

Evidence-Based
ONCOLOGY™AUGUST 2018
VOL. 24 • NO. 10

ALSO IN THIS ISSUE



RAISING FUNDS, AWARENESS, AND HOPE
A New Jersey family's effort to fund research for less toxic therapies for pediatric brain tumors shines a light on the long-term effects of treatment for childhood cancer survivors.

WHAT'S NEXT?

Our editor-in-chief Joseph Alvarnas, MD, writes how the coordination of cancer treatment must extend to the period that comes afterward, **S412**.



BEAUPIN

LOST TO FOLLOW-UP

A leader in the care of adolescent and young adult cancer survivors, Lynda Kwon Beaupin, MD, describes how physicians must do a better job of emphasizing the need for ongoing care, **SP419**.



GOTTLIEB

NCCN POLICY SUMMIT

Full coverage of the National Comprehensive Cancer Network (NCCN) Policy Summit, which included a keynote address from FDA Commissioner Scott Gottlieb, MD, and panel discussions on funding innovation and addressing narrow networks, featuring EBO™ editor-in-chief Joseph Alvarnas, MD, **SP423-SP426**.



ALVARNAS

AJMC™
TV

AJMCTV® INTERVIEWS

How financial stress during acute care affects patient outcomes in survivorship, and why oncologists should do more to address patients' sexual health needs, **SP436-SP437**.



DIZON



SALTZ



RUGO



O'MALLEY

CLINICAL PRACTICE

Survivorship Care Throughout the Cancer Journey

Don Champlain, MHA, RN, and Lucio Gordan, MD

THE NATIONAL CANCER INSTITUTE (NCI) describes cancer survivorship as a focus on the health and life of a person with cancer post treatment until the end of life. The survivorship experience encompasses the physical, psychosocial, and economic issues of cancer and includes family members, friends, and caregivers.¹

An estimated 15.5 million cancer survivors are currently living in the United States. The projected number of cancer survivors is 20.3 million by 2026.² Therefore, it is essential for practices to support the importance of survivorship and ensure that patients are offered services to help them navigate the multiple challenges related to cancer diagnosis, treatment, follow-up, and management of potential late physical complications, as well as nutrition, reengagement in workforce, psychological concerns, and financial considerations.

At Florida Cancer Specialists, we have created a survivorship program to meet the needs of our diverse population. We divide the program into 3 distinct phases: cancer diagnosis, cancer treatment, and life after treatment.

Survivorship Care Starts at Diagnosis

Many ask when to initiate survivorship and what services to provide. At Florida Cancer Specialists, we implement the first phase upon the diagnosis of cancer. We believe it is essential to introduce the concepts of survivorship early, which helps patients use the program most effectively as they move forward in the treatment phase and beyond.



Cancer survivors who received care at Florida Cancer Specialists take part in an event at a minor league ballpark.

CONTINUED ON SP438

COST PERSPECTIVE

Healthcare Costs and Access for Young Adult Cancer Survivors: A Snapshot Post ACA

Michelle S. Landwehr, MPH; Samantha E. Watson, MBA; and Maia Dolphin-Krute, BFA

Introduction

Although the conversation about cancer and financial toxicity has finally gained traction in recent years,¹ there is still a dearth of coverage in oncology literature on the population arguably hit hardest: young adult cancer survivors (YAs). In 15 years of providing direct financial assistance to the YA population, The Samfund has seen many ways in which financial toxicity manifests: forgoing follow-up care, making difficult choices between paying for rent or for prescriptions, and/or facing bankruptcy at an early age.

Ultimately, the high cost of healthcare affects YAs in unique ways due to their age and life stage (lack of financial stability before cancer, limited employment history/potential, etc).

CONTINUED ON SP440

PAYER PERSPECTIVE

CareMore's Togetherness Program Addresses a Symptom of Living With Chronic Illness: Loneliness

Robin Caruso, MSW, LCSW

OVER THE PAST CENTURY, America has endured numerous health epidemics affecting individuals, families, and communities: polio, diphtheria, whooping cough, and measles. Each resulted in the creation of vaccines, changes in health practice, and health education campaigns to help us address the epidemic.

Today we are facing an epidemic of a different nature. It is rooted not in a virus, bacterium, or toxin but in the soul. The epidemic is loneliness.

According to Sachin Jain, MD, MBA, chief executive officer of CareMore, the impact of loneliness on the emotional well-being of seniors is so great, it should be treated as a medical condition.¹

CONTINUED ON SP442

FROM THE EDITOR-IN-CHIEF



ALVARNAS

What Happens Next?

IN THE 1972 MOVIE *The Candidate*, Robert Redford stars as a political upstart who takes on an established politician in an impossible political race. Throughout the campaign, he is guided through every twist and turn by an acerbic, experienced political adviser played by Peter Boyle. At the end of the movie, after winning, Redford's character looks at Boyle's as the triumph sinks in and calls out to him with evident terror, "What do I do now?"

As patients navigate their cancer journey, many of their early steps are intensely guided by expert clinicians. Key treatment components, including surgery, chemotherapy, immuno-therapy, and radiation, are supervised and curated by a cadre of healthcare professionals, who are dedicated to ensuring that the right care is delivered—safely—and that patients and their families are supported through the logistics along the way.

When this part of the cancer journey ends, however, the integrated nature of the care experience frequently does also, and care becomes increasingly fragmented and disjointed, often delivered by healthcare professionals who are neither experts in cancer care nor fully prepared to effectively navigate and curate care for patients who have survived cancer. Survivorship care and wellness care following cancer, therefore, often becomes an unintentional afterthought as patients make their way through a highly fragmented healthcare system that is often indifferent to their unique needs. A 2005 Institute of Medicine (IOM) report entitled *From Cancer Patient to Cancer Survivor: Lost in Transition* highlights the importance of careful survivorship care following cancer treatment.¹ However, a recent study of adolescent and young adults with cancer (aged 18-39 years) led by Lynda Kwon Beaupin, who is interviewed in this issue on **SP419**, found that 37% of the patients did *not* receive survivorship care post treatment.² The impact of this lack of an effective survivorship care system is further reflected in this observation by the IOM: "Most cancer survivors will return to work following their treatment but approximately 1 in 5 will have cancer-related work limitations up to 5 years later."³ Lack of organized posttreatment care may not only compromise a patient's quality of life but also have a deleterious impact upon their ability to work and achieve a full restoration of function.

In considering the importance of survivorship and post-cancer wellness care, we need to realize the entire scope of these services. Effective survivorship care must include relapse monitoring, screening for the emergence of new or secondary cancers, and management of end-organ injury (cardiomyopathy, neuropathy, posttreatment cognitive

changes, reproductive organ effects, pulmonary dysfunction, and endocrine and bone health), as well as management of the emotional, spiritual, and psychological effects of having traversed such an intense part of the human experience. The National Comprehensive Cancer Network practice guidelines for survivorship care describe an enormous breadth of care needs that are all too often ignored in patients (and families) who have survived cancer.⁴

In this issue of *Evidence-Based Oncology*TM, we look at those who are working to make this type of care a reality for young survivors of cancer. A study by The Samfund tracks the impact of the Affordable Care Act on coverage and affordability of cancer care for young adults. Authors from Florida Cancer Specialists outline how survivorship care is integrated into clinical practice from a patient's first encounter and describe an initiative from CareMore Health, which seeks to address loneliness among seniors and help those recovering from cancer.

The end of cancer care marks the beginning of a life, albeit a different life—one in which some of our illusions about the nature of life are deeply challenged; among the young, this may include a dashed sense of invulnerability or immortality. The incontrovertible reality of cancer treatment is a path for these patients to a life that will, hopefully, go on well past that portion of their lives. Effective survivorship plans can empower patients and families in their ability to successfully and definitively answer the question "What do I do now?" ♦

REFERENCES

- Hewitt M, Greenfield S, Stovall E, eds. *From Cancer Patient to Cancer Survivor: Lost in Transition*. Washington, DC: The National Academies Press; 2006. nap.edu/catalog/11468/from-cancer-patient-to-cancer-survivor-lost-in-transition. Published 2006. Accessed August 6, 2018.
- Beaupin LM, Boldt A, Amato K. Come back: identifying targets to engage young adult survivors who have been lost to follow-up. Poster presented at: American Society of Clinical Oncology 2018 Cancer Survivorship Symposium; February 16-17, 2018; Orlando, FL. Abstract 29. meetinglibrary.asco.org/record/157765/abstract.
- Institute of Medicine. Cancer survivorship facts and figures. The National Academies of Science, Engineering, and Medicine website. nationalacademies.org/hmd/~media/Files/Report%20Files/2005/From-Cancer-Patient-to-Cancer-Survivor-Lost-in-Transition/factsheetfactsandfigures.pdf. Published November 2005. Accessed August 6, 2018.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Survivorship. Version 1.2018 – July 30, 2018. nccn.org/professionals/physician_gls/pdf/survivorship.pdf. Published July 30, 2018. Accessed August 6, 2018.

Joseph Alvarnas, MD
 EDITOR-IN-CHIEF

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.

Opinions expressed by authors, contributors, and advertisers are their own and not necessarily those of Clinical Care Targeted Communications, LLC, d/b/a Managed Care & Healthcare Communications, LLC, the editorial staff, or any member of the editorial advisory board. Clinical Care Targeted Communications, LLC, d/b/a Managed Care & Healthcare Communications, LLC, is not responsible for accuracy of dosages given in articles printed herein. The appearance of advertisements in this journal is not a warranty, endorsement, or approval of the products or services advertised or of their effectiveness, quality, or safety. Clinical Care Targeted Communications, LLC, d/b/a Managed Care & Healthcare Communications, LLC, disclaims responsibility for any injury to persons or property resulting from any ideas or products referred to in the articles or advertisements.

The content contained in this publication is for general information purposes only. The reader is encouraged to confirm the information presented with other sources. *Evidence-Based Oncology*TM makes no representations or warranties of any kind about the completeness, accuracy, timeliness, reliability, or suitability of any of the information, including content or advertisements, contained in this publication and expressly disclaims liability for any errors and omissions that may be presented in this publication. *Evidence-Based Oncology*TM reserves the right to alter or correct any error or omission in the information it provides in this publication, without any obligations. *Evidence-Based Oncology*TM further disclaims any and all liability for any direct, indirect, consequential, special, exemplary, or other damages arising from the use or misuse of any material or information presented in this publication. The views expressed in this publication are those of the authors and do not necessarily reflect the opinion or policy of *Evidence-Based Oncology*TM.

