Chicago, and in 2014, he was recruited to be the chief surgical officer and associate director for Clinical Sciences at the Rutgers Cancer Institute of New Jersey. Dr Kaufman has published over 200 peer-reviewed scientific papers, books, review articles, and abstracts, and serves on the editorial board of several biomedical journals. He is the editor-in-chief of the *Journal of Immunotherapy Applications* and is a senior associate editor at the *Journal of Translational Medicine*. He is a member of numerous professional societies, and was elected president of the Society for Immunotherapy of Cancer. Dr Kaufman has chaired several NIH grant review study sections and has been ap-

pointed to the boards of directors of several professional organizations, including the Melanoma Research Foundation, the American Cancer Society-Eastern Division, and the University of Illinois Chicago.

IRA M. KLEIN, MD, MBA, FACP

National Medical Director, Clinical Thought Leadership
Aetna, Inc

Dr Klein is a national medical director in the Office of the Chief Medical Officer at Aetna, holding the position of Clinical Thought Leadership, responsible for core program development across the enterprise. He recently transitioned from his previous role of almost 2 years as chief of staff to the chief medical officer at Aetna, having been in this role since 2011. He remains as part of the team responsible for communicating and deploying the strategic efforts of the CMO in multiple areas, including leveraging of business acquisitions, clinical integration, and clinical program development. He joined Aetna in 2006 as a medical director in the northeast region and transitioned to the corporate-level national accounts sales and support group in 2009, where he was involved in the development of new benefits designs, financial and clinical analytics for national accounts, and the evolution of oncology strategies. Prior to joining Aetna, Dr Klein was the medical director for quality and case management at Bayshore Community Health Services in New Jersey. Before that, he also served as the chief medical officer of Elderplan, an 11,000-member Medicare Social HMO that focused on the frail elderly. Dr Klein has his BS in pharmacy **and** an MBA from Rutgers University, and a doctor of medicine degree from the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School. He completed his residency in internal medicine at Brown University and Robert Wood Johnson University Hospital.

JOY LARSEN HAIDLE, MS, CGC

President, National Society of Genetic Counselors

Ms Haidle is a board-certified genetic counselor at the Humphrey Cancer Center in Robbinsdale, Minnesota, with 20 years of experience in counseling hereditary cancer genetics. She is also a policy and peer review consultant for Blue Cross Blue Shield of Minnesota and an expert resource for other Minnesota payers. Ms Larsen Haidle is a clinical preceptor in the Genetic, Cell Biology, and Development Department at the University of Minnesota, and president of the National Society of Genetic Counselors. She has a special interest in public policy, appropriate utilization of genetic tests, and identifying individuals/families at increased cancer risk that might benefit from heightened surveillance or risk reduction. She is recognized nationally for her contributions to the field of genetic counseling, including being the recipient of the National Society of Genetic Counselors Leadership Award: Outstanding Volunteer in 2012. She has co-authored several genetic counseling practice guidelines and has published extensively on a variety of topics including Lynch syndrome and juvenile polyposis.

LAURA LONG, MD, MPH

Chief Medical Officer, VP of Clinical Innovation
BCBS South Carolina

Dr Long is a graduate of Duke University, and received her doctor of medicine degree from the Medical College of Virginia and her MPH at the University of South Carolina (USC). After completing her residency at USC in preventive medicine and public health, she held several positions in geriatrics with increasing levels of management responsibility. She worked with Paul Eleazer, MD, as he enhanced the geriatric curriculum for residents and then established a fellowship training program in Geriatrics at USC. Ultimately, the JF Byrnes Center for Geriatric Medicine, Education and Research was established, and Dr Long served as clinical director; she continues to hold a faculty appointment at the Center. Prior to joining BlueChoice HealthPlan, Dr Long was responsible for the management of the 7-hospital system of the SC Department of Mental Health. Dr Long joined BlueChoice HealthPlan in 1996 as an associate medical director to start the Medicare managed care plan, Prime Companion. After promotions in 2002 and 2004, she joined Blue Cross Blue Shield South Carolina in 2008, where she led initiatives in disease management, pharmacy, transparency, and health innovation for Blue Cross and BlueChoice. In this role, she led the statewide rollout of the patient-centered medical home care delivery model. Most recently, in 2011, she was promoted to chief medical officer and vice president for clinical innovation. Dr Long serves on the boards for the National Institute for Quality Improvement and Education and the Consortium for Southeastern Hypertension Control Board of Directors, where she also functions as the board's secretary. She is also a member of the Family Connections of South Carolina Advisory Board, the Organizing for Health Vision Team, and the Colorectal Cancer Action committee. In her free time, she enjoys riding at her ranch in Chapin.

MEG MALEY, RN, BSN

Co-Founder /CEO
CanSurround

Twenty-six years of Ms Maley's 28-year healthcare career have been devoted to improving the lives of people living with cancer. A serial entrepreneur, she has founded, owned, operated, and sold oncology healthcare companies. She has also spent almost 5 years in the technology space, first as executive with WellDoc Inc and more recently with CanSurround. Born of her belief that people living with cancer deserve specialized care at home, Ms Maley's first company, Oncology Care Home Health Specialists, was the first and only oncology-specific home care company in the country and delivered hands-on multidisciplinary care for almost 17 years. Now, Oncology Care is focused on delivering a comprehensive turn-key solution for community-based healthcare providers seeking to implement cancer specialty programs. Recently, Ms Maley and 2 partners cofounded CanSurround, a technology start-up and public benefits corporation focused on reducing emotional distress and enhancing well-being for people living with cancer (patients and their caregivers). Ms Maley has always been passionate about helping to guide people to *healing* choices. CanSurround is the incarnation of this commitment. Ms Maley lives in Landenberg, Pennsylvania.

LEONARDO VIANA NICACIO, MD

Vice President, Oncology
Flatiron Health

Dr Nicacio, a medical oncologist, joined Flatiron Health in 2013. Flatiron operates a Big Data platform that aggregates, cleans, and structures real-world clinical and claims oncology data to deliver impactful value back to its partners. Parallel to the work that he develops at Flatiron, Dr Nicacio accumulates responsibilities as clinical lead of Project DataSphere, an initiative from the CEO Roundtable on Cancer. Before his tenure at Flatiron, he was senior medical director of oncology at Sanofi, responsible for activities related to medical affairs, business development, regulatory, and clinical development for North America Medical Affairs, Oncology. Previously, Dr Nicacio was the medical director of clinical affairs at YM Biosciences, Canada, and was responsible for clinical development, regulatory affairs, and pharmacovigilance. He received his medical degree in Brazil and did his residency at Hospital Sirio Libanes in Sao Paulo, Brazil. Prior to joining the biotech/pharmaceutical industry, he was an advisor of drug development for pharmaceutical companies and received training in molecular and clinical research at Memorial Sloan Kettering Cancer Center. He is currently a member of the American Society of Clinical Oncology; Life Sciences Consortium, CEO Roundtable on Cancer; and the European Society of Medical Oncology, and has joined Harvard Business School programs in leadership and strategy for pharmaceuticals and biotech.

TED OKON, MBA

Executive Director
Community Oncology Alliance

Mr Okon is a nationally recognized expert on the policy and politics of cancer care. He frequently testifies before Congress and comments in the press, especially on the topics of cancer treatment, healthcare reform, Medicare reimbursement, drug shortages, and the changing landscape of cancer care delivery in the United States. His expertise comes from a career devoted to healthcare business and policy; he worked for several pharmaceutical companies, including Merck and Warner Lambert, now part of Pfizer, and IMS Health. He co-founded and took public the healthcare information business Medical Marketing Group. He also founded 2 oncology companies and has traveled extensively overseas, analyzing and discussing cancer care delivery. As executive director of the Community Oncology Alliance, Mr Okon oversees the strategic direction of this nonprofit organization dedicated to patients and providers in the community cancer care setting, under the direction of a dedicated board of oncologists and practice administrators. Mr Okon also speaks to state oncology societies, professional organizations, and companies about the challenges facing the nation's cancer care delivery system. He holds a BS degree from Fairfield University and an MBA from the Carnegie-Mellon University Tepper School of Business. His wife is a full-time practicing oncology nurse.

DEBRA PATT, MD, MPH

Physician
Texas Oncology

Dr Patt is a specialist in medical oncology and hematology, and she is board-certified in internal medicine, hematology, and medical oncology. She also has clinical expertise in breast cancer. Dr Patt directs public policy for Texas Oncology, and serves as the medical director for Healthcare Informatics for McKesson Specialty Health, where she leads a team of physicians and researchers in health economic and outcomes research. She also serves as a medical director in outcomes research and leads the breast cancer team of the pathways task force for The US Oncology Network. She is an active participant and principal investigator in breast cancer clinical research. She completed her training in hematology and medical oncology at MD Anderson Cancer Center in Houston, Texas, and earned an MPA at the UT Health Science Center's School of Public Health in Houston, where she focused on cancer health policy and also completed the Cancer Prevention Program. Her doctor of medicine degree is from the Baylor College of Medicine in Houston, where she also completed her residency. She received both her BS and MBA from UT Austin. She completed the American Society of Clinical Oncology (ASCO) leadership development program in 2014 and is a member of ASCO's clinical practice and cancer education committees. She has served as chair for the Texas Medical Association's Cancer Committee and on the board of the Breast Cancer Resource Center.

BRUCE QUINN, MD, PHD, MBA

Senior Health Policy Advisor
Foley Hoag LLC

Dr Quinn is a national expert on Medicare policy, the impact of health reform on innovation, and the crafting of successful business strategies within the United States healthcare reimbursement system. Dr Quinn has worked successfully with both large and small companies in overcoming hurdles to commercialization through negotiation, understanding insightful ways to use the existing system to advantage and the mechanisms of policy change. Since 2008, he has been a full-time business strategist working with attorney and policy teams for healthcare and life sciences clients in the firm's Government Strategies practice.

DENNIS SCANLON, PHD

Professor of Health Policy and Administration
The Pennsylvania State University

Dr Scanlon is a professor of health policy and administration at The Pennsylvania State University, College of Health and Human Development. He serves as principal investigator for the Robert Wood Johnson Foundation's Aligning Forces for Quality evaluation and is a consultant on an Agency for Healthcare Research and Quality study, "Assessing a Statewide Multi-Stakeholder Chronic Care Model Implementation." Dr Scanlon also serves on the editorial board of several journals, including *BMC Health Services Research*, *International Scholarly Research Network Public Health*, *Health Services Research*, *The American Journal of Managed Care*, and *Medical Care Research and Review*. In 2002, he received the John D. Thompson Prize for Young Investigators, given annually by the Association of University Programs in Health Administration to an outstanding young investigator in the field of health services research. Dr Scanlon earned a master's degree in economics from the University of Pittsburgh and a doctorate in health services organization and policy from the University of Michigan. Dr Scanlon is widely published on a variety of topics in the health services field, with more than 60 journal articles and reports.

HEIDI SCHUMACHER, MD

Health Insurance Specialist
Centers for Medicare & Medicaid Services

Dr Schumacher is a clinical pediatrician and a program lead within the Patient Care Models Group at the Center for Medicare & Medicaid Innovation (CMMI). At CMMI, she heads the team developing the forthcoming oncology care model, an episode-based payment model for cancer. In addition to her work in payment reform, her policy work has included international research on the structure and funding of graduate medical education, as well as research on quality outcomes within urban mobile health programs. She attended medical school at the University of Vermont College of Medicine and completed her residency in pediatrics at the Children's National Health System in Washington, DC, where she continues to practice clinically.