EDITORIAL BOARD



EDITOR-IN-CHIEF

JOSEPH ALVARNAS, MD
 Vice President of Government Affairs
 Senior Medical Director, Employer Strategy
 Associate Clinical Professor, Hematology
 & Hematologic Cell Transplantation
 City of Hope
 Duarte, CA



MICHAEL E. CHERNEW, PHD
 Department of Health Care Policy
 Harvard Medical School
 Boston, MA



JONAS DE SOUZA, MD, MBA
 Medical Director, Office of the Chief Medical Officer
 Humana
 Louisville, Kentucky



JEFFREY D. DUNN, PHARM D, MBA
 Vice President, Clinical Strategy and Programs and
 Industry Relations
 Magellan Rx
 Salt Lake City, UT



BRUCE A. FEINBERG, DO
 Vice President and Chief Medical Officer
 Cardinal Health Specialty Solutions
 Atlanta, GA



A. MARK FENDRICK, MD
 Professor of Medicine and Health
 Management and Policy
 Schools of Medicine & Health
 University of Michigan
 Ann Arbor, MI



JOHN L. FOX, MD, MS
 Senior Medical Director and Vice President
 of Medical Affairs
 Priority Health
 Grand Rapids, MI



BO GAMBLE
 Director of Strategic Practice Initiatives
 Community Oncology Alliance
 Washington, DC



LUCIO GORDAN, MD
 Head, Quality and Medical Informatics
 Florida Cancer Specialists
 Gainesville, Florida



JOHN HORNBERGER, MD, MS
 Cedar Associates, LLC
 Menlo Park, CA



IRA M. KLEIN, MD, MBA
 Senior Director Quality
 Strategic Customer Group
 Janssen Pharmaceutical Companies



MICHAEL KOLODZIEJ, MD
 Vice President and Chief Innovation Officer
 ADVI Health LLC
 Washington, DC



KATHLEEN G. LOKAY
 CEO of Via Technology
 Pittsburgh, PA



ELLEN MATLOFF, MS, CGC
 President and CEO
 My Gene Counsel



JOSHUA J. OFMAN, MD, MSHA
 SVP, Global Value and Access
 Amgen, Inc
 Thousand Oaks, CA



DEBRA PATT, MD, MPH, MBA
 Texas Oncology Cancer Center
 Austin, TX



ANDREW L. PECORA, MD, FACP, CPE
 Chief Innovations Officer
 Vice President of Cancer Services
 John Theurer Cancer Center
 Hackensack, NJ



ERIN SULLIVAN, MPH, PHD
 Vice President, Health Economics and Outcomes Research
 Avalere Health
 Lexington, MA

 everyday
Verzenio[®]
abemaciclib
50 | 100 | 150 | 200 mg tablets
twice a day

Along the MBC journey* – explore Verzenio¹

Verzenio is indicated for the treatment of hormone receptor–positive (HR+), human epidermal growth factor receptor 2–negative (HER2–) advanced or metastatic breast cancer (MBC):

- In **combination with fulvestrant** for women with disease progression following endocrine therapy
- In **combination with an aromatase inhibitor (AI)** for postmenopausal women as initial endocrine-based therapy
- As a **single agent** for adult patients with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting

*Patients who received prior therapy with a CDK4 & 6 inhibitor were excluded from the MONARCH trials.²⁻⁴ There are currently no data regarding the use of Verzenio following use of another CDK4 & 6 inhibitor.



For patients with HR+, HER2– MBC, including those with concerning clinical characteristics^{1-14†}

†Disease characteristics that typically confer a less favorable prognosis. Visceral disease and progression on ET and prior chemotherapy in the metastatic setting were concerning clinical characteristics in MONARCH 1. Primary resistance and visceral disease were concerning clinical characteristics in MONARCH 2. Liver metastases and treatment-free interval <36 months were concerning clinical characteristics in MONARCH 3. Exploratory subgroup analyses of PFS were performed for patients with liver metastases and for patients with a treatment-free interval <36 months.²⁻¹⁴ CDK4 & 6=cyclin-dependent kinases 4 and 6; ET=endocrine therapy; PFS=progression-free survival.

Select Important Safety Information

Diarrhea occurred in 81% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 86% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and 90% of patients receiving Verzenio alone in MONARCH 1. Grade 3 diarrhea occurred in 9% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 13% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and in 20% of patients receiving Verzenio alone in MONARCH 1. Episodes of diarrhea have been associated with dehydration and infection.

Diarrhea incidence was greatest during the first month of Verzenio dosing. In MONARCH 3, the median time to onset of the first diarrhea event was 8 days, and the median duration of diarrhea for Grades 2 and 3 were 11 and 8 days, respectively. In MONARCH 2, the median time to onset of the first diarrhea event was 6 days, and the median duration of diarrhea for

Grades 2 and 3 were 9 days and 6 days, respectively. In MONARCH 3, 19% of patients with diarrhea required a dose omission and 13% required a dose reduction. In MONARCH 2, 22% of patients with diarrhea required a dose omission and 22% required a dose reduction. The time to onset and resolution for diarrhea were similar across MONARCH 3, MONARCH 2, and MONARCH 1.

Instruct patients that at the first sign of loose stools, they should start antidiarrheal therapy such as loperamide, increase oral fluids, and notify their healthcare provider for further instructions and appropriate follow-up. For Grade 3 or 4 diarrhea, or diarrhea that requires hospitalization, discontinue Verzenio until toxicity resolves to ≤Grade 1, and then resume Verzenio at the next lower dose.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information for Verzenio on the following pages.

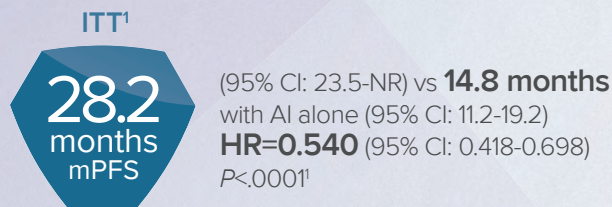
Lilly

Verzenio + AI

For women with HR+, HER2- MBC

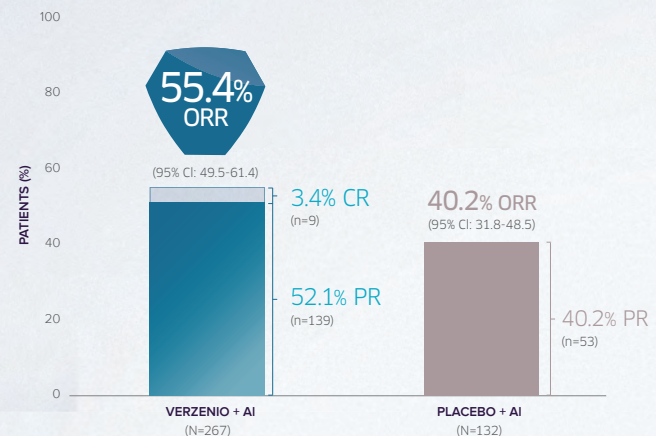
Verzenio + AI as first-line endocrine-based therapy^{1,3}

>28-month median PFS as initial endocrine-based therapy¹



- The percentage of events at the time of analysis was 42.1% (n=138) and 65.5% (n=108) in the Verzenio + AI and AI alone arms, respectively¹
- At the time of the PFS analysis, 19% of patients had died, and overall survival data were immature¹

ORR in patients with measurable disease^{1,3**†}



- ORR was defined as the proportion of patients with CR + PR and does not include stable disease¹

^{*}In patients with measurable disease; N=267 for the Verzenio + AI arm, N=132 for the AI alone arm.¹

^{**}Based upon confirmed responses.¹

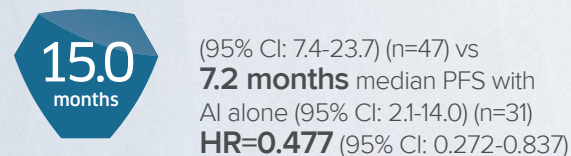
[†]PR defined as ≥30% reduction in target lesion size per RECIST 1.1.^{3,15}

Exploratory subgroup analyses

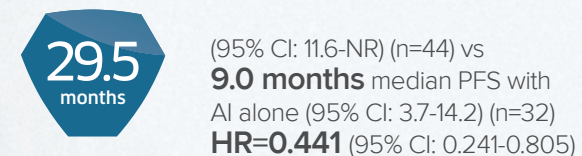
PFS results in women with concerning clinical characteristics were consistent with the ITT population^{1,3,9-14§}

[§]Disease characteristics that typically confer a less favorable prognosis. Liver metastases and treatment-free interval <36 months were concerning clinical characteristics in MONARCH 3.

Liver metastases¹³



Treatment-free interval <36 months¹⁴



- Exploratory subgroup analyses of PFS were performed for the subgroups of patients with liver metastases or with treatment-free interval <36 months after completion of adjuvant ET. Estimated HRs and CIs for the within group analyses that were adjusted for treatment interaction are shown. The analyses were not adjusted for multiplicity and the study was not powered to test the effect of Verzenio + AI among subgroups.^{13,14}

MONARCH 3 was a multicenter trial that enrolled 493 patients with HR+, HER2- locoregionally recurrent or MBC in combination with a nonsteroidal AI as initial endocrine-based therapy. The median patient age was 63 years (range, 32 to 88 years). Forty-seven percent of patients had received prior ET and 39% of patients had received chemotherapy in the adjuvant setting. Patients were randomized 2:1 to Verzenio + AI or placebo + AI. Patients received either letrozole (80%) or anastrozole (20%). Verzenio was dosed continuously until disease progression or unacceptable toxicity. The primary endpoint was PFS. Key secondary endpoints were ORR and DoR.^{1,3}

CI=confidence interval; CR=complete response; DoR=duration of response; HR=hazard ratio; ITT=intent-to-treat; NR=not reached; ORR=objective response rate; PR=partial response; RECIST 1.1= Response Evaluation Criteria in Solid Tumors version 1.1.

Select Important Safety Information (cont'd)

Neutropenia occurred in 41% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 46% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and 37% of patients receiving Verzenio alone in MONARCH 1. A Grade ≥3 decrease in neutrophil count (based on laboratory findings) occurred in 22% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 32% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and in 27% of patients receiving Verzenio alone in MONARCH 1. In MONARCH 3, the median time to first episode of Grade ≥3 neutropenia was 33 days, and in MONARCH 2 and MONARCH 1, was 29 days. In MONARCH 3, median duration of Grade ≥3 neutropenia was 11 days, and for MONARCH 2 and MONARCH 1 was 15 days.

Monitor complete blood counts prior to the start of Verzenio therapy, every 2 weeks for the first 2 months, monthly for the next 2 months,

and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

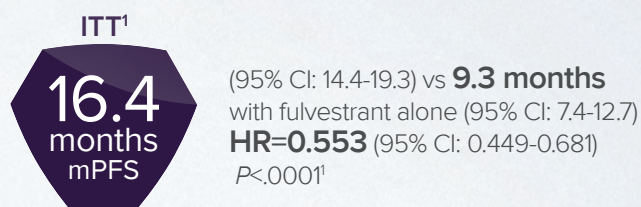
Febrile neutropenia has been reported in <1% of patients exposed to Verzenio in the MONARCH studies. Two deaths due to neutropenic sepsis were observed in MONARCH 2. Inform patients to promptly report any episodes of fever to their healthcare provider.

Grade ≥3 increases in **alanine aminotransferase (ALT)** (6% versus 2%) and **aspartate aminotransferase (AST)** (3% versus 1%) were reported in the Verzenio and placebo arms, respectively, in MONARCH 3. Grade ≥3 increases in ALT (4% versus 2%) and AST (2% versus 3%) were reported in the Verzenio and placebo arms respectively, in MONARCH 2.