PHYLLIS TORDA

Vice President, Quality Solutions Group
National Committee for Quality Assurance

Ms Torda is vice president for the Quality Solutions Group at the National Committee for Quality Assurance (NCQA). In that capacity, she leads NCQA's efforts to work with federal and state governments and private organizations on quality assessment issues. In her 17 years at NCQA, Ms Torda has led a wide variety of activities related to performance measurement, quality assessment, and reporting. She is the principal investigator for NCQA's contract with CMS to develop performance measures for the Medicare population and to evaluate Medicare special needs plans. She has also led NCQA's activities to develop measures of inpatient psychiatric care and cancer care for CMS and to develop measures for reporting from electronic health records for CMS and the Office of the National Coordinator for Health IT. Ms Torda led development of standards for how to measure care provided by physicians, which are used by the New York State Attorney General and others. She created NCQA's program for recognizing physician practices as patient-centered medical homes. Ms Torda has participated in development of the Consumer Assessment of Healthcare Providers and Systems surveys since the inception of that Agency for Healthcare Research and Quality initiative. Ms Torda holds a master's degree in history and a bachelor's degree in sociology.

BURTON F. VANDERLAAN, MD, FACP

Medical Director, Network Effectiveness
Priority Health

Dr VanderLaan is the medical director for network effectiveness at Priority Health. In this position, he is responsible for improved performance of the networks and delivery systems. His focus is on successful development and implementation of medical management programs in partnership with the organization's network of physicians and hospitals. Prior to joining Priority Health, he served as regional medical director for Aetna, Inc, for the Midwestern area.

RINA WOLF, MHA

VP Commercialization Strategies, Consulting & Industry Affairs
XIFIN, Inc

Ms Wolf is a nationally recognized expert in the field of laboratory commercialization and reimbursement, with over 20 years of experience in the diagnostic laboratory industry, specializing in molecular diagnostic laboratories. She lectures extensively on these topics and has consulted for major laboratories and laboratory associations throughout the United States. She is a former president and board member of the California Clinical Laboratory Association and is an active participant with the American Clinical Laboratory Association and the Personalized Medicine Coalition. Ms Wolf also advises and presents to investor audiences. Recent speaking engagements include Piper Jaffray, Cowen Group, and Bloomberg's G2 Intelligence Lab Investment Forum. Most recently, Ms Wolf held the position of vice president of reimbursement and regulatory affairs at Axial Biotech, Inc, where she was responsible for creating and implementing their successful reimbursement strategies. Prior to joining Axial Biotech, Inc, Ms Wolf held executive positions in the area of commercialization and reimbursement at RedPath Integrated Pathology, Inc; Genomic Health, Inc; and Esoterix (now LabCorp). Ms Wolf has a BA from the University of California, Los Angeles, and a master's of healthcare administration.

PETER P. YU, MD, FASCO, FACP

President
American Society of Clinical Oncology

Dr Yu is the 2014-2015 president of the American Society of Clinical Oncology (ASCO). He is a medical oncologist and hematologist, director of cancer research at Palo Alto Medical Foundation, and a member of the Alliance for Clinical Trials in Oncology and the Gynecologic Oncology Group. He is also the chair of ASCO's Research, Policy & Practice subcommittee, an ASCO liaison to the College of American Pathologists Cancer Biomarker Reporting Committee, and past chair of the ASCO Health Information Technology Work Group.

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For Better Quality of Life, Start Palliative Care Early in Process

Peter Page

If palliative care were a new cancer drug on the market it would be broadly embraced, heralded for its ability to improve the quality of life of cancer patients and, in the case of those with metastatic lung cancer, extend life by 2.7 months.[1] Instead, palliative care is a process unevenly funded by insurers and far from universally available, said **Marian Grant, DNP, RN, CRNP,** and assistant professor at the University of Maryland School of Nursing.

Grant's talk, "When Is the Right Time for Palliative Care?" began the first evening of Patient-Centered Oncology care in Baltimore, November 13, 2014. She answered her own topic question unequivocally: "The right time for palliative care is the sooner the better, and the evidence supports that," she said

Grant's talk at the 2-day session hosted by *The American Journal of Managed Care* outlined the many barriers to making palliative care a standard practice in cancer treatment. A lay person often confuses the term with hospice, which is a form of palliative care limited to those within the last 6 months of life, though in practice few patients get the full 6 months of hospice. One big reason is that the patient must make the wrenching decision to cease curative treatment to enter hospice.

"I have a background in sales and marketing," Grant said. "I am a pretty good salesman, but I can't sell anyone on the idea of ceasing treatment they believe is extending their life."

Palliative care, taken more holistically, is "an extra layer of support," she said, that meets the emotional and spiritual needs of both patients and their families, who both suffer from a wide range of stress in addition to pain and other physical symptoms. "That sounds a little fluffy, but when you explain it to patients and their families, it sounds pretty good to them," she said. Palliative care supports patients and families as they consider how to manage end-of-life treatment before events sweep the patient into intensive care they don't want and which can't extend their lives, Grant explained. In that way, palliative care saves money, but increasingly, the evidence shows that it actually extends life as well.

Grant cited a well-known study of lung cancer patients published in the *New England Journal of Medicine* in 2010. Half the patients were given usual standard of care and half were given an intervention of palliative care. The finding that those who received palliative care had better quality of life and less depression was not a surprise; but the improved survival time caught the attention of the medical world, including the American Society of Clinical Oncology.[1]

To fully achieve those benefits, palliative care needs to begin as early as diagnosis. "I get called all the time very late in the game," Grant said, adding that she is often not consulted until patients are in intensive care. "Families often tell me, 'You know, she never would have wanted any of this.'"

Options are changing with the Affordable Care Act. Pediatric patients can have curative treatment and hospice at the same time. The Center for Medicare and Medicaid Innovation is running trial studies to allow this option for adults, too, Grant said.

Grant believes the biggest challenge is the seemingly impossibile one of training enough specialists. There will never be enough specialists, and they will be concentrated in large hospitals and academic medical centers, so nurses and oncologists need to be "deputized" with training in the basics of palliative care to make it available in outpatient clinics and rural communities, Grant said.

"There's no evidence of harm, or excessive costs for doing so," she said. "There are a lot of pros and very few cons." **EBO**

Reference

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As Cancer Becomes a Chronic Condition, Payers Shift Focus to Survivorship

Peter Page

Payers can do more to promote survivorship, but most have already made a significant start, said **Ira Klein, MD, MBA, FACP,** national medical director, Clinical Thought Leadership, Aetna. Klein's talk, "Making the Grade on Survivorship: How are Payers Performing?" helped open Patient-Centered Oncology Care 2014, hosted by *The American Journal of Managed Care* in Baltimore, Maryland. While his remarks were specific to initiatives at Aetna, most insurers have a similar focus. The shift toward supporting survivorship is a natural result of more effective treatments, which means that cancer has become a chronic disease for many patients, requiring holistic, long-term management.

Patients receiving cancer treatment take an average 90 to 120 days of disability, and employers are looking for ways to help these patients return to work earlier to be fully productive, Klein said. Patients naturally seek "more peace, a longer life, and a more productive life." Grounding treatment in evidence-based approaches and survivorship programs can begin prior to chemotherapy to meet the goals of all concerned. Holistic survivorship begins with screening and informing individuals of their cancer risk. Screening requires educating patients and their families about genetic testing and whether a cancer has a hereditary component. To gauge patients' cancer risk, the Aetna website allows them to provide information on their family history of cancer. "Education on the genetics of cancer is an important part of screening," Klein informed attendees.

Aetna's approach to wellness includes risk identification, encouraging changes in diet and exercise, self-directed online virtual care, and 24-hour nurse support. "If you have cancer and you understand you need to keep taking a daily walk, you need to keep eating well, you can't pick up smoking again, you are going to come out better on the other end," Klein said.

Physicians invariably believe they are using evidence-based treatment, but Klein cited data from an internal Aetna study that found this was true just 62% of the time, The percentage increased to 87% in a pilot program within Aetna that provided doctors with a clinical decision support system, based on guidelines from the National Comprehensive Cancer Network and the American Society of Clinical Oncology.

HOW CAN PAYERS FOCUS ON SURVIVORSHIP?

- Create incentives for appropriate screening, including genetic testing, using evidence-based approaches.
- Promote wellness as a strategy, through multiple channels of engagement.
- Influence the care environment by aligning with evidence-based medicine for the best possible outcomes of treatment.
- Reward holistic cancer care within the Oncology Medical Home.
- Include patients with metastatic disease in the survivorship plan. "Leave no patient behind."

A study centered on patients with non-small cell lung cancer found that providers following guidelines and documenting their treatment reduced costs up to 35%. "The value equation is, 'What can you do to improve the quality and reduce the cost?' We've seen in studies you can reduce costs and have the same or better outcomes," Klein said.

The insurer is paying physicians for preparation of care summaries. "A lot of patient information" is an important aspect of evidence-based treatment to improve outcomes. "This is important because if the patient has a chaotic journey through their cancer treatment, they are not set up for good survivorship care," he said.

Effective case management is acutely important at diagnosis and discharge, the crucial transitions for patients. Navigators are important for guiding the patient through bewildering and often frightening treatments, and the practical considerations of undergoing chemotherapy. Aetna has programs to begin case management prior to chemotherapy, a time when navigators play an important role in helping patients with practical matters and setting the stage for survivorship.

The conclusion of treatment is a key juncture, particularly for patients requiring palliative care that is "still applied extremely unsystematically," Klein said. "Any time you see something that is not applied systematically and is all over the place, you can guess there are not best practices and efficiency applied." **EBO**

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Cost, Survival Time, or Quality of Life: the Debate in End-of-Life Care

Peter Page

Jan Berger, MD, MJ, moderator of the panel discussion "Payer, Provider, and Patient Roles for Understanding the End-of-Life Care Equation," opened the session asking the room filled with oncology health professionals and insurers for a show of hands: How many had advance directives?

About half did. She then told the story of a curious family dinner at her parents' home a dozen years earlier; her parents had invited an attorney, unknown to any of them, and instructed every family member to work with him to complete an advance directive before any could enjoy wine and the meal.

"We made fun of it for years. None of us realized that within the following 10 years, twice, with my father and my brother, we would need those advance directives," she said.

The panel was part of the November 13, 2014, session for Patient-Centered Oncology Care, held in Baltimore, hosted by *The American Journal of Managed Care*. Panelists included **Amy Berman, BS, RN,** of The John A. Hartford Foundation, who has received palliative care the past 4 years for her stage 4 inflammatory breast cancer; **Bruce Feinberg, DO,** of Cardinal Health Specialty Solutions; and **Patti Forest, MD, MBA,** senior medical director at Blue Cross Blue Shield of North Carolina. Each described a thicket of barriers—personal among patients and providers, institutional among payers, and cultural for all—that prevent the discussion of advance directives with cancer patients before it's too late for them to control the course of their treatment.

Berman began her remarks by telling the story of a pin she wore that belonged to her grandmother, Shirley Dinnerstein, the plaintiff in a landmark 1978 Massachusetts case that determined a person does not have to go to court to have his or her end-of-life wishes honored. "It is the precedent for the advanced directive," Berman said. She attributed the fundamental resistance to making advanced directives a normal part of healthcare planning, well before need, to a deep cultural reluctance to accept the inevitability of death. "Death is simply part of the life cycle, and we live in a denial mode," she said.

Feinberg said palliative care needs must become part of the curriculum for training doctors while, more broadly, a general shift in the culture must occur to accept advanced care planning as a normal part of medicine. He described data that showed 75% adults 65 years and older are not "health literate." Feinberg asked, "What is the education we can provide (patients), and can that education be received as it needs to be received so the patient can make the decision? I struggle with how to convey the information to them because, in the end, if it becomes the doctor making the decision, we have not accomplished the goal."

> *"What is the education we can provide, and can that education be received as it needs to be received so the patient can make the decision?"*
>
> —BRUCE FEINBERG, DO, CARDINAL HEALTH SPECIALTY SOLUTIONS

Said Forrest, "The fear from the payer perspective is even bringing (palliative care) up, for fear the patient or provider will think we are just trying to save money. That has held back many organizations in the past, but the time is ripe for the conversation around it." She said one thing payers can do is to simply begin to pay doctors for having conversations with patients about palliative care.

Berger, who said her family experience has made her "a passionate zealot" for advance directives, noted the allegation made during debate over the Affordable Care Act that compensating doctors for discussions of palliative and hospice care amounted to creating "death panels." "We took a few steps backward then," she said.

Forrest, summarizing the consensus of the panel, said the best rebuttal to those who denigrate discussion of palliative care is the research that supports it. "I would say 'look at the evidence.' Not only can quality of life be improved, but survival can be improved. It's not about withholding care. The more we educate people, the better," she said. **EBO**

PROVIDER KEYNOTE

ASCO's Yu Outlines How the "Changing Value Proposition" Is Redefining the Oncologist's Role

Mary K. Caffrey

The rising cost of cancer care in the United States, and the need to listen to what cancer patients want, is not only transforming the way Americans deal with health insurers, but also the way physicians practice medicine, **Peter P. Yu, MD, FACP, FASCO,** president of the American Society of Clinical Oncology (ASCO), told a multistakeholder meet at Patient-Centered Oncology Care 2014.

Peter Paul Yu, MD, FACP, FASCO

Yu gave the morning keynote address, "Value in Cancer Care: Achieving Patient Centered Care in Today's Environment," which offered the providers' view to the third annual gathering of payers, providers, policy leaders, and representatives from the pharmaceutical sector sponsored by *The American Journal of Managed Care*. The meeting in Baltimore, Maryland, aimed to seek better solutions for cancer patients at a time when patterns of insurance coverage are changing, and as payers demand proof that new therapies are worth the high cost.

The changing value proposition is causing oncologists to ask, "What does it mean to be a doctor in the United States?" Yu said in opening his talk. A physician, he said, can no longer be someone who does things *to* patients, but must be someone who does things *with* patients to try to achieve an outcome. Yu emphasized that the cancer patient must be part of the decision-making because the implications of care have changed so much.

WHERE IS THE VALUE?

Citing an Institute of Medicine report, Yu reviewed elements that are driving up healthcare spending in the United States without adding value: $210 billion in unnecessary medical interventions, $190 billion in excess administrative costs, and $130 billion in inefficient care delivery. He dubbed this, "Doing the right thing, but doing it the wrong way."[1]

To stop this trajectory, healthcare reformers seek to measure quality. However, "We don't really have robust outcomes measures, and this is a major problem," Yu said. "If you don't have outcomes measures, how can we decide what value is? We focus mostly on process measures."

In cancer care, diagnostics have added a new, expensive element to the cost equation. "Diagnostics are as important, if not more important, than therapeutics because they increasingly drive the decision for therapeutics," Yu said.

COSTS CANNOT BE IGNORED

The ASCO president said the rising cost of cancer care has changed the dynamic between doctors and patients. Historically, discussing the price of therapy with patients was verboten for physicians, but in 2014, ASCO took on the dual issues of value and quality as priorities. Last spring, CMS agreed to use ASCO's quality standards as a clinical data registry. ASCO collected data from payers and engaged in extended dis-

cussions, and the group is now working with Congress to redesign Medicare reimbursement to be less complex and to reward quality.

There's simply no avoiding that rising prices for specialty drugs are the biggest cost drivers in cancer care, Yu said. He shared data from Blue Cross Blue Shield Association showing a 900% escalation in cancer drugs between 1996 and 2010, and data from PriceWaterhouse Coopers showing that the current $87.1-billion expenditure on specialty drugs is expected to quadruple by 2020.

On a more critical note, out-of-pocket costs for patients are rising: 34% of employers now charge at least a $60 co-pay for specialty drugs. How does that play out in cancer care? It means a patient who needs to take 1 pill a day for chronic myeloid leukemia might take that pill every other day, and that person becomes likely to relapse when there's no reason for that to happen, Yu said. "We need to consider more than the price of the drug," he said. "We need to consider using or not using the drug."

At the practice level, regulatory pressures, the price and delivery of cancer drugs, and the trend toward consolidation have made it difficult for small oncology practices to stay afloat, Yu said. This can hurt access to care in rural areas, where the community oncology clinic may be the only option. Clinical care pathways, which payers use to control the costs, can be designed with software that incorporates patient preferences, Yu said. He was optimistic about the role of Big Data in the future of cancer care.

Yu then discussed principles of the payment reform initiative that ASCO is pursuing with Congress:

- Reimbursement must not only move away from fee-for-service toward value, but also from the idea that payment must be tied to the physician touching the patient. Work by nurses, nutritionists, and other team members is essential and should be reimbursed.
- Contact with the patient outside the office visit—especially during the survivorship stage—needs to be recognized.
- Flexible payment models must match the transition to value-based care. Excessive documentation is wasteful. Documentation should be streamlined and predictable.
- A model advocated by ASCO trims codes from 58 to 11.
- A bundled model can work, but the period of the bundle should be 1 month, since cancer patients' status can change rapidly.
- The model must support clinical trials and transitions in care. **EBO**

> *"We need to consider more than the price of the drug, we need to consider using or not using the drug."*
>
> —PETER P. YU, MD, FACP, FASCO, AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO), PRESIDENT

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PRACTICE & PAYMENT MODELS

Surveys Find Agreement in What Stakeholders Want From Cancer Care, and Oncology Medical Homes Deliver

Peter Page

Evidence is mounting that the oncology medical home (OMH), in which cancer patients receive all of their treatments in a coordinated fashion through a single practice, lowers costs and maintains, or even improves, the quality of care. In his presentation, "Early Findings of the Oncology Medical Home," **Ted Okon, MBA,** executive director of the Community Oncology Alliance, told stakeholders at Patient-Centered Oncology Care 2014, hosted by *The American Journal of Managed Care* in Baltimore, Maryland, that surveys, pilot studies, and conversations with patients, payers, and providers fundamentally agree on what each wants from cancer care—and the OMH satisfies them all.


Ted Okon, MBA

Both Medicare and commercial insurers are clamoring for quality, cost control, accountability, and predictability, Okon said. In fact, surveys find that patients and providers want improvements in how care is delivered. The OMH, where one primary focus is avoiding unnecessary emergency department (ED) visits and hospital admissions, meets all of these goals. For example, surveys find patients want to be educated about their diagnosis and treatment; physicians want to be paid for cognitive services, such as treatment, survivorship planning, and end-of-life care; and providers demand productivity with a focus on survivorship.

"It is remarkably similar what the 3 stakeholders want," Okon said. He presented a summary of a 3-year pilot study by UnitedHealthcare of 5 medical oncology groups that treated 810 patients with breast, colon, and lung cancers. The oncologists were reimbursed upfront for an entire cancer treatment program, regardless of the drugs administered to the patient, based on the expected cost of a standard treatment predetermined by the doctor. Patient visits were individually reimbursed using the fee-for-service contract rates, and chemotherapy treatments were reimbursed based on the average sales price. Although the pilot was designed to remove any incentive for prescribing costly cancer drugs, drug spending actually increased 275%, while overall costs per patient shrank 34%, primarily from reduced ED visits and hospital admissions.

> *"You have to change basic care processes. This isn't just saying you are going to change. You really have to change. The practice has to focus on change that, for example, keeps patients out of the ER and hospitals, and that requires an investment in technology and people. Timely, regular feedback from the payer is key."*
>
> —TED OKON, MBA COMMUNITY ONCOLOGY ALLIANCE

Oncology practices typically coordinate care with all physicians treating their patients, which is a key feature of the OMH, but don't provide 24-hour access for triage, the same level of information support, or measurements of quality, value, and patient satisfaction. The UnitedHealthcare pilot study found all of these factors to be essential for maintaining quality of care while simultaneously reducing costs.

"You have to change basic care processes," Okon said. "This isn't just saying you are going to change. You really have to change. The practice has to focus on change that, for example, keeps patients out of the ER and hospitals, and that requires an investment in technology and people. Timely, regular feedback from the payer are key."

The Commission on Cancer has set a target of early 2015 for accrediting OMHs, which will include infrastructure and process requirements, specific measures of progress, data submission with benchmarking, and site surveys.

"You can contain costs and increase quality, but don't kid yourself; this takes work," Okon said. **EBO**

Cost Matters to Cancer Patients, and Care Costs More in Hospitals, Panel Agrees

Mary K. Caffrey


Jan Berger, MD, MJ


Ted Okon, MBA


Stacie Dusetzina, PhD


Debra Patt, MD, MPH

The transition to payment models in cancer care that reward quality might do more than save money. In some cases, the change might improve relationships between patients and oncologists. Whether this happens or not, there's no denying that therapy costs are driving decisions in cancer care, both by patients and, in some unpleasant cases, by the institutions pledged to serve them. The economics of cancer care are playing out on the front lines, and they *do* affect outcomes, according to a panel moderated by **Jan Berger, MD, MJ,** editor-in-chief of *The American Journal of Pharmacy Benefits*.

The panel, featuring **Ted Okon, MBA,** executive director of the Community Oncology Alliance; **Debra Patt, MD, MPH,** of Texas Oncology; and **Stacie Dusetzina, PhD,** an epidemiologist from the University of North Carolina at Chapel Hill, covered "Perspectives on Economics and Outcomes of Community vs Hospital Oncology Practice."

> *"The average person equates high cost with high value and doesn't grasp that when an insurer might want to withhold an expensive therapy, it's because of evidence it won't work, not because it's expensive and the insurer doesn't want to pay for it."*
>
> —STACIE DUSETZINA, PHD

At the start, Berger observed that today's movement toward measuring quality and building payment structures around quality metrics stands apart from past reform efforts in that it seeks to build on the best of prior models rather than discard everything and start over. To that end, she asked the panelists how current reforms might change patient-provider relationships, especially from the perspective of cancer treatment in a community practice compared with a hospital.

Dusetzina, who has studied the impact of therapy cost on patients, said that the difference in setting can have a compelling effect on relationships. "Care costs more for everyone in hospital-affiliated clinics," she said, due to facility charges. Getting that extra bill, she said, can negatively harm the relationship with the oncologist.

Okon expressed concern about the consolidation and "corporatization" of hospital-based care, especially with the expansion of the 340B drug pricing program. This initiative, run by the Health Resources and Services Administration, was set to allow "safety net" hospitals to obtain cancer drugs at deep discounts so those medications can be offered to vulnerable patient populations. However, he asserts that 340B has been allowed to expand far beyond its intended purpose, at the expense of community practices unable to obtain drug discounts. The situation, he said, is forcing the closure or consolidation of community oncology practices, leaving some remote areas without coverage, and "is unsustainable."

Okon said he hears "horror stories" of patients being asked to sign waivers agreeing to cover drug costs for off-label uses at prices well above what the hospital would have paid. "The bottom line is, this is really bad medicine," he said. This corporate culture in hospital-based cancer care, he said, is coming "in an era when we're thinking more about quality, when we're thinking more about value and more about measurement for the first time."

"There's no question," said Patt, that oncology care needs a transition from current incentives to a "more population-based model." Her theme throughout the panel discussion was the need for oncology practices to embrace a team-based approach, one that does not require all information to flow from the oncologist, but instead distributes care and decision making among several professionals, including social workers, nurse practitioners, care coordinators, and even psychologists.

But Patt acknowledged this is hard on a community practice. "This requires infrastructure investments. Most oncology clinics have small margins by which they derive revenue. For each incremental investment you make, you have to demonstrate return," she said.

Without reimbursement reform that rewards practices for a team-based approach, hospitals alone might find it easier to make these investments. And yet, Patt said, she sees more innovation happening at the community level because it comes from practice culture and is not seen as a directive from the hospital administration. She would be concerned if an oncology home model became just a set of metrics for a practice to follow. "Then you're not really changing how you're delivering care," she said.