For women with HR+, HER2- MBC

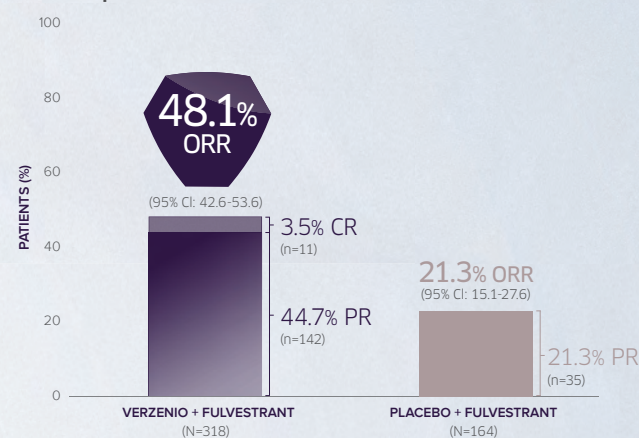
Verzenio + fulvestrant in patients who recurred or progressed on or after ET¹

>16-month median PFS in women who recurred or progressed on or after ET¹



- The percentage of events at the time of analysis was 49.8% (n=222) and 70.4% (n=157) in the Verzenio + fulvestrant and fulvestrant alone arms, respectively¹
- At the time of the primary analysis of PFS, overall survival data were not mature (20% of patients had died)¹

ORR in patients with measurable disease^{1,2,††}



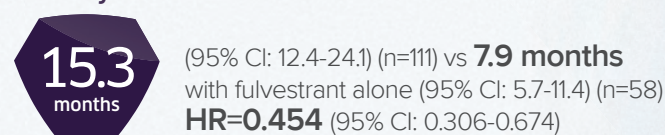
- ORR was defined as the proportion of patients with CR + PR, and does not include stable disease^{1,5†}

[†]N=318 for the Verzenio + fulvestrant arm; N=164 for the fulvestrant alone arm.
^{††}PR defined as ≥30% reduction in target lesion size per RECIST 1.1.^{2,5}

PFS results in women with concerning clinical characteristics were consistent with the ITT population^{1,2,5-8‡}

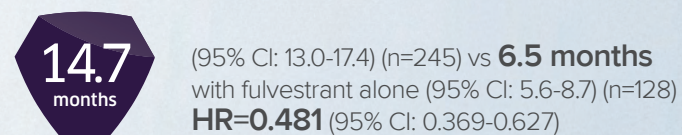
[‡]Disease characteristics that typically confer a less favorable prognosis. Primary resistance and visceral disease were concerning clinical characteristics in MONARCH 2.

Primary resistance¹⁶



- Primary resistance is defined as relapse while on the first 2 years of adjuvant endocrine therapy, or progressive disease within the first 6 months of first-line endocrine therapy for metastatic breast cancer¹
- Preplanned subgroup analyses of PFS were performed for stratification factors of disease site, including visceral disease, and endocrine resistance, including primary resistance. The analyses were not adjusted for multiplicity and the study was not powered to test the effect of Verzenio + fulvestrant among subgroups¹⁶

Visceral disease¹⁶



- Visceral disease was defined as at least 1 lesion on an internal organ or in the third space and could have included lung, liver, pleural, or peritoneal metastatic involvement¹⁷

MONARCH 2 was a phase III, randomized, double-blind, placebo-controlled trial that enrolled 669 patients with HR+, HER2- MBC who progressed on ET. Patients were randomized 2:1 to Verzenio + fulvestrant or placebo + fulvestrant. Verzenio was dosed on a continuous dosing schedule until disease progression or unacceptable toxicity. The primary endpoint was PFS. Key secondary endpoints were ORR, overall survival, and DoR.^{1,2}

Select Important Safety Information (cont'd)

In MONARCH 3, for patients receiving Verzenio plus an aromatase inhibitor with Grade ≥3 increases in ALT or AST, median time to onset was 61 and 71 days, respectively, and median time to resolution to Grade <3 was 14 and 15 days, respectively. In MONARCH 2, for patients receiving Verzenio plus fulvestrant with Grade ≥3 increases in ALT or AST, median time to onset was 57 and 185 days, respectively, and median time to resolution to Grade <3 was 14 and 13 days, respectively.

For assessment of potential **hepatotoxicity**, monitor liver function tests (LFTs) prior to the start of Verzenio therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, dose discontinuation, or delay in starting treatment cycles is recommended for patients who develop persistent or recurrent Grade 2, or Grade 3 or 4, hepatic transaminase elevation.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information for Verzenio on the following pages.

Venous thromboembolic events were reported in 5% of patients treated with Verzenio plus an aromatase inhibitor as compared to 0.6% of patients treated with an aromatase inhibitor plus placebo in MONARCH 3. Venous thromboembolic events were reported in 5% of patients treated with Verzenio plus fulvestrant in MONARCH 2 as compared to 0.9% of patients treated with fulvestrant plus placebo. Venous thromboembolic events included deep vein thrombosis, pulmonary embolism, pelvic venous thrombosis, cerebral venous sinus thrombosis, subclavian and axillary vein thrombosis, and inferior vena cava thrombosis. Across the clinical development program, deaths due to venous thromboembolism have been reported.

everyday
Verzenio
 abemaciclib
 50 | 100 | 150 | 200 mg tablets
 twice a day

Single agent

For heavily pretreated women with HR+, HER2- MBC

The only CDK4 & 6 inhibitor approved as a single agent¹

ORR¹



(95% CI: 13.3-27.5)
per investigator assessment¹
ORR was defined as the proportion of patients with CR + PR, and does not include stable disease^{1,15*}

- 17.4% ORR (95% CI: 11.4-25.0), per independent review¹

MONARCH 1 was a single-arm, open-label, multicenter study in 132 women with measurable HR+, HER2- MBC whose disease progressed during or after ET, had received a taxane in any setting, and who received 1 or 2 prior chemotherapy regimens in the metastatic setting. Patients had an Eastern Cooperative Oncology Group Performance Status of 0 (55% of patients) or 1 (45% of patients). Patients took 200 mg of Verzenio orally twice daily on a continuous schedule unless disease progression or unacceptable toxicity occurred. The primary endpoint was ORR. A key secondary endpoint was DoR.^{1,4}

Select Important Safety Information (cont'd)

Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate.

Verzenio can cause **fetal harm** when administered to a pregnant woman based on findings from animal studies and the mechanism of action. In animal reproduction studies, administration of abemaciclib to pregnant rats during the period of organogenesis caused teratogenicity and decreased fetal weight at maternal exposures that were similar to the human clinical exposure based on area under the curve (AUC) at the maximum recommended human dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Verzenio and for at least 3 weeks after the last dose. There are no data on the presence of Verzenio in human milk or its effects on the breastfed child or on milk production. Advise lactating women not to breastfeed during Verzenio treatment and for at least 3 weeks after the last dose because of the potential for serious adverse reactions in breastfed infants. Based on findings in animals, Verzenio may impair fertility in males of reproductive potential.

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 3 for Verzenio plus anastrozole or letrozole** and **≥2% higher than placebo plus anastrozole or letrozole vs placebo plus anastrozole or letrozole** were diarrhea (81% vs 30%), neutropenia (41% vs 2%), fatigue (40% vs 32%), infections (39% vs 29%), nausea (39% vs 20%), abdominal pain (29% vs 12%), vomiting (28% vs 12%), anemia (28% vs 5%), alopecia (27% vs 11%), decreased appetite (24% vs 9%), leukopenia (21% vs 2%), creatinine increased (19% vs 4%), constipation (16% vs 12%), ALT increased (16% vs 7%), AST increased (15% vs 7%), rash (14% vs 5%), pruritus (13% vs 9%), cough (13% vs 9%), dyspnea (12% vs 6%), dizziness (11% vs 9%), weight decreased (10% vs 3%), influenza-like illness (10% vs 8%), and thrombocytopenia (10% vs 2%).

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 2 for Verzenio plus fulvestrant** and **≥2% higher than**

Median duration of response (mDoR)^{1†}



- **3.7-month** median time to response (range: 1.1-14.2 months)^{4,18}
- **7.2-month mDoR** (95% CI: 5.6-NR), per independent review¹

*PR defined as ≥30% reduction in target lesion size per RECIST 1.1.^{4,15}

[†]Among 26 patients (investigator assessed) and 23 patients (independent review) who had a PR.¹

placebo plus fulvestrant vs placebo plus fulvestrant were diarrhea (86% vs 25%), neutropenia (46% vs 4%), fatigue (46% vs 32%), nausea (45% vs 23%), infections (43% vs 25%), abdominal pain (35% vs 16%), anemia (29% vs 4%), leukopenia (28% vs 2%), decreased appetite (27% vs 12%), vomiting (26% vs 10%), headache (20% vs 15%), dysgeusia (18% vs 3%), thrombocytopenia (16% vs 3%), alopecia (16% vs 2%), stomatitis (15% vs 10%), ALT increased (13% vs 5%), pruritus (13% vs 6%), cough (13% vs 11%), dizziness (12% vs 6%), AST increased (12% vs 7%), peripheral edema (12% vs 7%), creatinine increased (12% vs <1%), rash (11% vs 4%), pyrexia (11% vs 6%), and weight decreased (10% vs 2%).

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 1** with Verzenio were diarrhea (90%), fatigue (65%), nausea (64%), decreased appetite (45%), abdominal pain (39%), neutropenia (37%), vomiting (35%), infections (31%), anemia (25%), thrombocytopenia (20%), headache (20%), cough (19%), leukopenia (17%), constipation (17%), arthralgia (15%), dry mouth (14%), weight decreased (14%), stomatitis (14%), creatinine increased (13%), alopecia (12%), dysgeusia (12%), pyrexia (11%), dizziness (11%), and dehydration (10%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 3** were neutropenia (22% vs 2%), diarrhea (9% vs 1%), leukopenia (8% vs <1%), ALT increased (7% vs 2%), and anemia (6% vs 1%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 2** were neutropenia (27% vs 2%), diarrhea (13% vs <1%), leukopenia (9% vs 0%), anemia (7% vs 1%), and infections (6% vs 3%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** from **MONARCH 1** with Verzenio were neutropenia (24%), diarrhea (20%), fatigue (13%), infections (7%), leukopenia (6%), anemia (5%), and nausea (5%).

Abemaciclib (Verzenio®): recommended by the National Comprehensive Cancer Network® (NCCN®)¹⁹

Abemaciclib (Verzenio): the only CDK4 & 6 inhibitor recommended by NCCN in combination with fulvestrant or an AI and as a single agent¹⁹

CATEGORY 1*

Abemaciclib (Verzenio) + fulvestrant^{19†}

Recommended option for the treatment of postmenopausal women with HR+, HER2- MBC after disease progression on prior ET

Abemaciclib (Verzenio) + an AI^{19†}

Recommended option for the treatment of postmenopausal women with HR+, HER2- MBC as initial endocrine-based therapy

CATEGORY 2A‡

Abemaciclib (Verzenio) as a single agent^{19†}

Recommended option for the treatment of postmenopausal women with HR+, HER2-MBC after disease progression on prior ET and prior chemotherapy in the metastatic setting

*Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.¹⁹

†If there is disease progression while on CDK4 & 6 inhibitor therapy, there are no data to support an additional line of therapy with another CDK4 & 6-containing regimen.

‡Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.¹⁹

NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Select Important Safety Information (cont'd)

Lab abnormalities (all grades; Grade 3 or 4) for MONARCH 3 in ≥10% for Verzenio plus anastrozole or letrozole and ≥2% higher than placebo plus anastrozole or letrozole vs placebo plus anastrozole or letrozole were increased serum creatinine (98% vs 84%; 2% vs 0%), decreased white blood cells (82% vs 27%; 13% vs <1%), anemia (82% vs 28%; 2% vs 0%), decreased neutrophil count (80% vs 21%; 22% vs 3%), decreased lymphocyte count (53% vs 26%; 8% vs 2%), decreased platelet count (36% vs 12%; 2% vs <1%), increased ALT (48% vs 25%; 7% vs 2%), and increased AST (37% vs 23%; 4% vs <1%).

Lab abnormalities (all grades; Grade 3 or 4) for MONARCH 2 in ≥10% for Verzenio plus fulvestrant and ≥2% higher than placebo plus fulvestrant vs placebo plus fulvestrant were increased serum creatinine (98% vs 74%; 1% vs 0%), decreased white blood cells (90% vs 33%; 23% vs 1%), decreased neutrophil count (87% vs 30%; 33% vs 4%), anemia (84% vs 33%; 3% vs <1%), decreased lymphocyte count (63% vs 32%; 12% vs 2%), decreased platelet count (53% vs 15%; 2% vs 0%), increased ALT (41% vs 32%; 5% vs 1%), and increased AST (37% vs 25%; 4% vs 4%).