But change has to come, and community oncology practices do, as a group, deliver care at a lower cost than hospitals and academic centers. "The cost issue is real," Patt said. "I've had patients say, 'I can't pay for that oral chemotherapy for my renal cell carcinoma. I've decided it's in the best interest for my family for me to die.'"

Berger than asked the panel to address some of the tougher issues in oncology care today: how to educate patients and providers on when palliative care might be best and how to deal with transparency issues, so that "doing less" does not come across as "withholding care."

Change in healthcare is never easy, Patt said. "There is always the '*New York Times*' test," she said. For some audiences, any mention of palliative care will come across as a "death panel" conversation. "Nothing like cancer pulls more at your heart strings…society is very polarized about it." That reality, she said, means it's the oncology community's job to change how people think about cancer care. For some today, it can become a chronic disease, "but many people do die of cancer."

Okon agreed that education is very much needed, but also among providers: both on what he called the "macro level," about the business of cancer care, and on the "micro level," about issues such as end-of-life planning. Dusetzina said one of the barriers to having good conversations with patients about their options is the lack of understanding about the associated risks.

The average person equates high cost with high value, she said, and doesn't grasp that when an insurer might want to withhold an expensive therapy, it's because of evidence it won't work, "not because it's expensive and the insurer doesn't want to pay for it."

The panelists agreed that the oncology medical home model, with a team-based approach, should be the wave of the future. Okon said change must start with the oncologist, who must abandon the "queen bee" model of being the only decision maker, because it's too inefficient. "They have to change their mind-set," he said. **EBO**

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Payers Seek Quality Measures That Matter to Patients, Fox Says

Mary K. Caffrey

Efforts to improve quality in cancer care by creating standards of measurement abound, including the Quality Oncology Practice Initiative (QOPI), launched in 2006 by the American Society of Clinical Oncology (ASCO).[1] But although measuring quality with the goal of improving patient care is important, it's essential for healthcare leaders to grasp what is being measured and to ensure that it actually matter to patients.

"The triple aim of increased patient satisfaction, improved population health, and a downward pressure on healthcare costs can be achieved. The challenge is that while various parts of the system may want to work cooperatively, the imperative today is for each to satisfy our primary stakeholders and not society as a whole." That challenge has created an upward tick in healthcare spending, in general, and cancer care, in particular.

—JOHN L. FOX, MD, MHA

TABLE. QOPI Certification Measures

CORE MEASURES	PROCESS/OUTCOME	IOM DOMAIN
Pathology report confirming malignancy	process	effective
Staging documented within one month of first office visit	process	effective
Pain addressed appropriately (defect-free measure)	outcome	PC
Documented plan for chemotherapy, including doses, etc.	process	effective
Chemotherapy intent (curative vs palliative) documented	process	effective
Cigarette smoking status documented by second office visit	process	effective
Patient emotional well-being assessed by second office visit	process	PC
Symptom/Toxicity Management Module measures	process	effective
Corticosteroids and serotonin antagonist prescribed with moderate/high emetic risk chemotherapy	process	effective
Infertility risks discussed prior to chemotherapy with patients of reproductive age	outcome	PC

SOURCE:

That was the message from **John Fox, MD, MHA,** associate vice president of Medical Affairs at Priority Health, who gave the talk, "Payer Perspectives on the Role and Impact of QOPI Certification." At the outset, Fox said that healthcare tends to value those things that are easiest to measure, although "They are not necessarily the things that are the most important."

So which measurements matter? "We have to measure things that are important to *patients*," he said, rather than what matters most to providers and payers. Doing this likely means integrating data from sources beyond the doctor's office or the healthcare system itself, such as death registries that will tell healthcare systems exactly when and where patients died.

The triple aim of increased patient satisfaction, improved population health, and a downward pressure on healthcare costs can be achieved, Fox said. The challenge is that while various parts of the system may want to work cooperatively, "The imperative today is for each to satisfy our primary stakeholders and not society as a whole." That challenge has created an upward tick in healthcare spending, in general, and cancer care, in particular, something that ASCO is determined to address.

John L. Fox, MD, MHA

Fox pointed to a graphic that showed that the amount middle-class Americans are spending on healthcare is simply not sustainable, especially with a diagnosis like cancer. He referenced the 2001 Institute of Medicine (IOM) report, "Crossing the Quality Chasm,"[2] which calls for a healthcare delivery system along 6 domains that Fox said are still relevant today: according to the IOM care must be safe, effective, patient-centered, timely, efficient, and equitable.

Fox elaborated on the elements of safety and efficiency in cancer care, defining efficiency as "the absence of waste." He shared a figure showing how waste in the system contributes to healthcare's rate of spending continuing to outpace the US gross national product: fraud, along with failures in care delivery, care coordination, and pricing, all contribute, but the biggest problem areas were overtreatment and too much administration.

Does any of this matter to patients? Some of it might, Fox said, noting the example, "overtreatment that patients wouldn't have wanted had they known differently." What patients care most about, however, are outcomes. However, most quality care measurements focus on process and structure, not outcomes, he said. He listed the 10 core QOPI quality measures, of which 8 are process measures (See **Table**), while 2 measure outcomes. Within the IOM framework, 7 involve effectiveness, and 3 concern whether care is patient-centered. All this might speak to why payers are not yet funding QOPI, he explained. It's not that QOPI may not be important; Fox said, it's that payers don't care as much about process or structure *unless* there is a clear correlation with how it affects patient outcomes. QOPI, he said, has 200 measures, and Fox said it can be difficult to see at first how many of these, which are process measures, translate to things that bring value to patients. Fox went through numerous other examples, including research that highlighted spectacular disconnects between what he called "box-checking" by physicians and what patients understood to be happening in their care. By contrast, other research involving practices that received Patient-Centered Medical Home (PCMH) designation form the National Committee on Quality Assurance reported a 5% reduction in total Medicare payments compared with their nonaccredited counterparts, with 62% of the decline due to a reduction in payments to acute care hospitals.

Fox sees hope for PCMHs, but he also warned that the conflicting standards of measurement being put forth by QOPI, the Commission on Cancer, the Community Oncology Alliance, and CMS' Center for Medicare and Medicaid Innovation could create confusion among oncologists.

"We have to measure things that matter to patients," he said. "Not everyone can measure everything—it takes collaboration between oncologists and payers. We will get farther, faster, if we can agree on a common set of metrics." **EBO**

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Resistance to Guidelines Ebbs, but "Less Is More" Approach May Help Cancer Care Providers

Mary K. Caffrey

Today's cancer specialist faces a proliferation of clinical care pathways, which payers see as a way to help control costs. Pathways, which may offer incentives if physicians follow them, exist alongside guidelines from the National Comprehensive Cancer Network (NCCN) or the American Society of Clinical Oncology, and now quality measures. All are well intended, but how much is too much? And where do patients fit in? Moderator **Jan Berger, MD, MJ,** editor-in-chief of *The American Journal of Pharmacy Benefits*, explored these themes with panelists who had different perspectives on cancer care guidelines and measurement in the discussion, "Defining Quality in Oncology: Is There a Common Ground?"

Berger started the discussion by comparing adult cancer care with pediatric cancer care, noting that guidelines for children have existed for more than 30 years without the pushback or complaints of "cookbook medicine" sometimes heard among oncologists who treat adults. She invited thoughts on this dynamic. **Phyllis Torda,** vice president for quality solutions at the National Committee for Quality Assurance, said this may be because pediatric oncology was historically concentrated in "centers of excellence" and involved fewer cancers; pediatric oncology offered a haven for clinicians to develop patient registries and best practices.

The issue behind Berger's question—the juxtaposition between the "wiggle room" within guidelines and the need for precise measurement—is a huge challenge, Torda said. It is very difficult to develop measurements that can accurately gauge quality while allowing for varied, though legitimate, choices for doctors in consultation with patients. These disconnects are wider in some cancers than in others, Torda said.

Dennis Scanlon, PhD, professor of health policy and administration at Penn State University, drew distinctions among the types of measures and reasons for them, some of which do not relate to quality. Measurements occur for accountability, quality improvement, surveillance, and payment, and these are not always "synergistic," he said. "Measures for accountability tend to be low bar…not measures that necessarily get us to innovation, which is what this field is striving for." Getting to innovation in patient-centered care requires innovation in measurement itself, he noted, "and is something we probably can't strictly regulate." He mentioned the Geisinger Health System in Pennsylvania, where the OpenNotes project is an example of engaging patients in order to improve quality.

Laura Long, MD, MPH, chief medical officer and vice president of clinical innovation at BlueCross BlueShield of South Carolina, said the "good news" is that unlike a decade ago, today she rarely experiences pushback over clinical guidelines. The "bad news," however, is that the healthcare system lacks the technology to adequately measure what's meaningful.

It's not enough just to measure how well clinicians or practices are delivering evidence-based care, or providing access or efficiency; it's also necessary to know whether what they are delivering is important to patients, Long said. "We're just figuring this out; we're in our infancy," she said.

Assuming that compliance with these criteria can be measured, how can the resulting information be given back to physicians at the point of care in a timely way?

At NCCN, guidelines are hardly "cookbook medicine," said **Jessica DeMartino, PhD,** the network's manager of health policy programs. Guidelines often include choices, including those based on what patients want, and NCCN now includes material to help engage patients in decision making. Evidence-based guidelines can suffer implementation due to a lack of robust data, DeMartino said. NCCN is trying to get its guidelines integrated into electronic health record systems and into pathways to improve care and curtail costs.

Berger invited comment for how to better engage patients in their care. At the point of care, Torda said, measurements are tracking patient-reported outcomes and whether patients understand treatment. Some practices are working with patient advisory councils with surprising success: Scanlon added that his colleagues are experimenting with measures that ask only a few critical questions, but ask them more frequently, including questions from cancer patients' families. Healthcare policymakers and practice teams should ask whether the doctor is always the best person to deliver certain news, Scanlon said. "If we really want to understand how the patient is doing, there are untapped measurement opportunities," he added.

Long agreed with this patient-centered approach: physicians may not have been trained to engage patients in the most effective way, or to understand their goals. She and Scanlon both spoke about issues of health literacy and meeting divergent patient needs based on language barriers, education levels, cultural differences, and the distance a patient must travel for care.

It's not enough just to measure how well clinicians or practices are delivering evidence-based care, or providing access to efficiency; Laura Long, MD, MPH, said it's also necessary to know whether what they are delivering is important to patients.

During the question period, the panel was also asked how to get payers, professional societies, and accrediting groups to set common standards for adult oncology. Torda pointed to the demonstration project at the Center for Medicare & Medicaid Innovation (CMMI), since Medicare handles 51% of the patients who have cancer, and CMMI is also working with commercial payers. (In 2012, CMMI awarded $19.8 million to Barbara McEneny, MD, and Innovation Oncology Business Solutions to launch the Community Oncology Medical Home or COME HOME project at 7 sites.)[1]

Long echoed the sentiment that physicians desperately need consensus on what constitutes quality. "Less is more," she said. "It is too overwhelming for physicians in practice today." Alignment is critical; fortunately, it is starting to happen, with specialty societies playing an important role, she added. "The patient is still a little left out. This conversation is exactly what is needed." **EBO**

PHYLLIS TORDA of the National Committee on Quality Assurance answers a question from the moderator while fellow panelists DENNIS SCANLON, PHD; LAURA LONG, MD, MPH; and JESSICA DEMARTINO, PHD, listen.

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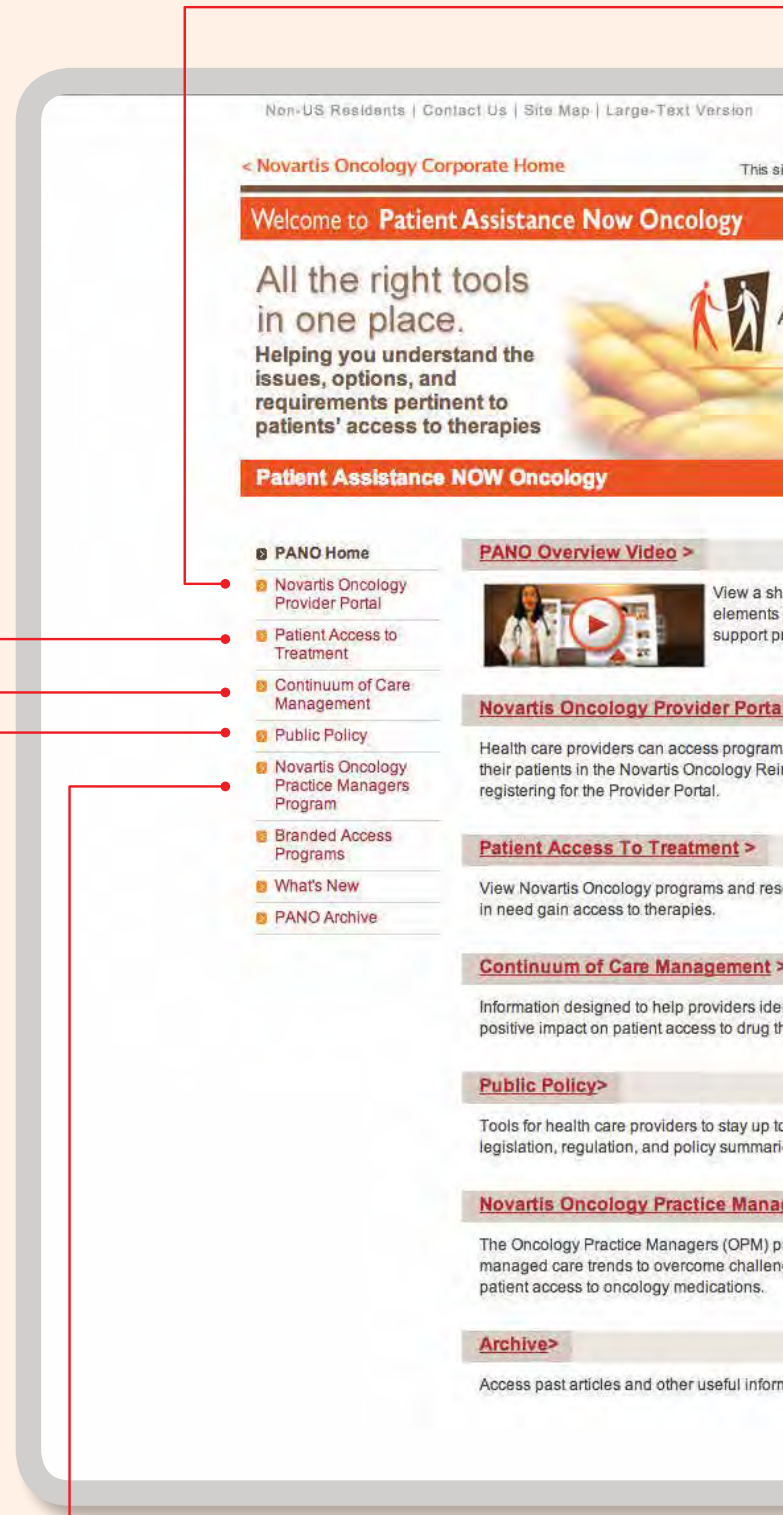

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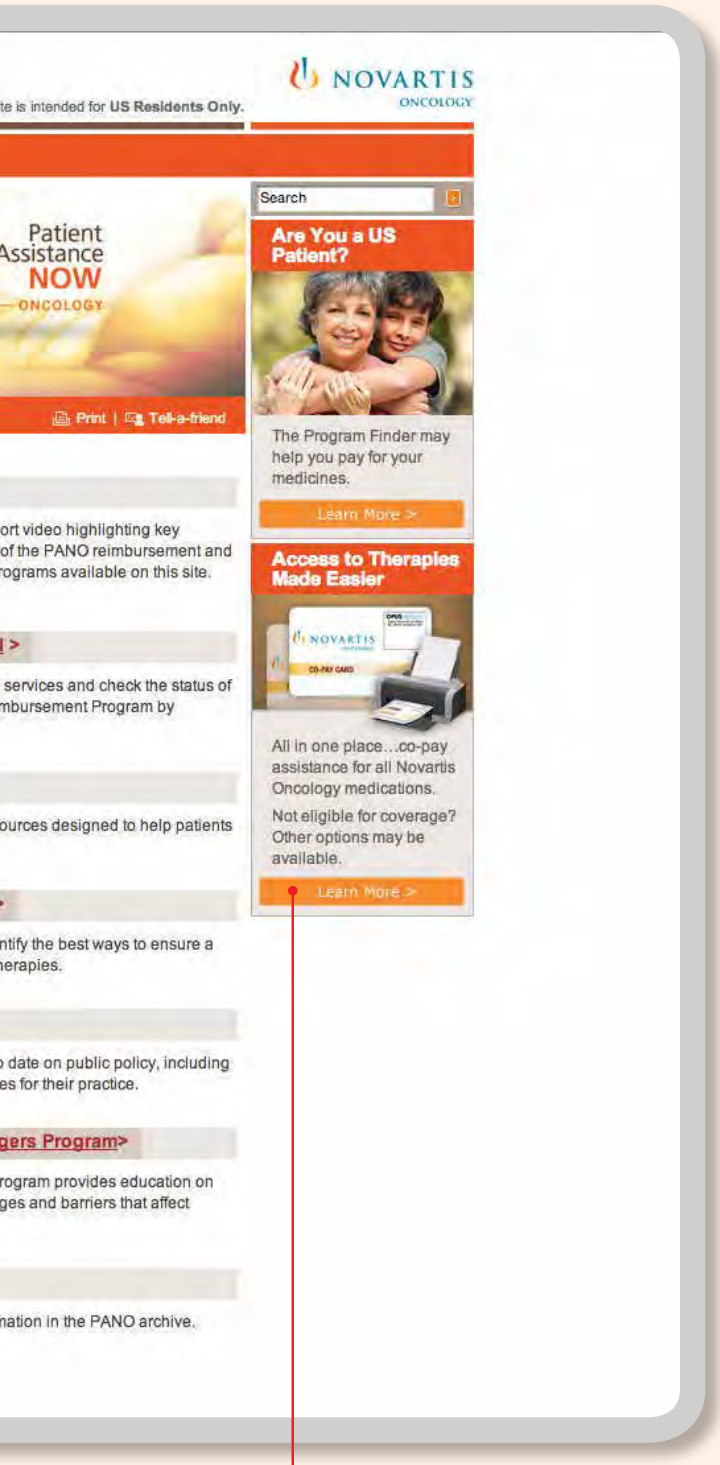

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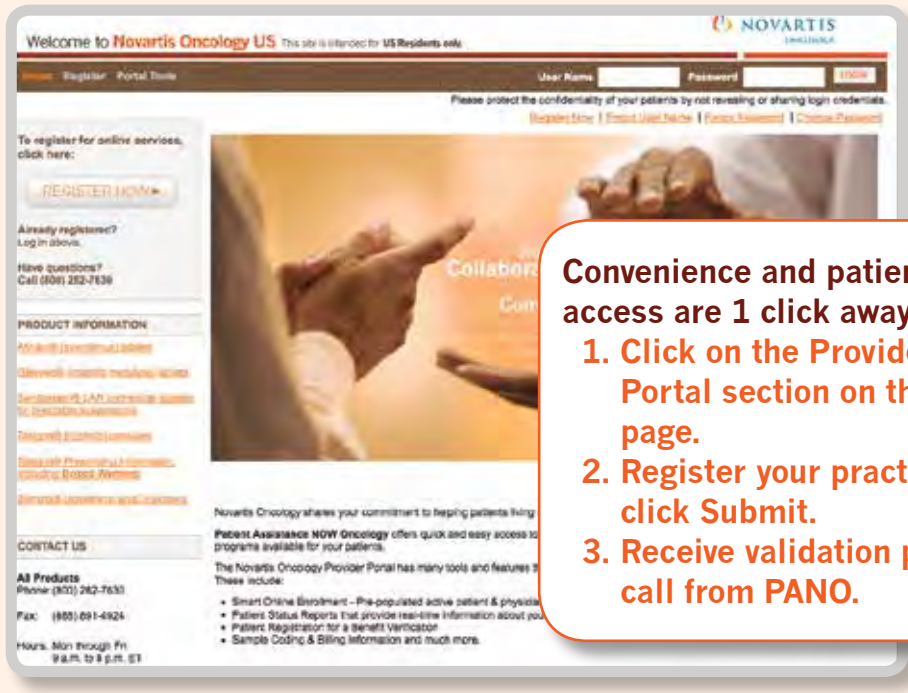

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How the ACA Is Changing Oncology Practice on the Ground

Mary K. Caffrey

The Affordable Care Act (ACA) is still relatively new, but it's already changing the way patient populations gain access to healthcare coverage. This has important implications for oncology, according to **Burton VanderLaan, MD, FACP,** medical director for Priority Health.

VanderLaan delivered the afternoon keynote—the payer perspective—on November 14 at Patient-Centered Oncology Care 2014, and he offered an early view of how the payer mix is changing as the ACA takes hold.

In looking at the population of Michigan, where Priority Health is based, VanderLaan presented data showing that 900,000 people joined the ranks of the insured, while Medicaid enrollment grew by 600,000. "Some of the movement into Medicaid is from employers, but most of it is from the newly insured," he said **(Figure 1).** Many who signed up on the health insurance exchange websites were able to do so because of "the attractiveness of the subsidies," which held down the cost, VanderLaan said.

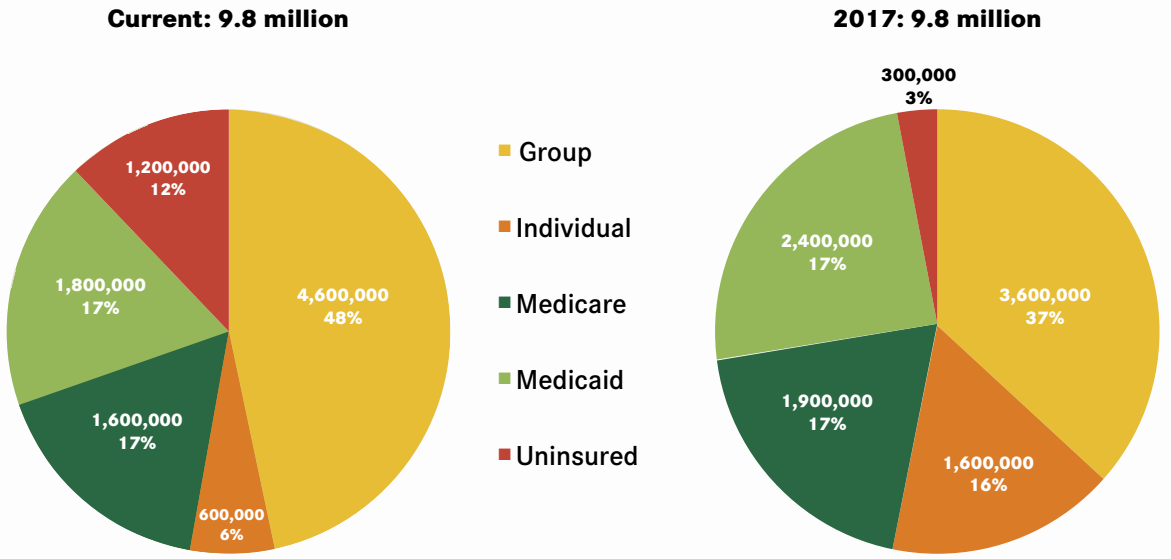
As a group, those signing up for insurance on the exchanges tend to be older—most of those who signed up in Michigan were between the ages of 45 and 64 years. Data from Priority Health's pharmacy benefit managers show those who signed up also tended to be sicker, based on the number of prescriptions they were having filled. "Many had some prior insurance, but because they were able to get a premium subsidy, there was an impetus to move to the exchanges," VanderLaan said, asking, "What are the implications of that? Think of those implications to an oncology practice."