Lab abnormalities (all grades; Grade 3 or 4) for MONARCH 1 with Verzenio were increased serum creatinine (98%; <1%), decreased white blood cells (91%; 28%), decreased neutrophil count (88%; 27%), anemia (68%; 0%), decreased lymphocyte count (42%; 14%), decreased platelet count (41%; 2%), increased ALT (31%; 3%), and increased AST (30%; 4%).

Strong CYP3A inhibitors increased the exposure of abemaciclib plus its active metabolites to a clinically meaningful extent and may lead to increased toxicity. Avoid concomitant use of ketoconazole. Ketoconazole

is predicted to increase the AUC of abemaciclib by up to 16-fold. In patients with recommended starting doses of 200 mg twice daily or 150 mg twice daily, reduce the Verzenio dose to 100 mg twice daily with concomitant use of other strong CYP3A inhibitors. In patients who have had a dose reduction to 100 mg twice daily due to adverse reactions, further reduce the Verzenio dose to 50 mg twice daily with concomitant use of other strong CYP3A inhibitors. If a patient taking Verzenio discontinues a strong CYP3A inhibitor, increase the Verzenio dose (after 3 to 5 half-lives of the inhibitor) to the dose that was used before starting the strong inhibitor. Patients should avoid grapefruit products.

Avoid concomitant use of strong CYP3A inducers and consider alternative agents. Coadministration of Verzenio with rifampin, a strong CYP3A inducer, decreased the plasma concentrations of abemaciclib plus its active metabolites and may lead to reduced activity.

With severe hepatic impairment (Child-Pugh Class C), reduce the Verzenio dosing frequency to once daily. The pharmacokinetics of Verzenio in patients with **severe renal impairment** (CLcr <30 mL/min), end stage renal disease, or in patients on dialysis **is unknown**. No dosage adjustments are necessary in patients with mild or moderate hepatic (Child-Pugh A or B) and/or renal impairment (CLcr ≥30-89 mL/min).

AL HCP ISI 26FEB2018

Please see Brief Summary of full Prescribing Information for Verzenio on the following pages.

everyday
Verzenio
abemaciclib
50 | 100 | 150 | 200 mg tablets
twice a day



Please see Brief Summary of full Prescribing Information for Verzenio on the following pages.

References: **1.** Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2018. **2.** Sledge GW Jr, Toi M, Neven P, et al. MONARCH 2: abemaciclib in combination with fulvestrant in women with HR+/HER2- advanced breast cancer who had progressed while receiving endocrine therapy. *J Clin Oncol.* 2017;35:2875-2884. **3.** Goetz MP, Toi M, Campone M, et al. MONARCH 3: abemaciclib as initial therapy for advanced breast cancer. *J Clin Oncol.* 2017;35:3638-3646. **4.** Dickler MN, Tolaney SM, Rugo HS, et al. MONARCH 1, a phase II study of abemaciclib, a CDK4 and CDK6 inhibitor, as a single agent, in patients with refractory HR+/HER2- metastatic breast cancer. *Clin Cancer Res.* 2017;23:5218-5224. **5.** Imkamp A, Bendall S, Bates T. The significance of the site of recurrence to subsequent breast cancer survival. *Eur J Surg Oncol.* 2007;33:420-423. **6.** Largillier R, Ferrero JM, Doyen J, et al. Prognostic factors in 1038 women with metastatic breast cancer. *Ann Oncol.* 2008;19:2012-2019. **7.** Solomayer EF, Diel IJ, Meyberg GC, Gollan C, Bastert G. Metastatic breast cancer: clinical course, prognosis and therapy related to the first site of metastasis. *Breast Cancer Res Treat.* 2000;59:271-278. **8.** Cardoso F, Costa A, Senkus E, et al. 3rd ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 3). *Breast.* 2017;31:244-259. **9.** Gerratana L, Fanotto V, Bonotto M, et al. Pattern of metastasis and outcome in patients with breast cancer. *Clin Exp Metastasis.* 2015;32:125-133. **10.** Vogel CL, Azevedo S, Hilsenbeck S, East DR, Ayub J. Survival after first recurrence of breast cancer: the Miami experience. *Cancer.* 1992;70:129-135. **11.** Chang J, Clark GM, Allred DC, Mohsin S, Chamness G, Elledge RM. Survival of patients with metastatic breast carcinoma: importance of prognostic markers of the primary tumor. *Cancer.* 2003;97:545-553. **12.** Yamamoto N, Watanabe T, Katsumata N, et al. Construction and validation of a practical prognostic index for patients with metastatic breast cancer. *J Clin Oncol.* 1998;16:2401-2408. **13.** Data on file. Lilly USA, LLC. ONC20180108a. **14.** Data on file. Lilly USA, LLC. ONC20180328a. **15.** Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer.* 2009;45:228-247. **16.** Data on file. Lilly USA, LLC. ONC20180103a. **17.** Data on file. Lilly USA, LLC. ONC20171128a. **18.** Data on file. Lilly USA, LLC. ONC20171201a. **19.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.1.2018. © National Comprehensive Cancer Network, Inc. 2018. All rights reserved. Accessed March 22, 2018. To view the most recent and complete version of the guideline, go online to NCCN.org.

PP-AL-US-0970 05/2018 ©Lilly USA, LLC 2018. All rights reserved. Verzenio® is a registered trademark owned or licensed by Eli Lilly and Company, its subsidiaries or affiliates.

Verzenio[®]
abemaciclib
50 | 100 | 150 | 200 mg tablets

VERZENIO™ (abemaciclib) tablets, for oral use
Initial U.S. Approval: 2017

BRIEF SUMMARY: Consult the package insert for complete prescribing information.

INDICATIONS AND USAGE

VERZENIO™ (abemaciclib) is indicated:

- in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.
- in combination with fulvestrant for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.
- as monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS

Diarrhea

Diarrhea occurred in 81% of patients receiving VERZENIO plus an aromatase inhibitor in MONARCH 3, 86% of patients receiving VERZENIO plus fulvestrant in MONARCH 2, and 90% of patients receiving VERZENIO alone in MONARCH 1. Grade 3 diarrhea occurred in 9% of patients receiving VERZENIO plus an aromatase inhibitor in MONARCH 3, 13% of patients receiving VERZENIO plus fulvestrant in MONARCH 2, and in 20% of patients receiving VERZENIO alone in MONARCH 1. Episodes of diarrhea have been associated with dehydration and infection.

Diarrhea incidence was greatest during the first month of VERZENIO dosing. In MONARCH 3, the median time to onset of the first diarrhea event was 8 days, and the median duration of diarrhea for Grades 2 and 3 were 11 and 8 days, respectively. In MONARCH 2, the median time to onset of the first diarrhea event was 6 days, and the median duration of diarrhea for Grades 2 and 3 were 9 days and 6 days, respectively. In MONARCH 3, 19% of patients with diarrhea required a dose omission and 22% required a dose reduction. The time to onset and resolution for diarrhea were similar across MONARCH 3, MONARCH 2, and MONARCH 1.

Instruct patients that at the first sign of loose stools, they should start antidiarrheal therapy such as loperamide, increase oral fluids, and notify their healthcare provider for further instructions and appropriate follow up. For Grade 3 or 4 diarrhea, or diarrhea that requires hospitalization, discontinue VERZENIO until toxicity resolves to ≤Grade 1, and then resume VERZENIO at the next lower dose.

Neutropenia

Neutropenia occurred in 41% of patients receiving VERZENIO plus an aromatase inhibitor in MONARCH 3, 46% of patients receiving VERZENIO plus fulvestrant in MONARCH 2, and 37% of patients receiving VERZENIO alone in MONARCH 1. A Grade ≥3 decrease in neutrophil count (based on laboratory findings) occurred in 22% of patients receiving VERZENIO plus an aromatase inhibitor in MONARCH 3, 32% of patients receiving VERZENIO plus fulvestrant in MONARCH 2, and in 27% of patients receiving VERZENIO in MONARCH 1. In MONARCH 3, the median time to first episode of Grade ≥3 neutropenia was 33 days, and in MONARCH 2 and MONARCH 1 was 29 days. In MONARCH 3, median duration of Grade ≥3 neutropenia was 11 days, and for MONARCH 2 and MONARCH 1 was 15 days.

Monitor complete blood counts prior to the start of VERZENIO therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Febrile neutropenia has been reported in <1% of patients exposed to VERZENIO in the MONARCH studies. Two deaths due to neutropenic sepsis were observed in MONARCH 2. Inform patients to promptly report any episodes of fever to their healthcare provider.

Hepatotoxicity

In MONARCH 3, Grade ≥3 increases in ALT (6% versus 2%) and AST (3% versus 1%) were reported in the VERZENIO and placebo arms, respectively. In MONARCH 2, Grade ≥3 increases in ALT (4% versus 2%) and AST (2% versus 3%) were reported in the VERZENIO and placebo arms, respectively.

In MONARCH 3, for patients receiving VERZENIO plus an aromatase inhibitor with Grade ≥3 ALT increased, median time to onset was 61 days, and median time to resolution to Grade <3 was 14 days. In MONARCH 2, for patients receiving VERZENIO plus fulvestrant with Grade ≥3 ALT increased, median time to onset was 57 days, and median time to resolution to Grade <3 was 14 days. In MONARCH 3, for patients receiving VERZENIO plus an aromatase inhibitor with Grade ≥3 AST increased, median time to onset was 71 days, and median time to resolution was 15 days. In MONARCH 2, for patients receiving VERZENIO plus fulvestrant with Grade ≥3 AST increased, median time to onset was 185 days, and median time to resolution was 13 days.

Monitor liver function tests (LFTs) prior to the start of VERZENIO therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, dose discontinuation, or delay in starting treatment cycles is recommended for patients who develop persistent or recurrent Grade 2, or Grade 3 or 4, hepatic transaminase elevation.

Venous Thromboembolism

In MONARCH 3, venous thromboembolic events were reported in 5% of patients treated with VERZENIO plus an aromatase inhibitor as compared to 0.6% of patients treated with an aromatase inhibitor plus placebo. In MONARCH 2, venous thromboembolic events were reported in 5% of patients treated with VERZENIO plus fulvestrant as compared to 0.9% of patients treated with fulvestrant plus placebo. Venous thromboembolic events included deep vein thrombosis, pulmonary embolism, pelvic venous thrombosis, cerebral venous sinus thrombosis, subclavian and axillary vein thrombosis, and inferior vena cava thrombosis. Across the clinical development program, deaths due to venous thromboembolism have been reported.

VERZENIO™ (abemaciclib) tablets, for oral use

AL HCP BS 26FEB2018

Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate.

Embryo-Fetal Toxicity

Based on findings from animal studies and the mechanism of action, VERZENIO can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of abemaciclib to pregnant rats during the period of organogenesis caused teratogenicity and decreased fetal weight at maternal exposures that were similar to the human clinical exposure based on area under the curve (AUC) at the maximum recommended human dose.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with VERZENIO and for at least 3 weeks after the last dose.

ADVERSE REACTIONS

Clinical Studies 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.

MONARCH 3: VERZENIO in Combination with an Aromatase Inhibitor (Anastrozole or Letrozole) as Initial Endocrine-Based Therapy

Postmenopausal Women with HR-positive, HER2-negative locoregionally recurrent or metastatic breast cancer with no prior systemic therapy in this disease setting

MONARCH 3 was a study of 488 women receiving VERZENIO plus an aromatase inhibitor or placebo plus an aromatase inhibitor. Patients were randomly assigned to receive 150 mg of VERZENIO or placebo orally twice daily, plus physician's choice of anastrozole or letrozole once daily. Median duration of treatment was 15.1 months for the VERZENIO arm and 13.9 months for the placebo arm. Median dose compliance was 98% for the VERZENIO arm and 99% for the placebo arm.