VanderLaan walked the audience through projections, showing that eventually up to two-thirds will be covered as individuals, not through their employers (ie, through a group plan). As a group, those with individual coverage are less likely to pay premiums on time, less likely to buy full coverage, and more likely to change coverage frequently.


Burton VanderLaan, MD, FACP

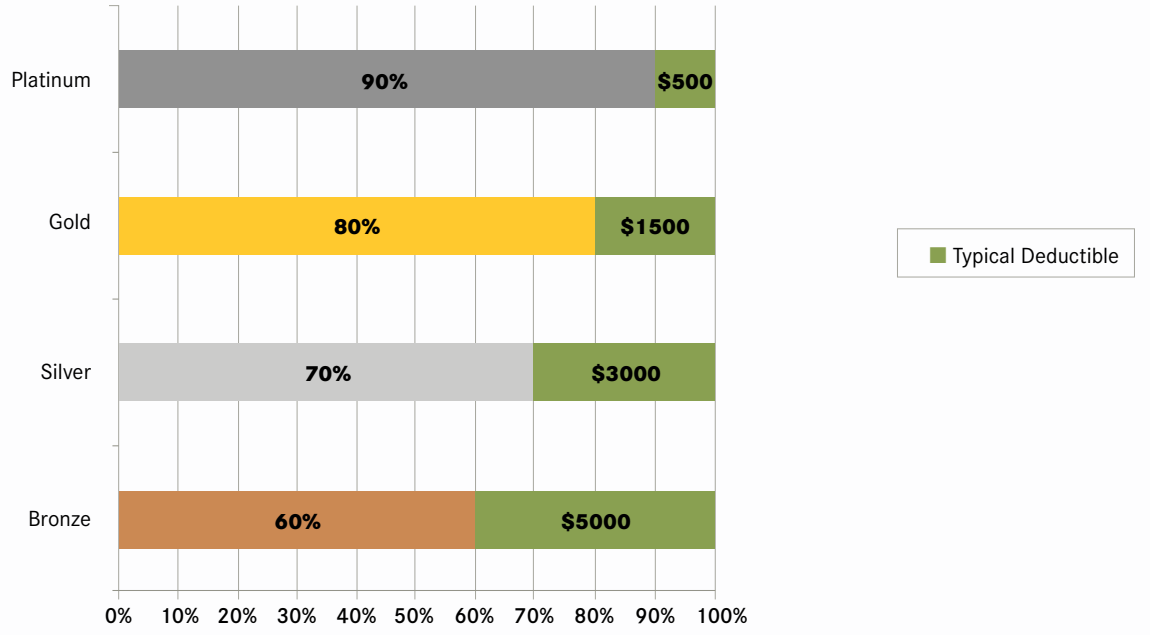
"An individual is more likely to miss a payment than a corporation," VanderLaan said. "For terms of the ACA, if an individual doesn't pay, the insurer honors the claims for 30 days. If you're that provider seeing that patient, you see them for 30 days; then it pends for 60 days. It raises the whole issue of bad debt that might be injected into the system."

FIGURE 1. Impact of the Affordable Care Act: Shifting the Mix of Healthcare Coverage; State of Michigan Example



SOURCE: Burton VanderLaan, MD, FACP, Priority Health. Presentation at Patient-Centered Oncology Care, Baltimore, MD; November 14, 2014.

FIGURE 2. Types of Affordable Care Act Plans



SOURCE: Burton VanderLaan, MD, FACP, Priority Health. Presentation at Patient-Centered Oncology Care, Baltimore, MD; November 14, 2014.

VanderLaan is not the first to raise this issue. Groups, including the Community Oncology Alliance, along with oncologists from academic medical centers who spoke last spring at the National Comprehensive Cancer Network annual meeting, raised the specter of challenges from the "underinsured." This group, distinct from those who are known upfront to need charity care, might have some coverage but face steep deductibles or co-payments for cutting-edge therapies. "Lower cost plans come with a lot of cost sharing," he said.

With the ACA Silver plans being the most popular, the out-of-pocket costs when a patient faces a cancer diagnosis might be more than the person can handle. "Most Silver plans come with a $3000 deductible," he said. "Out-of-pocket maximums may offer some protection, but that may be in-network only." **(Figure 2.)**

Thus, VanderLaan raised another emerging issue: "narrow networks," which are efforts by exchanges in some states to limit where patients seek care, all done in an effort to control costs. "Academic medical centers and cancer centers are particularly vulnerable," he said. VanderLaan discussed an Associated Press survey that found only 4 of 19 nationally recognized cancer centers reported that patients had access to care through their exchanges.[1]

"There has been a backlash," he said. "CMS has definitely had a backlash." Indeed, VanderLaan cited outcry in California over access-to-care issues, which that state's exchange said it tried to address by adding more choices for consumers in 2015.

With an aging population, oncology is going to face ever-increasing demands. "It's unclear where this is going to end up," VanderLaan said. **EBO**

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Turning That Cell Phone Into a Tool for Oncology Care

Mary K. Caffrey

What is the optimal solution for the healthcare industry if it must address the increased complexity and cost of cancer care at a time when labor is scarce? Perhaps harness the power of that cellphone most people already have with them, according to **Meg Maley, RN, BSN,** who gave the talk, "The Role of mHealth in Oncology," at the third Patient-Centered Oncology Care Meeting hosted by *The American Journal of Managed Care*.

When Maley hears of the need for stakeholders to work together to address patient needs, she sees a vital role for mobile health, or "mHealth," in large part because it takes advantage of technology that patients already have at their fingertips. Bringing mHealth into the cancer care equation starts with understanding where patients are emotionally when they receive a cancer diagnosis, Maley said. "Many patients describe their inaugural experience, as well as repeat experiences in their cancer journey, as being enveloped in a dense fog. That fog breeds uncertainty and anxiety." Each patient's cancer journey is different, Maley said. Even though patients may know that others have treaded the path before them, "It is still *your* singular experience."

For all the information that the Internet provides, it can also overwhelm patients, Maley said. With mobile technology, an app designed for cancer patients to give bite-size pieces of information tailored to individual needs can provide just the right level of support without leaving patients confused. Maley discussed such an app, called CanSurround.

mHealth can help patients manage the feeling of being overwhelmed, of having to deal with multiple doctors, appointments, nurse navigators, and even well-intentioned family and friends. Maley said patients in metropolitan areas often have providers in multiple healthcare delivery systems; 1 told her that managing cancer "has become her fulltime job. That is a sad statement."

Why is mHealth the answer? Because cell phones are already ubiquitous, Maley said. Studies show that people check their cell phones 150 times a day, she pointed out. And mHealth isn't just about an app that lets a patient manage a schedule; it's also about sensors that take vitals or an electrocardiogram. The FDA is clearing medical devices, and other agencies are protecting consumers from illicit advertising. mHealth will be big business, and Maley said it's already seen a huge investment.

What's key, she said, is that mHealth isn't just grabbing data for data's sake. With today's analytics, "Data can be analyzed and served back to the provider, the case manager," Maley said. "Data are transformed into knowledge that has the power to influence actions and outcomes."

"There is wisdom here," she said. Apps are no longer experimental; they are being "prescribed" and listed on formularies. With CanSurround, mHealth has the potential to help with medica-

tion management, symptom management and documentation, scheduling, and patient education on a schedule that suits the patient. Some cancer patients cannot absorb information about treatment choices in their physicians' offices and need time for it to sink in, perhaps after the shock of the bad news has worn off.

The CanSurround technology can even take patients through meditation exercises, give nutrition information, or provide instructions on dealing with stress based on feedback from the patient, she said. Patients can connect with others in similar circumstances for emotional and social support; they want "someone to pay attention to me as more than a tumor."

Providers and payers are embracing mHealth, Maley said, because they know they need new tools to drive better outcomes and reduce costs. They need to improve communication, and they need new ways to collect patient-reported data. As much as mHealth helps on the patient side, it also can help providers and case managers triage patients. In the home health sector, mHealth can collect data from patients and feed them to a nurse who receives alerts on which patients need immediate attention; this process eliminates hours of phone calls to make status checks. This way, when the nurse sees the patients, there's already a threshold understanding of what's happening. "By the time the patient shows up, there's time for a deeper conversation," Maley said. **EBO**

As Use of Diagnostics Rises, Challenges Remain in Education, Reimbursement

Mary K. Caffrey

Increasingly, molecular diagnostic tests direct which therapy is best for cancer treatment or whether a therapy should even be used. This fact has raised a host of issues in cancer care: how do payers decide which tests they will cover? How can oncologists and genetic counselors involve patients in the testing process without overwhelming them? Most of all, how can physicians keep up with this fast-moving field, so that the promise of precision medicine moves beyond academic centers and into community practices?

Panelists led by moderator **Ira M. Klein, MD, MBA, FACP,** national medical director, Clinical Thought Leadership, Aetna, examined these questions in "The Road to Personalized Medicine: Clinical Utility and Reimbursement

in Molecular Diagnostics," an area in which regulators are racing to keep pace with developments in science. Panelists included **Bruce Quinn, MD, PhD, MBA,** a former Medicare official who is now senior health policy specialist for Foley Hoag, LLC; **Rina Wolf, MHA,** vice president for Commercialization Strategies with Xifin, a revenue cycle management company that supports about 70% of the molecular diagnostics claims in the United States; **Howard L. Kaufman, MD, FACS,** associate director for Clinical Sciences at Rutgers Cancer Institute of New Jersey; and **Joy Larsen-Haidle, MS, CGC,** president of the National Society of Genetic Counselors.

The promise of personalized medicine—the opportunity to tailor treatments to patients—has run headlong into cost concerns from payers, CMS chief among them, as diagnostics have become a major part of balance sheets in oncology care. Especially since 2011, payers have begun to demand not just proof of clinical validity—that is, evidence that a test showed what it said it would show—but also clinical utility, or proof that tests shape physician decision making and patient outcomes.

Klein referenced earlier speakers' descriptions of how data that shape physician decisions don't always get to the right place, or meet patient needs. How, he asked, can the field of molecular diagnostics fill some of these gaps, and what are the challenges?

Wolf said cancer patients are most helped when there is a truly definitive diagnosis, and it is the predictive value of molecular testing that helps physicians decide on the best course of treatment. She said she had been surprised earlier in the conference to learn that

51% of patients were not receiving tests for EGFR mutations, "which is standard of care."

Educating physicians, in addition to payers and regulators, so they stay abreast of scientific advances in molecular diagnostics and next-generation sequencing (NGS) is a huge challenge, Wolf said, and all stakeholders must work together on this. While the scientific community races ahead with NGS, Wolf said her firm still struggles with CMS and its contractors, in addition to commercial payers, just to get molecular diagnostic claims paid.

Wolf and Quinn also discussed specific examples of bundling rules and other policies that work against patients by discouraging tests from happening in a timely manner. It would be better to take a public health approach in certain common cancers and test everyone who is diagnosed, Quinn said, rather than risk costly delays. "Turnaround times are a much bigger problem than people think," he said.

At Rutgers, precision medicine is proving its value, Kaufman said, and that is making discussions with payers easier. "On complicated tumors and resistant cancers, we are doing full genomic sequencing and finding unexpected mutations, and there may be drugs available that target that specific mutation," he said. In some cases, academic physicians must work with patients to include them in a clinical trial so they gain access to drugs that will work on those mutations.

"We looked at the first 100 patients in the precision medicine program, and we changed the clinical treatment plan for 40% of the patients based on the diagnostic information that came in,"

Kaufman said.

While he said Rutgers' discussions with payers have been fruitful, he recognized that what gets approved in an academic center might not get approved in a community setting. Rutgers is now working to move its precision medicine model into community hospitals. "If it becomes more widespread, I am not sure what will happen," Kaufman added.

Quinn is not surprised that payers want to see evidence before they are willing to offer reimbursement. He described instances in which early clinical results looked promising but time proved otherwise, so waiting for convincing evidence is prudent. But patients suffer, he and Wolf agreed, when Medicare policies discourage or delay testing, so there needs to be a better framework for who is tested and under what circumstances.

Larsen-Haidle said that genetic counselors are increasingly working side-by-side with oncologists to guide treatment. Counselors start the process by talking with patients about their family history, asking, "What are the odds there is a genetic component to the cancer you have developed?"

> *"We looked at the first 100 patients in the precision medicine program, and we changed the clinical treatment plan for 40% of the patients based on the diagnostic information that came in."*
>
> —HOWARD KAUFMAN, MD, FACP
> RUTGERS CANCER INSTITUTE
> OF NEW JERSEY

It's important for patients to be empowered and to understand what tests can and cannot tell them. "Most important," Larsen-Haidle said, "how are they going to use it?" Tests also provide information for family members, "So for that same healthcare dollar, we have the opportunity to provide information for more people."

Kaufman said that at Rutgers, he is sending more patients to genetic counselors to identify germline mutations that could affect other family members. Testing is becoming more mainstream. "We have to balance what's experimental and still needs to be done under the guise of a clinical trial, but we also have to push the field forward," he said. Oncologists "have the ability to get this data now," and should start using it. **EBO**

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- The Patient Lens on Precision Medicine
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**subject to change*

Groundbreaking Decision on Genomic Profiling Coverage Comes With No Fanfare

Mary K. Caffrey

A key CMS contractor has issued an apparent precedent-setting decision outlining how it will make coverage determinations for laboratory-developed tests (LDTs) that use sequence-based genetic profiling to guide treatment for persons with non-small cell lung cancer (NSCLC). However, the decision, known as a local coverage determination (LCD), came with no warning, press release, or announcement, so it remains to be seen if the policy will become standard across Medicare.


Bruce Quinn, MD, PhD, MBA

As reported in *The Cancer Letter* January 23, 2015, Palmetto GBA posted on its website on January 22, 2015, "well after the close of business," an LCD titled "Comprehensive Genomic Profiling for Non-Small Cell Lung Cancer."[1] The move came in the aftermath of President Obama's State of the Union address, which mentioned a precision medicine initiative later outlined at the White House.

While the Obama administration did not draw a link between the 2 items, *The New York Times* mentioned the Palmetto policy change in its coverage of the larger effort to develop treatments tailored to patients' individual genetic characteristics. Bruce Quinn, MD, PhD, MBA, a former Medicare official and consultant for Foley Hoag, told the *Times* that the LCD was a "watershed event."[2]

What does the Palmetto change mean? Strictly speaking, it applies only to treatment decisions in the Carolinas, Virginia, and West Virginia. In a broader sense, as *The Cancer Letter* notes, Palmetto's decision to develop the MolDx program and gain expertise in developing standards for making payment decisions in molecular diagnostics could elevate its status due to a 2014 law that would allow CMS to use its LCDs to establish policies for all such tests.

According to *The Cancer Letter*, the decision focuses on coverage of somatic comprehensive genomic profiling for patients with metastatic NSCLC. Tests are limited to those who are lifetime nonsmokers or former light smokers and who have tested negative for *EGFR* mutations and EML4-ALK rearrangements. This will allow patients to be treated with a targeted therapy for which they would have been ineligible.[1]

As experts told *The Cancer Letter*,[1] and as Quinn and Rina Wolf, MHA, vice president of XIFIN, told stakeholders gathered in Baltimore at Patient-Centered Oncology Care in November 2014, sponsored by *The American Journal of Managed Care*,[3] the issue of reimbursement in next-generation sequencing is increasingly important.[3] Both Wolf, in addressing the Baltimore meeting, and sources who spoke to *The Cancer Letter*, said the comprehensive sequencing technologies could render moot challenges that arise when tissue samples are depleted before all tests are run.[1,3]

Vincent Miller, chief medical officer of Foundation Medicine Inc, a company that stands to be a winner under the Palmetto decision, called it "potentially transformative," and specifically cited the distinction between a comprehensive genetic profile and panels of multiple genes.[1] In mid-January, Roche spent just over $1 billion for a 56% share in Foundation Medicine, *Forbes* reported.[4]

If Palmetto's move is a harbinger of what CMS will do more broadly, it could signal less uncertainty in both the reimbursement and regulation of diagnostic testing, which may not make everyone happy. In early January, the FDA held a 2-day workshop to outline a framework for regulating up to 11,000 LDTs that fall under a relatively small number of Medicare codes. Most reach the market with oversight from agencies, although the FDA has granted clearance for some companion diagnostics.[5]

Pharmaceutical firms have sought to bring order to this situation, and reports indicate they were represented at the White House announcement of the precision medicine initiative.[6] Some funding in the $215-million plan will aid FDA efforts to regulate to the industry.[7] **EBO**

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Medicare to Cover LDCT Screening for Lung Cancer

Mary K. Caffrey

Certain patients can now receive Medicare coverage for lung cancer screening with low-dose computed tomography (LDCT), after CMS issued a national coverage determination (NCD) on February 5, 2015.[1] Coverage is effective immediately.

The decision will allow Medicare beneficiaries to receive LDCT screening once a year if they meet all of the following criteria:

- They are age 55 to 77 years and are either current smokers or have quit smoking within the past 15 years.
- They have a tobacco smoking history of at least 30 pack years, which is at least a pack a day for 30 years. (If a person smoked 2 packs a day for 15 years that equals 30 pack years.)
- The person receives a written order from a physician or qualified non-physician practitioner that meets certain requirements, which are contained in the NCD.[1]

According to a press release from CMS, coverage will include a visit for counseling on the benefits and risks of LDCT screening. The announcement also included requirements for data collection and eligibility requirements for radiologists and imaging centers, consistent with the National Lung Screening Trial (NLST) Protocol.

The CMS announcement comes a little more than a year after the US Preventive Services Task Force (USPSTF) finalized its "B" recommendation for annual lung cancer screenings with LDCT; that recommendation was for adults ages 55 to 80 years who had smoked 30 pack years.[2] USPSTF's recommendation was based on results of the NLST, which found that patients who received screening had a 15% to 20% lower risk of dying from lung cancer; results published in 2013 showed that the targeted screening toward those at greatest risk produced the most effective results.[3]

However, the decision to pay for widespread screening is not without controversy. In a paper published in *JAMA Internal Medicine* in December 2014, authors SH Woolf, et al, expressly discouraged CMS from paying for screening. This is difficult under the Affordable Care Act, since the law requires commercial insurers to pay due to the B recommendation. The authors argued that screening in the general population may not be limited to high-risk smokers outside a clinical trial, and may cause unnecessary harm due to radiation and false positives. **EBO**

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AKYNZEO® (netupitant and palonosetron) capsules, for oral use

BRIEF SUMMARY OF PRESCRIBING INFORMATION

DOSAGE AND ADMINISTRATION

Highly Emetogenic Chemotherapy, including Cisplatin Based Chemotherapy

The recommended dosage in adults is one capsule of AKYNZEO administered approximately 1 hour prior to the start of chemotherapy with dexamethasone 12 mg administered orally 30 minutes prior to chemotherapy on day 1 and 8 mg orally once daily on days 2 to 4.

Anthracyclines and Cyclophosphamide Based Chemotherapy and Chemotherapy Not Considered Highly Emetogenic

The recommended dosage in adults is one capsule of AKYNZEO approximately 1 hour prior to the start of chemotherapy with dexamethasone 12 mg administered orally 30 minutes prior to chemotherapy on day 1. Administration of dexamethasone on days 2 to 4 is not necessary.

AKYNZEO can be taken with or without food.

WARNINGS AND PRECAUTIONS

Hypersensitivity: Hypersensitivity reactions, including anaphylaxis, have been reported with or without known hypersensitivity to other 5-HT_3 receptor antagonists.

Serotonin Syndrome: The development of serotonin syndrome has been reported with 5-HT_3 receptor antagonists. Most reports have been associated with concomitant use of serotonergic drugs (e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors, mirtazapine, fentanyl, lithium, tramadol, and intravenous methylene blue). Some of the reported cases were fatal. Serotonin syndrome occurring with overdose of another 5-HT_3 receptor antagonist alone has also been reported. The majority of reports of serotonin syndrome related to 5-HT_3 receptor antagonist use occurred in a post-anesthesia care unit or an infusion center.

Symptoms associated with serotonin syndrome may include the following combination of signs and symptoms: mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, with or without gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Patients should be monitored for the emergence of serotonin syndrome, especially with concomitant use of AKYNZEO and other serotonergic drugs. If symptoms of serotonin syndrome occur, discontinue AKYNZEO and initiate supportive treatment. Patients should be informed of the increased risk of serotonin syndrome, especially if AKYNZEO is used concomitantly with other serotonergic drugs.

ADVERSE REACTIONS

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 overall safety of AKYNZEO was evaluated in 1538 cancer patients and healthy volunteers in clinical trials. The data described below reflect exposure to AKYNZEO in 1169 cancer patients, receiving at least one cycle of cancer chemotherapy in 3 active-controlled trials, including 782 exposed to AKYNZEO for at least 4 cycles and 321 exposed for at least 6 cycles, up to a maximum of 12 cycles of chemotherapy. The median age was 55, 79% were female, 83% were White, 13% were Asian, and 4% were Hispanic. All patients received a single oral dose of AKYNZEO 1 hour prior to the start of each chemotherapy cycle. In all studies, dexamethasone was co-administered with AKYNZEO.

Cisplatin Based Highly Emetogenic Chemotherapy: In a single-cycle study of patients receiving cisplatin-based highly emetogenic chemotherapy, 136 patients were treated with AKYNZEO. Table 1 shows adverse reactions defined as adverse events reported at an incidence of at least 3% and for which the AKYNZEO rate exceeded palonosetron alone.

Table 1: Adverse Reactions Occurring in ≥3% of Cancer Patients Receiving AKYNZEO and Cisplatin Based Highly Emetogenic Chemotherapy (Cycle 1)

Adverse Reactions	AKYNZEO netupitant 300 mg/ palonosetron 0.5 mg (N=136)	Palonosetron 0.5 mg (N=136)
Dyspepsia	4%	2%
Fatigue	4%	2%
Constipation	3%	1%
Erythema	3%	2%

Anthracyclines and Cyclophosphamide Based Chemotherapy: In a study of patients receiving anthracycline and cyclophosphamide based chemotherapy, 725 patients were treated with AKYNZEO during Cycle 1, and 635 of these patients continued for up to 8 cycles in a multiple-cycle extension. Table 2 shows adverse reactions defined as adverse events reported at an incidence of at least 3% and for which the AKYNZEO rate exceeded palonosetron alone during Cycle 1. The adverse reaction profile in subsequent cycles was similar to that observed in Cycle 1.

Table 2: Adverse Reactions Occurring in ≥3% of Cancer Patients Receiving AKYNZEO and Anthracyclines and Cyclophosphamide Based Chemotherapy (Cycle 1)

Adverse Reactions	AKYNZEO netupitant 300 mg/ palonosetron 0.5 mg (N=725)	Palonosetron 0.5 mg (N=725)
Headache	9%	7%
Asthenia	8%	7%
Fatigue	7%	5%

In addition to the adverse reactions shown above, there were reports of concomitant elevations of transaminases > 3 x ULN and total bilirubin in both arms of the two trials that compared AKYNZEO to oral palonosetron, and the frequency of these elevations was comparable between treatment groups. See Table 3.