Dose reductions due to an adverse reaction occurred in 43% of patients receiving VERZENIO plus anastrozole or letrozole. Adverse reactions leading to dose reductions in ≥5% of patients were diarrhea and neutropenia. VERZENIO dose reductions due to diarrhea of any grade occurred in 13% of patients receiving VERZENIO plus an aromatase inhibitor compared to 2% of patients receiving placebo plus an aromatase inhibitor. VERZENIO dose reductions due to neutropenia of any grade occurred in 11% of patients receiving VERZENIO plus an aromatase inhibitor compared to 0.6% of patients receiving placebo plus an aromatase inhibitor.

Permanent treatment discontinuation due to an adverse event was reported in 13% of patients receiving VERZENIO plus an aromatase inhibitor and in 3% placebo plus an aromatase inhibitor. Adverse reactions leading to permanent discontinuation for patients receiving VERZENIO plus an aromatase inhibitor were diarrhea (2%), ALT increased (2%), infection (1%), venous thromboembolic events (VTE) (1%), neutropenia (0.9%), renal impairment (0.9%), AST increased (0.6%), dyspnea (0.6%), pulmonary fibrosis (0.6%) and anemia, rash, weight decreased and thrombocytopenia (each 0.3%).

Deaths during treatment or during the 30-day follow up, regardless of causality, were reported in 11 cases (3%) of VERZENIO plus an aromatase inhibitor treated patients versus 3 cases (2%) of placebo plus an aromatase inhibitor treated patients. Causes of death for patients receiving VERZENIO plus an aromatase inhibitor included: 3 (1%) patient deaths due to underlying disease, 3 (0.9%) due to lung infection, 3 (0.9%) due to VTE event, 1 (0.3%) due to pneumonitis, and 1 (0.3%) due to cerebral infarction.

The most common adverse reactions reported (≥20%) in the VERZENIO arm and ≥2% than the placebo arm were diarrhea, neutropenia, fatigue, infections, nausea, abdominal pain, anemia, vomiting, alopecia, decreased appetite, and leukopenia (Table 6). The most frequently reported (≥5%) Grade 3 or 4 adverse reactions were neutropenia, diarrhea, leukopenia, increased ALT, and anemia. Diarrhea incidence was greatest during the first month of VERZENIO dosing. The median time to onset of the first diarrhea event was 8 days, and the median durations of diarrhea for Grades 2 and for Grade 3 were 11 days and 8 days, respectively. Most diarrhea events recovered or resolved (88%) with supportive treatment and/or dose reductions. Nineteen percent of patients with diarrhea required a dose omission and 13% required a dose reduction. The median time to the first dose reduction due to diarrhea was 38 days.

Table 6: Adverse Reactions ≥10% of Patients Receiving VERZENIO Plus Anastrozole or Letrozole and ≥2% Higher Than Placebo Plus Anastrozole or Letrozole in MONARCH 3

	VERZENIO plus Anastrozole or Letrozole N=327			Placebo plus Anastrozole or Letrozole N=161		
	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
Gastrointestinal Disorders						
Diarrhea	81	9	0	30	1	0
Nausea	39	<1	0	20	1	0
Abdominal pain	29	1	0	12	1	0
Vomiting	28	1	0	12	2	0
Constipation	16	<1	0	12	0	0
Infections and Infestations						
Infections ^a	39	4	<1	29	2	<1
Blood and Lymphatic System Disorders						
Neutropenia	41	20	2	2	<1	<1
Anemia	28	6	0	5	1	0
Leukopenia	21	7	<1	2	0	<1
Thrombocytopenia	10	2	<1	2	<1	0

VERZENIO™ (abemaciclib) tablets, for oral use

AL HCP BS 26FEB2018

Table 6: Adverse Reactions ≥10% of Patients Receiving VERZENIO Plus Anastrozole or Letrozole and ≥2% Higher Than Placebo Plus Anastrozole or Letrozole in MONARCH 3 (Cont.)

	VERZENIO plus Anastrozole or Letrozole N=327			Placebo plus Anastrozole or Letrozole N=161		
	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
General Disorders and Administration Site Conditions						
Fatigue	40	2	0	32	0	0
Influenza like illness	10	0	0	8	0	0
Skin and Subcutaneous Tissue Disorders						
Alopecia	27	0	0	11	0	0
Rash	14	<1	0	5	0	0
Pruritus	13	0	0	9	0	0
Metabolism and Nutrition Disorders						
Decreased appetite	24	1	0	9	<1	0
Investigations						
Blood creatinine increased	19	2	0	4	0	0
Alanine aminotransferase increased	16	6	<1	7	2	0
Aspartate aminotransferase increased	15	3	0	7	1	0
Weight decreased	10	<1	0	3	<1	0
Respiratory, Thoracic, and Mediastinal Disorders						
Cough	13	0	0	9	0	0
Dyspnea	12	<1	<1	6	<1	0
Nervous System Disorders						
Dizziness	11	<1	0	9	0	0

^a Includes all reported preferred terms that are part of the Infections and Infestations system organ class. Most common infections (>1%) include upper respiratory tract infection, lung infection, and pharyngitis.

Additional adverse reactions in MONARCH 3 include venous thromboembolic events (deep vein thrombosis, pulmonary embolism, and pelvic venous thrombosis), which were reported in 5% of patients treated with VERZENIO plus anastrozole or letrozole as compared to 0.6% of patients treated with anastrozole or letrozole plus placebo.

Table 7: Laboratory Abnormalities ≥10% in Patients Receiving VERZENIO Plus Anastrozole or Letrozole and ≥2% Higher Than Placebo Plus Anastrozole or Letrozole in MONARCH 3

Laboratory Abnormality	VERZENIO plus Anastrozole or Letrozole N=327			Placebo plus Anastrozole or Letrozole N=161		
	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
Creatinine increased	98	2	0	84	0	0
White blood cell decreased	82	13	0	27	<1	0
Anemia	82	2	0	28	0	0
Neutrophil count decreased	80	19	3	21	3	0
Lymphocyte count decreased	53	7	<1	26	2	0
Platelet count decreased	36	1	<1	12	<1	0
Alanine aminotransferase increased	48	6	<1	25	2	0
Aspartate aminotransferase increased	37	4	0	23	<1	0

Creatinine Increased

Abemaciclib has been shown to increase serum creatinine due to inhibition of renal tubular secretion transporters, without affecting glomerular function. Across the clinical studies, increases in serum creatinine (mean increase, 0.2-0.3 mg/dL) occurred within the first 28-day cycle of VERZENIO dosing, remained elevated but stable through the treatment period, and were reversible upon treatment discontinuation. Alternative markers such as BUN, cystatin C, or calculated GFR, which are not based on creatinine, may be considered to determine whether renal function is impaired.

MONARCH 2: VERZENIO in Combination with Fulvestrant

Women with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression on or after prior adjuvant or metastatic endocrine therapy

The safety of VERZENIO (150 mg twice daily) plus fulvestrant (500 mg) versus placebo plus fulvestrant was evaluated in MONARCH 2. The data described below reflect exposure to VERZENIO in 441 patients with HR-positive, HER2-negative advanced breast cancer who received at least one dose of VERZENIO plus fulvestrant in MONARCH 2.

Median duration of treatment was 12 months for patients receiving VERZENIO plus fulvestrant and 8 months for patients receiving placebo plus fulvestrant.

Dose reductions due to an adverse reaction occurred in 43% of patients receiving VERZENIO plus fulvestrant. Adverse reactions leading to dose reductions in ≥5% of patients were diarrhea and neutropenia. VERZENIO dose reductions due to diarrhea of any grade occurred in 19% of patients receiving VERZENIO plus fulvestrant compared to 0.4% of patients receiving placebo and fulvestrant. VERZENIO dose reductions due to neutropenia of any grade occurred in 10% of patients receiving VERZENIO plus fulvestrant compared to no patients receiving placebo plus fulvestrant.

VERZENIO™ (abemaciclib) tablets, for oral use

AL HCP BS 26FEB2018

Permanent study treatment discontinuation due to an adverse event was reported in 9% of patients receiving VERZENIO plus fulvestrant and in 3% of patients receiving placebo plus fulvestrant. Adverse reactions leading to permanent discontinuation for patients receiving VERZENIO plus fulvestrant were infection (2%), diarrhea (1%), hepatotoxicity (1%), fatigue (0.7%), nausea (0.2%), abdominal pain (0.2%), acute kidney injury (0.2%), and cerebral infarction (0.2%).

Deaths during treatment or during the 30-day follow up, regardless of causality, were reported in 18 cases (4%) of VERZENIO plus fulvestrant treated patients versus 10 cases (5%) of placebo plus fulvestrant treated patients. Causes of death for patients receiving VERZENIO plus fulvestrant included: 7 (2%) patient deaths due to underlying disease, 4 (0.9%) due to sepsis, 2 (0.5%) due to pneumonitis, 2 (0.5%) due to hepatotoxicity, and one (0.2%) due to cerebral infarction.

The most common adverse reactions reported (≥20%) in the VERZENIO arm were diarrhea, fatigue, neutropenia, nausea, infections, abdominal pain, anemia, leukopenia, decreased appetite, vomiting, and headache (Table 8). The most frequently reported (≥5%) Grade 3 or 4 adverse reactions were neutropenia, diarrhea, leukopenia, anemia, and infections.

Table 8: Adverse Reactions ≥10% in Patients Receiving VERZENIO Plus Fulvestrant and ≥2% Higher Than Placebo Plus Fulvestrant in MONARCH 2

	VERZENIO plus Fulvestrant N=441			Placebo plus Fulvestrant N=223		
	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
Gastrointestinal Disorders						
Diarrhea	86	13	0	25	<1	0
Nausea	45	3	0	23	1	0
Abdominal Pain ^a	35	2	0	16	1	0
Vomiting	26	<1	0	10	2	0
Stomatitis	15	<1	0	10	0	0
Infections and Infestations						
Infections ^b	43	5	<1	25	3	<1
Blood and Lymphatic System Disorders						
Neutropenia ^c	46	24	3	4	1	<1
Anemia ^d	29	7	<1	4	1	0
Leukopenia ^e	28	9	<1	2	0	0
Thrombocytopenia ^f	16	2	1	3	0	<1
General Disorders and Administration Site Conditions						
Fatigue ^g	46	3	0	32	<1	0
Edema peripheral	12	0	0	7	0	0
Pyrexia	11	<1	<1	6	<1	0
Metabolism and Nutrition Disorders						
Decreased appetite	27	1	0	12	<1	0
Respiratory, Thoracic and Mediastinal Disorders						
Cough	13	0	0	11	0	0
Skin and Subcutaneous Tissue Disorders						
Alopecia	16	0	0	2	0	0
Pruritus	13	0	0	6	0	0
Rash	11	1	0	4	0	0
Nervous System Disorders						
Headache	20	1	0	15	<1	0
Dysgeusia	18	0	0	3	0	0
Dizziness	12	1	0	6	0	0
Investigations						
Alanine aminotransferase increased	13	4	<1	5	2	0
Aspartate aminotransferase increased	12	2	0	7	3	0
Creatinine increased	12	<1	0	<1	0	0
Weight decreased	10	<1	0	2	<1	0

^a Includes abdominal pain, abdominal pain upper, abdominal pain lower, abdominal discomfort, abdominal tenderness.

^b Includes upper respiratory tract infection, urinary tract infection, lung infection, pharyngitis, conjunctivitis, sinusitis, vaginal infection, sepsis.

^c Includes neutropenia, neutrophil count decreased.

^d Includes anemia, hematocrit decreased, hemoglobin decreased, red blood cell count decreased.

^e Includes leukopenia, white blood cell count decreased.

^f Includes platelet count decreased, thrombocytopenia.

^g Includes asthenia, fatigue.

Additional adverse reactions in MONARCH 2 include venous thromboembolic events (deep vein thrombosis, pulmonary embolism, cerebral venous sinus thrombosis, subclavian vein thrombosis, axillary vein thrombosis, and DVT inferior vena cava), which were reported in 5% of patients treated with VERZENIO plus fulvestrant as compared to 0.9% of patients treated with fulvestrant plus placebo.

VERZENIO™ (abemaciclib) tablets, for oral use

AL HCP BS 26FEB2018

Table 9: Laboratory Abnormalities ≥10% in Patients Receiving VERZENIO Plus Fulvestrant and ≥2% Higher Than Placebo Plus Fulvestrant in MONARCH 2

	VERZENIO plus Fulvestrant N=441			Placebo plus Fulvestrant N=223		
	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
Creatinine increased	98	1	0	74	0	0
White blood cell decreased	90	23	<1	33	<1	0
Neutrophil count decreased	87	29	4	30	4	<1
Anemia	84	3	0	33	<1	0
Lymphocyte count decreased	63	12	<1	32	2	0
Platelet count decreased	53	<1	1	15	0	0
Alanine aminotransferase increased	41	4	<1	32	1	0
Aspartate aminotransferase increased	37	4	0	25	4	<1

Creatinine Increased

Abemaciclib has been shown to increase serum creatinine due to inhibition of renal tubular secretion transporters, without affecting glomerular function. In clinical studies, increases in serum creatinine (mean increase, 0.2 mg/dL) occurred within the first 28-day cycle of VERZENIO dosing, remained elevated but stable through the treatment period, and were reversible upon treatment discontinuation. Alternative markers such as BUN, cystatin C, or calculated glomerular filtration rate (GFR), which are not based on creatinine, may be considered to determine whether renal function is impaired.

VERZENIO Administered as a Monotherapy in Metastatic Breast Cancer (MONARCH 1)

Patients with HR-positive, HER2-negative breast cancer who received prior endocrine therapy and 1-2 chemotherapy regimens in the metastatic setting

Safety data below are based on MONARCH 1, a single-arm, open-label, multicenter study in 132 women with measurable HR+, HER2- metastatic breast cancer. Patients received 200 mg VERZENIO orally twice daily until development of progressive disease or unmanageable toxicity. Median duration of treatment was 4.5 months.

Ten patients (8%) discontinued study treatment from adverse reactions due to (1 patient each) abdominal pain, arterial thrombosis, aspartate aminotransferase (AST) increased, blood creatinine increased, chronic kidney disease, diarrhea, ECG QT prolonged, fatigue, hip fracture, and lymphopenia. Forty-nine percent of patients had dose reductions due to an adverse reaction. The most frequent adverse reactions that led to dose reductions were diarrhea (20%), neutropenia (11%), and fatigue (9%).

Deaths during treatment or during the 30-day follow up were reported in 2% of patients. Cause of death in these patients was due to infection.

The most common reported adverse reactions (≥20%) were diarrhea, fatigue, nausea, decreased appetite, abdominal pain, neutropenia, vomiting, infections, anemia, headache, and thrombocytopenia (Table 10). Severe (Grade 3 and 4) neutropenia was observed in patients receiving abemaciclib.

Table 10: Adverse Reactions (≥10% of Patients) in MONARCH 1

	VERZENIO N=132		
	All Grades %	Grade 3 %	Grade 4 %
Gastrointestinal Disorders			
Diarrhea	90	20	0
Nausea	64	5	0
Abdominal pain	39	2	0
Vomiting	35	2	0
Constipation	17	<1	0
Dry mouth	14	0	0
Stomatitis	14	0	0
Infections and Infestations			
Infections	31	5	2
General Disorders and Administration Site Conditions			
Fatigue ^a	65	13	0
Pyrexia	11	0	0
Blood and Lymphatic System Disorders			
Neutropenia ^b	37	19	5
Anemia ^c	25	5	0
Thrombocytopenia ^d	20	4	0
Leukopenia ^e	17	5	<1
Metabolism and Nutrition Disorders			
Decreased appetite	45	3	0
Dehydration	10	2	0
Respiratory, Thoracic and Mediastinal Disorders			
Cough	19	0	0

VERZENIO™ (abemaciclib) tablets, for oral use

AL HCP BS 26FEB2018

Table 10: Adverse Reactions (≥10% of Patients) in MONARCH 1 (Cont.)

	VERZENIO N=132		
	All Grades %	Grade 3 %	Grade 4 %
Musculoskeletal and Connective Tissue Disorders			
Arthralgia	15	0	0
Nervous System Disorders			
Headache	20	0	0
Dysgeusia	12	0	0
Dizziness	11	0	0
Skin and Subcutaneous Tissue Disorders			
Alopecia	12	0	0
Investigations			
Creatinine increased	13	<1	0
Weight decreased	14	0	0

^a Includes asthenia, fatigue.

^b Includes neutropenia, neutrophil count decreased.

^c Includes anemia, hematocrit decreased, hemoglobin decreased, red blood cell count decreased.

^d Includes platelet count decreased, thrombocytopenia.

^e Includes leukopenia, white blood cell count decreased.

Table 11: Laboratory Abnormalities for Patients Receiving VERZENIO in MONARCH 1

	VERZENIO N=132		
	All Grades %	Grade 3 %	Grade 4 %
Creatinine increased	98	<1	0
White blood cell decreased	91	28	0
Neutrophil count decreased	88	22	5
Anemia	68	0	0
Lymphocyte count decreased	42	13	<1
Platelet count decreased	41	2	0
ALT increased	31	3	0
AST increased	30	4	0

Creatinine Increased

Abemaciclib has been shown to increase serum creatinine due to inhibition of renal tubular secretion transporters, without affecting glomerular function. In clinical studies, increases in serum creatinine (mean increase, 0.3 mg/dL) occurred within the first 28-day cycle of VERZENIO dosing, remained elevated but stable through the treatment period, and were reversible upon treatment discontinuation. Alternative markers such as BUN, cystatin C, or calculated GFR, which are not based on creatinine, may be considered to determine whether renal function is impaired.

DRUG INTERACTIONS

Effect of Other Drugs on VERZENIO

Strong CYP3A Inhibitors

Strong CYP3A inhibitors increased the exposure of abemaciclib plus its active metabolites to a clinically meaningful extent and may lead to increased toxicity.

Ketoconazole

Avoid concomitant use of ketoconazole. Ketoconazole is predicted to increase the AUC of abemaciclib by up to 16-fold.

Other Strong CYP3A Inhibitors

In patients with recommended starting doses of 200 mg twice daily or 150 mg twice daily, reduce the VERZENIO dose to 100 mg twice daily with concomitant use of other strong CYP3A inhibitors. In patients who have had a dose reduction to 100 mg twice daily due to adverse reactions, further reduce the VERZENIO dose to 50 mg twice daily with concomitant use of other strong CYP3A inhibitors. If a patient taking VERZENIO discontinues a strong CYP3A inhibitor, increase the VERZENIO dose (after 3-5 half-lives of the inhibitor) to the dose that was used before starting the strong inhibitor. Patients should avoid grapefruit products.

Strong CYP3A Inducers

Coadministration of VERZENIO with rifampin, a strong CYP3A inducer, decreased the plasma concentrations of abemaciclib plus its active metabolites and may lead to reduced activity. Avoid concomitant use of strong CYP3A inducers and consider alternative agents.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on findings in animals and its mechanism of action, VERZENIO can cause fetal harm when administered to a pregnant woman. There are no available human data informing the drug-associated risk. Advise pregnant women of the potential risk to a fetus. In animal reproduction studies, administration of abemaciclib during organogenesis was

VERZENIO™ (abemaciclib) tablets, for oral use

AL HCP BS 26FEB2018

teratogenic and caused decreased fetal weight at maternal exposures that were similar to human clinical exposure based on AUC at the maximum recommended human dose (see Data). Advise pregnant women of the potential risk to a fetus.

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

Data

Animal Data

In an embryo-fetal development study, pregnant rats received oral doses of abemaciclib up to 15 mg/kg/day during the period of organogenesis. Doses ≥ 4 mg/kg/day caused decreased fetal body weights and increased incidence of cardiovascular and skeletal malformations and variations. These findings included absent innominate artery and aortic arch, malpositioned subclavian artery, unossified sternebra, bipartite ossification of thoracic centrum, and rudimentary or nodulated ribs. At 4 mg/kg/day in rats, the maternal systemic exposures were approximately equal to the human exposure (AUC) at the recommended dose.

Lactation

Risk Summary

There are no data on the presence of abemaciclib in human milk, or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed infants from VERZENIO, advise lactating women not to breastfeed during VERZENIO treatment and for at least 3 weeks after the last dose.

Females and Males of Reproductive Potential

Pregnancy Testing

Based on animal studies, VERZENIO can cause fetal harm when administered to a pregnant woman. Pregnancy testing is recommended for females of reproductive potential prior to initiating treatment with VERZENIO.

Contraception

Females

VERZENIO can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during VERZENIO treatment and for at least 3 weeks after the last dose.

Infertility

Males

Based on findings in animals, VERZENIO may impair fertility in males of reproductive potential.

Pediatric Use

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

Geriatric Use

Of the 900 patients who received VERZENIO in MONARCH 1, MONARCH 2, and MONARCH 3, 38% were 65 years of age or older and 10% were 75 years of age or older. The most common adverse reactions ($\geq 5\%$) Grade 3 or 4 in patients ≥ 65 years of age across MONARCH 1, 2, and 3 were neutropenia, diarrhea, fatigue, nausea, dehydration, leukopenia, anemia, infections, and ALT increased. No overall differences in safety or effectiveness of VERZENIO were observed between these patients and younger patients.

Renal Impairment

No dosage adjustment is required for patients with mild or moderate renal impairment (CLcr ≥ 30 -89 mL/min, estimated by Cockcroft-Gault [C-G]). The pharmacokinetics of abemaciclib in patients with severe renal impairment (CLcr < 30 mL/min, C-G), end stage renal disease, or in patients on dialysis is unknown.

Hepatic Impairment

No dosage adjustments are necessary in patients with mild or moderate hepatic impairment (Child-Pugh A or B). Reduce the dosing frequency when administering VERZENIO to patients with severe hepatic impairment (Child-Pugh C).

OVERDOSAGE

There is no known antidote for VERZENIO. The treatment of overdose of VERZENIO should consist of general supportive measures.

Rx only.

Additional information can be found at www.verzenio.com.



Eli Lilly and Company, Indianapolis, IN 46285, USA

Copyright ©2018, Eli Lilly and Company. All rights reserved.