Table 3: Liver Function Laboratory Abnormalities

Laboratory Changes	AKYNZEO netupitant 300 mg/palonosetron 0.5 mg (N=861)	Palonosetron 0.5 mg (N=861)
AST > 3 x ULN and/or ALT > 3 x ULN with Total Bilirubin > ULN	3 (0.3%)	5 (0.6%)
AST > 10 x ULN and/or ALT > 10 x ULN with Total Bilirubin > ULN	–	2 (0.2%)
AST > 3 x ULN and/or ALT > 3 x ULN with Total Bilirubin ≥ 2 x ULN	1 (0.1%)	1 (0.1%)

In a multi-cycle safety study of 412 patients, the safety profile of AKYNZEO (n = 308) was comparable to aprepitant and palonosetron (n = 104) in patients undergoing initial and repeat cycles (median 5 cycles, range of 1-14 cycles) of chemotherapy, including carboplatin, cisplatin, oxaliplatin, and doxorubicin regimens. There were no reports of concomitant elevations of transaminases > 3 x ULN and total bilirubin in this study in either arm.

In a randomized, clinical non-inferiority study, that compared oral palonosetron 0.5 mg to intravenous palonosetron 0.25 mg in cancer patients scheduled to receive highly emetogenic cisplatin (≥70 mg/m^2) based chemotherapy, there were two patients (0.5%; 2/369) in the intravenous palonosetron arm who had concomitant elevations of transaminases and total bilirubin. Neither experienced transaminase elevations of > 10 x ULN.

DRUG INTERACTIONS

Effects of AKYNZEO on other drugs

Interaction with CYP3A4 substrates:

Netupitant, a component of AKYNZEO is a moderate inhibitor of CYP3A4.

AKYNZEO should be used with caution in patients receiving concomitant medications that are primarily metabolized through CYP3A4. The plasma concentrations of CYP3A4 substrates can increase when co-administered with AKYNZEO. The inhibitory effect on CYP3A4 can last for multiple days.

Dexamethasone: A two-fold increase in the systemic exposure of dexamethasone was observed 4 days after single dose of netupitant. The duration of the effect was not studied beyond 4 days. Administer a reduced dose of dexamethasone with AKYNZEO.

Midazolam: When administered with netupitant, the systemic exposure to midazolam was significantly increased. Consider the potential effects of increased plasma concentrations of midazolam or other benzodiazepines metabolized via CYP3A4 (alprazolam, triazolam) when administering these drugs with AKYNZEO.

Interaction with chemotherapeutic agents: The systemic exposure of chemotherapy agents metabolized by CYP3A4 can increase when administered with AKYNZEO. Chemotherapy agents that are known to be metabolized by CYP3A4 include docetaxel, paclitaxel, etoposide, irinotecan, cyclophosphamide, ifosfamide, imatinib, vinorelbine, vinblastine, and vincristine. Caution and monitoring for chemotherapeutic related adverse reactions are advised in patients receiving chemotherapy agents metabolized primarily by CYP3A4.

Interaction with oral contraceptives: Clinically significant effect of AKYNZEO on the efficacy of the oral contraceptive containing levonorgestrel and ethinyl estradiol is unlikely.

Effects of other drugs on AKYNZEO

Netupitant, a component of AKYNZEO is mainly metabolized by CYP3A4.

In vitro metabolism studies have suggested that CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in the metabolism of palonosetron.

CYP3A4 Inducers: Avoid concomitant use of AKYNZEO in patients who are chronically using a strong CYP3A4 inducer such as rifampin. A strong CYP3A inducer can decrease the efficacy of AKYNZEO by substantially reducing plasma concentrations of the netupitant component.

CYP3A4 Inhibitors: Concomitant use of AKYNZEO with a strong CYP3A4 inhibitor (e.g., ketoconazole) can significantly increase the systemic exposure to the netupitant component of AKYNZEO. However, no dosage adjustment is necessary for single dose administration of AKYNZEO.

Serotonergic Drugs: Serotonin syndrome (including altered mental status, autonomic instability, and neuromuscular symptoms) has been described following the concomitant use of 5-HT_3 receptor antagonists and other serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs)

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C

Risk Summary: Adequate and well-controlled studies with AKYNZEO have not been conducted in pregnant women. In animal reproduction studies, no effects on embryo-fetal development were observed following daily administration of netupitant in pregnant rats during the period of organogenesis at doses up to 3.7 times the human AUC (area under the plasma concentration-time curve) at the recommended single human dose to be given with each cycle of chemotherapy. However, a dose-dependent increase in adverse effects on embryo-fetal development was observed following daily administration of netupitant in pregnant rabbits during the period of organogenesis with doses at least 0.2 times the human AUC at the recommended single human dose to be given with each cycle of chemotherapy. Daily administration of netupitant in rats up to 3.7 times the human AUC at the recommended human dose during organogenesis through lactation produced no adverse effects in the offspring. In animal reproduction studies with palonosetron, no effects on embryo-fetal development were observed following oral administration during the period of organogenesis at doses up to 921 and 1841 times the recommended human oral dose in rats and rabbits, respectively. AKYNZEO should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data: Daily administration of up to 30 mg/kg netupitant in rats (3.7 times the human AUC at the recommended single human dose to be given with each cycle of chemotherapy) during the period of organogenesis produced no effects on embryo-fetal development. However, an increased incidence of external and skeletal abnormalities in rabbit fetuses was observed following daily administration of netupitant in rabbits at 10 mg/kg/day and higher (0.2 times the human AUC at the recommended single human dose to be given with each cycle of chemotherapy) during the period of organogenesis. These abnormalities included positional abnormalities in the limbs and paws, and fused sternebrae. Reduction in fetal rabbit weight occurred at 30 mg/kg/day. Maternal toxicity in rabbits (i.e. loss of bodyweight during the treatment period) was also observed at 30 mg/kg/day. Daily administration of up to 30 mg/kg netupitant (3.7 times the human AUC at the recommended human dose) in rats during organogenesis through lactation produced no adverse effects in the offspring.

In animal reproduction studies with palonosetron, no effects on embryo-fetal development were observed in pregnant rats given oral doses up to 60 mg/kg/day (921 times the recommended human oral dose based on body surface area) or pregnant rabbits given oral doses up to 60 mg/kg/day (1841 times the recommended human oral dose based on body surface area) during the period of organogenesis.

Nursing Mothers: It is not known whether AKYNZEO is present in human milk. Because many drugs are present in human milk and because of the potential for tumorigenicity shown for palonosetron in the rat carcinogenicity study, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in patients below the age of 18 years have not been established.

Geriatric Use: Of the 1169 adult cancer patients treated with AKYNZEO in clinical studies, 18% were aged 65 and over, while 2% were aged 75 years and over. The nature and frequency of adverse reactions were similar in elderly and younger patients. Exploratory analyses of the impact of age on efficacy were performed in the two trials that compared AKYNZEO to palonosetron. In Study 1 in patients treated with cisplatin chemotherapy, among the patients less than age 65 years, 115 were treated with AKYNZEO and 116 were treated with palonosetron alone. Among the patients 65 years or older, 20 were treated with AKYNZEO and 20 were treated with palonosetron alone. The difference in Complete Response (CR) rates between AKYNZEO and palonosetron alone was similar between the two age groups in both the acute and delayed phases. In Study 2 in patients treated with anthracyclines plus cyclophosphamide chemotherapy, among the patients less than age 65 years, 608 were treated with AKYNZEO and 602 were treated with palonosetron alone. Among the patients 65 years or older, 116 were treated with AKYNZEO and 123 were treated with palonosetron alone. The difference in CR rates between AKYNZEO and palonosetron alone (4% in <65 years and 2% in ≥65 years) was similar between the two age groups in the acute phase. In the delayed phase, the difference in CR rates between AKYNZEO and palonosetron alone (9% in <65 years and 1% in ≥ 65 years) was numerically higher in patients <65 years. This difference between age groups in the delayed phase of Study 2 may be explained, in part, by higher CR in the delayed phase associated with palonosetron alone in the older age group (81%) relative to the younger patients treated with palonosetron alone (67%).

In general, use caution when dosing elderly patients as they have a greater frequency of decreased hepatic, renal or cardiac function and concomitant disease or other drug therapy.

Hepatic Impairment: No dosage adjustment for AKYNZEO is necessary for patients with mild to moderate hepatic impairment (Child-Pugh score 5 to 8). Limited data are available with AKYNZEO in patients with severe hepatic impairment (Child-Pugh score >9)/ Avoid use of AKYNZEO in patients with severe hepatic impairment.

Renal Impairment: No dosage adjustment for AKYNZEO is necessary in patients with mild to moderate renal impairment. The pharmacokinetics and safety of netupitant has not been studied in patients with severe renal impairment, although severe renal impairment did not substantially affect pharmacokinetics of palonosetron. The pharmacokinetics for netupitant and palonosetron was not studied in patients with end-stage renal disease requiring hemodialysis.

OVERDOSAGE: No specific information is available on the treatment of overdosage with AKYNZEO. In the event of overdose, AKYNZEO should be discontinued and general supportive treatment and monitoring should be provided. Because of the antiemetic activity of AKYNZEO, drug-induced emesis may not be effective. Dialysis studies have not been performed; due to the large volume of distribution, dialysis is unlikely to be an effective treatment for AKYNZEO overdose.

A total of 33 adult cancer patients were administered oral palonosetron at a dose of 90 µg/kg (equivalent to 6 mg fixed dose), as part of a dose ranging study. This is approximately 12 times the recommended oral dose of 0.5 mg palonosetron. This dose group had a similar incidence of adverse events compared to the other dose groups and no dose response effects were observed. The highest dose of netupitant administered to 1169 cancer patients was 300 mg. The highest dose of netupitant administered to 49 healthy subjects was 600 mg. A similar incidence of adverse events was observed when compared to lower doses of netupitant in the respective populations of cancer patients and healthy subjects.

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Indication

AKYNZEO is indicated for prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

Important Safety Information

Warning and Precautions

- Hypersensitivity reactions, including anaphylaxis, have been reported with or without known hypersensitivity to other 5-HT_3 receptor antagonists
- Serotonin syndrome has been reported with 5-HT_3 receptor antagonists alone but particularly with the use of serotonergic drugs. Symptoms associated with serotonin syndrome may include the following combination of signs and symptoms: mental status changes, autonomic instability, neuromuscular symptoms, seizures, and gastrointestinal symptoms. Patients should be monitored for the emergence of serotonin syndrome, and if symptoms occur, discontinue AKYNZEO and initiate supportive treatment

Adverse Reactions

- Most common adverse reactions (≥3% and greater than palonosetron): headache, asthenia, dyspepsia, fatigue, constipation and erythema

Drug Interactions

- Use with caution in patients receiving concomitant medications primarily metabolized by CYP3A4. The inhibitory effect on CYP3A4 can last for multiple days
  - —Dexamethasone doses should be reduced when given with AKYNZEO
  - —Consider the potential effects of increased plasma concentrations of midazolam or other benzodiazepines metabolized via CYP3A4 (alprazolam, triazolam) when administering with AKYNZEO
  - —Caution and monitoring for chemotherapy-related adverse events are advised in patients receiving chemotherapy agents metabolized primarily by CYP3A4 including docetaxel, paclitaxel, etoposide, irinotecan, cyclophosphamide, ifosfamide, imatinib, vinorelbine, vinblastine, and vincristine
- Avoid concomitant use of AKYNZEO in patients on chronic use of a strong CYP3A4 inducer such as rifampin as this may decrease the efficacy of AKYNZEO

Use in Specific Populations

- Avoid use of AKYNZEO in patients with severe hepatic impairment, severe renal impairment, or end-stage renal disease

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

Eisai HELSINN