AL HCP BS 26FEB2018

PP-AL-US-0833

VERZENIO™ (abemaciclib) tablets, for oral use

AL HCP BS 26FEB2018

SPECIAL ISSUE / Survivorship

AUGUST 2018

VOLUME 24, ISSUE 10

PUBLICATION STAFF

SENIOR VICE PRESIDENT,
MANAGED MARKETS
Jeff Prescott, PharmD

COPY CHIEF
Jennifer Potash

ASSOCIATE EDITORIAL
DIRECTOR
**Surabhi Dangi-Garimella,
PhD**

COPY EDITORS
**Maggie Shaw
Rachelle Laliberte
Paul Silverman**

MANAGING EDITOR
Mary Caffrey

DESIGNER
Brianna Gibb

ASSISTANT EDITOR
Samantha DiGrande

SALES & MARKETING

DIRECTOR OF SALES
Gilbert Hernandez

NATIONAL ACCOUNTS
ASSOCIATE
Ryan O'Leary

OPERATIONS & FINANCE

CIRCULATION DIRECTOR
Jon Severn

VICE PRESIDENT, FINANCE
Leah Babitz, CPA

CONTROLLER
Katherine Wyckoff

CORPORATE OFFICERS

CHAIRMAN AND CEO
Mike Hennessy, Sr

VICE PRESIDENT, CORPORATE
DEVELOPMENT AND
INTEGRATION
Dave Heckard

VICE CHAIRMAN
Jack Lepping

VICE PRESIDENT, EDITORIAL
SERVICES AND PRODUCTION
Kerrie Keegan

PRESIDENT
Mike Hennessy, Jr

VICE PRESIDENT,
DIGITAL MEDIA
Jung Kim

CHIEF OPERATING OFFICER
George Glatcz

CHIEF CREATIVE OFFICER
Jeff Brown

CHIEF FINANCIAL OFFICER
Neil Glasser, CPA/CFE

DIRECTOR, HUMAN
RESOURCES
Shari Lundenberg

SENIOR VICE PRESIDENT,
OPERATIONS
Tom Tolvé



Scan here to subscribe
ajmc.com/subscribe.



2 Clarke Drive, Suite 100
Cranbury, NJ 08512 • (609) 716-7777

Copyright © 2018 by Managed Care & Healthcare Communications, LLC
The American Journal of Managed Care® ISSN 1088-0224 (print) & ISSN 1936-2692 (online) is published monthly by Managed Care & Healthcare Communications, LLC, 2 Clarke Drive, Suite 100, Cranbury, NJ 08512. Copyright © 2018 by Managed Care & Healthcare Communications, LLC.
All rights reserved. As provided by US copyright law, no part of this publication may be reproduced, displayed, or transmitted in any form or by any means, electronic or mechanical, without the prior written permission of the publisher. For subscription inquiries or change of address, please call 888-826-3066. For permission to photocopy or reuse material from this journal, please contact the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923; Tel: 978-750-8400; Web: www.copyright.com. Reprints of articles are available in minimum quantities of 250 copies.
To order custom reprints, please contact Jeff Prescott, The American Journal of Managed Care®, jprescott@ajmc.com; Tel: 609-716-7777. The American Journal of Managed Care is a registered trademark of Managed Care & Healthcare Communications, LLC. www.ajmc.com • Printed on acid-free paper.



INSIDE THIS ISSUE
SP421

Boomer, the mascot for the Trenton Thunder minor league baseball team, greets board members and supporters of Thea's Star of Hope during a benefit in June. In the center are members of the Danze family: Lilly, age 6; Trisha; Thea, age 11; and Jeff. Thea's Star of Hope raises funds to find treatments for pediatric brain tumors with fewer side effects.



Trisha Danze, center; Jeff Danze, right, with Thea, and board members present a check to Children's Hospital of Philadelphia.



Board members and supporters of Thea's Star of Hope at the Trenton Thunder benefit pregame ceremony, held June 10.

FEATURES

SP438
CLINICAL PRACTICE
Survivorship Care Throughout the Cancer Journey

DON CHAMPLAIN, MHA, RN,
AND LUCIO GORDAN, MD

SP440
COST PERSPECTIVE
Healthcare Costs and Access for Young Adult Cancer Survivors: A Snapshot Post ACA

MICHELLE S. LANDWEHR, MPH;
SAMANTHA E. WATSON, MBA;
AND MAIA DOLPHIN-KRUTE, BFA

SP442
PAYER PERSPECTIVE
CareMore's Togetherness Program Addresses a Symptom of Living With Chronic Illness: Loneliness

ROBIN CARUSO, MSW, LCSW

INSIDE THE ISSUE

SP406
FROM THE EDITOR-IN-CHIEF
What Happens Next?

JOSEPH ALVARNAS, MD

SP418
FROM THE CHAIRMAN
Success of Cancer Treatment Means Rethinking Survivorship

SP419
ADOLESCENTS AND YOUNG ADULTS
Survivorship Care in AYA Patients: Battling the Loss to Follow-up

WITH LYNDA KWON BEAUPIN, MD

SP421
REDUCING ADVERSE EFFECTS
A Family's Search for Better Treatment, Survival From Pediatric Brain Tumors



CareMore client Virta Woodward, right, meets with CareMore Care Connector Armando Contreras at Woodward's home in California. The CareMore Togetherness program seeks to address loneliness in seniors with chronic conditions, to improve health outcomes and reduce costs.

SP423-SP426
AJMC® STAFF CONFERENCE
COVERAGE: NCCN POLICY
SUMMIT 2018

Gottlieb Calls on Payers to Share Data to Aid Drug Innovation

Paying for Innovation in Cancer Care Means No Easy Answers

Narrow Networks in Cancer Care: Tough on Patients but Here to Stay

Cancer Survivors Caucus Seeks to Find Common Ground in Congress



SP427-SP429
MANAGED CARE UPDATES
Feedback on the Direction, Challenges of the OCM

Experts Suggest Prioritizing Price and Benefit, Allowing Negotiations for Targeted Cancer Drugs

Study Suggests HPV Test More Accurate Than Pap Smear for Cervical Cancer Screening

Senate Judiciary Committee Votes to Advance CREATES Act

SP429-SP431
CLINICAL UPDATES
BrainChild-01 Will Evaluate CART Cells in Pediatric CNS Tumors

Research Highlights Long-Term Survival and Health-Related QoL in Patients With Newly Diagnosed MM

Glasdegib Receives Priority Review Based on Results That Show Nearly Doubled OS in AML

PTAB Denies Samsung Bioepis' Request for IPR on Herceptin Patent

Progress Continues for Celltrion on Trastuzumab and Subcutaneous Infliximab Biosimilars



SP436-SP437
AJMC®TV INTERVIEWS
Denalee O'Malley, PhD, LSW, Instructor, Department of Family Medicine and Community Health, Research Division, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey

Don Dizon, MD, FACP, Director of Women's Cancers, Lifespan Cancer Institute; Clinical Director, Gynecologic Medical Oncology and Director of Medical Oncology, Rhode Island Hospital in Providence

Leonard B. Saltz, MD, Executive Director of Clinical Value and Sustainability, Head of Colorectal Oncology Section, Memorial Sloan Kettering Cancer Center

Hope Rugo, MD, Director of the Breast Oncology Clinical Trials Program at the University of California at San Francisco

Success of Cancer Treatment Means Rethinking Survivorship

CANCER KILLS. But thanks to extraordinary scientific advances and better therapies, many who are diagnosed with cancer have life spans that were once unimaginable. Five-year survival rates for all cancers have jumped from 49% to 69% since the 1970s, and the rates for breast and prostate cancer are now above 90%, according to federal data analyzed by the American Cancer Society.¹

With that success comes the need to help those who have survived cancer live productively and restore life before cancer as much as possible. Survivorship care has emerged as a priority, as both researchers and payers recognize that proactive steps to address medical and behavioral health, as well as social needs, not only improve quality of life but also translate into healthcare savings. In this issue, we hear from a leading community oncology group, Florida Cancer Specialists, where survivorship care is an art fueled by modern data tools.

Despite success, gaps remain. There's still much we don't know, for example, about the long-term effects of some treatments on our youngest patients. In this issue, we learn the story of the Danze family. After seeing the effects of treatment for a slow-growing glioma on their oldest daughter, Thea, Trisha and Jeff Danze of Robbinsville, New Jersey, created a foundation to raise money to develop less toxic therapies for children with cancer.

Increasingly, the financial toll of cancer affects both the health and life choices of adolescent and young adult patients. Authors from The Samfund offer a snapshot of the challenges this age group faces. Although passage of the Affordable Care Act has given thousands of survivors access to healthcare, coverage can be costly and restrictive, and patients shared with researchers some horror stories of having to abandon medical teams because of benefit changes. An expert on survivors in this age group, Lynda Kwon Beaupin, MD, says that physicians often fail to emphasize the need for follow-up care, and too many young adults don't get the information they need to help them make key decisions about future fertility.

Rethinking survivorship means planning for life. It means survivorship care starts at diagnosis and continues with proper care management and shared decision making. It means educating physicians to have informed, productive conversations with patients about their goals. It means taking a team-based approach to care so that patients have access to nursing, mental health, and nutrition experts who will help them stay healthy and out of the hospital.

It means letting survivors know they are not alone. ♦

REFERENCE

American Cancer Society. Cancer facts and figures 2018. American Cancer Society website. cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2018.html#. Accessed July 19, 2018.

Sincerely,

Mike Hennessy, Sr
CHAIRMAN AND CEO

ADOLESCENTS AND YOUNG ADULTS

Survivorship Care in AYA Patients: Battling the Loss to Follow-up

Samantha DiGrande

CANCER SURVIVORS OF ANY age are at risk of many adverse effects once their treatment is completed, but 1 risk is often overlooked: being “lost to follow-up.”

Adolescent and young adult (AYA) cancer survivors are at a particularly high risk of being lost to follow-up, which means the patient has not had any form of contact with a physician since completion of treatment. If cancer survivors are not being seen for routine care, their primary care physicians are no longer aware of conditions or risk factors that these patients may be exhibiting. That’s a problem, because this population has unique risks for certain heart problems, infertility, and secondary cancers that may arise from previous treatment.

The AYA cancer population is defined as patients aged 15 to 39 years. Within this cohort, about 70,000 people are diagnosed with cancer each year in the United States, accounting for about 5% of total cancer diagnoses in the United States.¹ In recent years, investigators found that AYA patients with cancer are now expected to live past the 5-year mark, though survival and health outcomes seem to differ by disease type, according to recent research.²

For insights on this issue, *Evidence-Based Oncology*TM spoke with Lynda Kwon Beaupin, MD, a pediatric hematologist-oncologist who recently became the director of CanSurvive, the pediatric cancer survivorship program at Johns Hopkins All Children’s Hospital in St. Petersburg, Florida. Beaupin and her colleagues in the Consortium of Adolescent and Young Adult Cancer Centers, which includes oncologists from major cancer centers including Johns Hopkins,³ are working to address the nuances that come with treating AYA patients with cancer and looking for ways to improve their quality of life.

The AYA Cohort: A Different Breed of Patient

The concept of survivorship care is fairly new among young adult patients with cancer, according to Beaupin. For pediatric patients, the transition to surveillance and long-term care after completing treatment has become standard—that’s been done in the field for many years. However, for a young adult or adolescent cancer survivor, the years after treatment may be approached quite differently.

Pediatric centers tend to unify young patients who are being treated for similar diseases. Conversely, in the “adult cancer world,” Beaupin said, patients are unified by age, not by disease type or where they were once treated, and the focus is generally on the type of treatment they receive. Once treatment ends, there isn’t a defined period of long-term survivorship care, as is traditionally seen in pediatric cancer, she said.

“I think maybe the lack of stressing that they have ongoing risks beyond finishing their cancer treatment hasn’t been at the forefront, and therefore, [the importance of follow-up is] not obvious to them,” Beaupin said. “In turn, we’re not seeing them as much as we would like, years from their diagnosis and completion of treatment.”

Physicians often do not stress to AYA patients the need for follow-up visits after the conclusion of treatment, she said, noting that oncologists should advocate for their patients to return for annual well visits.

Fertility and Cancer Care

Certain dangers around being pregnant or potentially becoming pregnant, both during and after cancer treatment, are common

concerns among older AYA patients. Fertility risks associated with treatment often go undiscussed in younger patients, but patients should be having these conversations with their doctors, Beaupin said.

“A distinct risk for younger patients is the fertility aspect,” she said, which depends on the type of therapy and radiation used. “That’s been linked with quality-of-life issues down the road, as well. So, I think we have to do more in terms of letting our younger population know that this is a risk they may have later on.”

“Their hair might grow back. [and] if they were working before, they certainly strive [to go back] to work. By all outward appearances, for their friends, families, and colleagues, they may look like they’re back to normal, and people may expect that of them. But what we’ve learned from survivors is that they still feel different, either vastly or just a little bit, and it’s not obvious to anyone physically on the outside, which makes it even harder.”

—Lynda Kwon Beaupin, MD

Beaupin stressed that after completion of chemotherapy treatment, physicians should reassess individual fertility risks so that, as patients enter their reproductive years and consider family planning, they understand their options. Fertility risks to address by gender:

- **Women:** Certain treatments, such as chemotherapy, radiation therapy, or surgery can affect fertility. Experts recommend meeting with a reproductive endocrinologist to address cancer-related fertility issues and options, such as freezing eggs. In some cases, cancer treatment can cause early menopause. In other cases, menstrual periods stop during treatment but return later, preserving the ability to have children.⁴

Children and young women have a larger ovarian reserve, or amount of eggs in the ovaries, than older women do and therefore are less likely to experience immediate menopause and infertility after chemotherapy.

- **Men:** Treatments such as chemotherapy, radiation therapy, and surgery also can cause fertility-related adverse effects (AEs) in men. For some men, cancer treatment can lead to permanent infertility. Other men report that treatment stops or slows down sperm production for years, and though the ability may return, it may not be the same as before treatment.

Boys who receive treatment before reaching puberty may have less sperm damage. However, stronger treatments or those at a higher dose, such as chemotherapy for a bone marrow transplant, could cause permanent future infertility. The American Society of Clinical Oncology (ASCO) recommends freezing and storing semen, or sperm banking, for the preservation of fertility.⁵

- **Everyone:** In addition, practicing safe sex is extremely



BEAUPIN

Lynda Kwon Beaupin, MD, specializes in pediatric hematology-oncology and is the director of CanSurvive at Johns Hopkins All Children’s Hospital, St. Petersburg, Florida.

ADOLESCENTS AND YOUNG ADULTS

important, particularly for patients receiving chemotherapy, because treatment breakdown and by-products are excreted through bodily fluid. All patients should practice safe sex and use some form of contraception, for their own protection and that of their partners.

Beaupin noted that even if physicians aren't discussing fertility with their AYA patients, she has noticed that some have preconceived notions about fertility among patients with cancer or survivors: "Sometimes they automatically assume that their offspring will have either an increased risk for cancer or have more defects—physical or cognitive—because of their history of cancer, and many may elect not to have children."

In a recent study,⁶ investigators sought to identify just how many cancer survivors elected to have children. The findings revealed that regardless of cancer type, survivors achieved fewer pregnancies. Specifically, the chance of a woman becoming pregnant more than 5 years after diagnosis was notably lower in women with breast, cervical, and brain/central nervous system tumors and leukemia.

The investigators recommended appropriate fertility counseling of all females of reproductive age at the time of diagnosis and going forward. This affirms Beaupin's beliefs that physicians must do a better job of addressing the fertility aspect of treatment for AYA patients with cancer—both men and women—and inform them not only of their risks but also their fertility options.

The Importance of Survivorship in Cancer Care

In 2006, the Institute of Medicine (now the National Academies of Medicine) recommended that every cancer patient receive an individualized survivorship care plan that includes guidelines for monitoring and maintaining health.⁷ Since then, cancer survivorship care—defined as a care plan that helps a patient, oncologist, and primary healthcare providers work together to address medical and psychosocial challenges that may arise post treatment—has grown tremendously.

Emphasizing the importance of survivorship care, Beaupin said that a plan improves the quality of life for cancer survivors. Having a support system and follow-up after treatment is crucial because some of the effects of cancer treatment can be long-lasting.

According to CDC data, AYA cancer survivors in the United States are more prone to a number of adverse effects. In a survey conducted in all 50 states and 3 US territories, researchers collected data from more than 400,000 respondents.⁸ The study found that compared with respondents who never had cancer, more AYA cancer survivors had higher rates of heart disease (14% vs 7%), diabetes (12% vs 9%), asthma (15% vs 8%), disability (36% vs 18%), and high blood pressure (35% vs 29%).⁹

"The importance, really, is that we need to recognize that although our focus when [a patient] is initially diagnosed is that we cure them—and I do think that's an important priority to have—these survivors are telling us that many years later, they still have a lot of effects," Beaupin said.

AEs Among Survivors

Some effects are seen commonly among cancer survivors regardless of disease state, such as what is referred to as chemo brain. Patients use this term to describe the cognitive effects of treatment, such as when they can no longer efficiently perform tasks that they completed with ease before treatment. Memory can be affected, as well.

Another AE of treatment is fatigue, which can be long-lasting. It can be difficult for physicians to determine the cause for why certain patients experience it. Often, after treatment is completed, a patient may experience AEs that aren't apparent to others.

"Their hair might grow back, [and] if they were working before, they certainly strive [to go back] to work," Beaupin said. "By all outward appearances, for their friends, families, and colleagues, they may look like they're back to normal, and people may expect that of them. But what we've learned from survivors is that they still feel different, either vastly or just a little bit, and it's not obvious to anyone physically on the outside, which makes it even harder."

In Beaupin's experience, this can leave survivors feeling disappointed because they believe they shouldn't continue to notice the effects of treatment. Sometimes patients themselves don't expect to have symptoms years later, either, and don't know where they can go to share these concerns.

"That's the whole point of why we now have survivorship clinics offered around the country: to try [to] learn more about survivors and how to address these issues—how to identify them, really," she said.

Beaupin's Research: Using Social Media to Engage AYA Patients With Cancer

Earlier this year, at ASCO's annual Cancer Survivorship Symposium held in Orlando, Florida, in February, Beaupin had the opportunity to share what she has learned about survivors.

Her research documented how nearly half of the 2367 AYA cancer survivors she studied were being lost to follow-up after even just a few years post treatment.¹⁰ Since presenting her research, Beaupin has sought to find ways to engage this cohort of patients and bring them back to cancer centers.

Beaupin and her team facilitated an informative paper mailing in an attempt to educate patients about the risks, as well as invite them back to the center, but her efforts fell on deaf ears.

"Although a simple mailing would have worked perhaps for another population, certainly, for this population, it hasn't," she said. "We still need to work together as a medical community to understand how we can reach out to this population and engage and involve them in this process."

A second attempt, however, saw more success.

In collaboration with the University of Buffalo and Roswell Park Cancer Institute (Beaupin's former workplace), both in Buffalo, New York, the team developed Photographs of Meaning. This program for AYA survivors is based on an app called Pixtory, which allows the user to post a photograph with either a vocal or written narrative for why they chose it. The user then shares it in an online platform

with other survivors, who respond in the form of "likes" or comments.

"What we've learned from them is that they have a lot of psychosocial issues and a lot of distress related to having gone through their cancer treatment that we aren't necessarily addressing very well," Beaupin said. "Again, I think it has a lot to do with this population being very difficult to engage and learn about."

"So, we've introduced this Photographs of Meaning program through this online app to try, and we're onto our second cohort, but it looks like it's quite beneficial for young adult survivors to remotely connect with us using this method," she said. "We're actually very excited about it, because it's traditionally been done with actual photos that people take, and then they get together in a support group setting and talk about their photos."

Support groups can be hard for people in general, but especially young adults, to attend. Through this tool, Beaupin gives adolescents the opportunity to share their experiences and meet other cancer survivors who can relate to what they're going through.

Her overall message was clear: engaging AYA patients is an uphill battle. To address their ongoing medical and emotional needs, physicians must first bring them back to the cancer centers. Although there is no "right way" to achieve this, Beaupin said, oncologists and healthcare professionals must come together to bring patients back for routine follow-ups, so they can receive the healthcare and treatment they deserve but may not know they need. ♦

REFERENCES

1. Adolescents and young adults with cancer. National Cancer Institute website. [cancer.gov/types/aya](https://www.cancer.gov/types/aya). Published January 31, 2018. Accessed July 16, 2018.
2. Anderson C, Smitherman AB, Nichols HB. Conditional relative survival among long-term survivors of adolescent and young adult cancers [published online May 9, 2018]. *Cancer*. doi: 10.1002/cncr.31529.
3. About CAYACC. Consortium of Adolescent and Young Adult Cancer Centers website. [cayacc.com/about](https://www.cayacc.com/about). Accessed July 16, 2018.
4. Fertility concerns and preservation for women. Cancer.Net website. [cancer.net/navigating-cancer-care/dating-sex-and-reproduction/fertility-concerns-and-preservation-women](https://www.cancer.net/navigating-cancer-care/dating-sex-and-reproduction/fertility-concerns-and-preservation-women). Published April 2018. Accessed July 16, 2018.
5. Oktay K, Harvey BE, Partridge AH, et al. Fertility preservation in patients with cancer: ASCO clinical practice guideline update. *J Clin Oncol* 2018;36(19):1994-2001. doi:10.1200/JCO.2018.78.1914.
6. Anderson RA, Brewster DH, Wood R, et al. The impact of cancer on subsequent chance of pregnancy: a population-based analysis. *Hum Reprod*. 2018;33(7):1281-1290. doi: 10.1093/humrep/dey216.
7. Survivorship care plans. American Cancer Society website. [cancer.org/treatment/survivorship-during-and-after-treatment/survivorship-care-plans.html](https://www.cancer.org/treatment/survivorship-during-and-after-treatment/survivorship-care-plans.html). Accessed July 16, 2018.
8. About BRFS. CDC website. [cdc.gov/brfss/about/](https://www.cdc.gov/brfss/about/). Accessed July 16, 2018.
9. Adolescent and young adult cancer survivors. CDC website. [cdc.gov/cancer/dcpc/research/articles/adolescent_young.htm](https://www.cdc.gov/cancer/dcpc/research/articles/adolescent_young.htm). Updated August 6, 2012. Accessed July 16, 2018.
10. Beaupin, L. Come back: identifying targets to engage young adult survivors who have been lost to follow-up. Presented at: ASCO 2018 Cancer Survivorship Symposium; February 16-17, 2018; Orlando, FL. Abstract 29. meetinglibrary.asco.org/record/157765/abstract.

REDUCING ADVERSE EFFECTS



Board members for Thea's Star of Hope appear with a check for Children's Hospital of Philadelphia during an event held near the Danzes' home in New Jersey. Trisha Danze is in the center; Jeff Danze is at the far right, holding Thea.

A Family's Search for Better Treatment, Survival From Pediatric Brain Tumors

Mary Caffrey

FOR THEA DANZE, the trip to Children's Hospital of Philadelphia (CHOP) on July 13, 2018, was a milestone long in the making.

The 11-year-old had spent over 7 years—more than two-thirds of her life—living with a port that delivered therapy to fight a brain tumor discovered when she was 4 months old. But on this day, the port was coming out.

In March 2017, Thea's doctors at CHOP decided she was doing well enough that she could stop receiving half doses of bevacizumab every 4 weeks. They would wait and watch and hope that her tumor would remain stable. A magnetic resonance imaging (MRI) scan in August 2017 wasn't promising, but by February 2018, the tumor appeared stable, and by this summer, it was better still. The tumor—a low-grade, or slow-growing, glioma—wasn't progressing.

Being off treatment was a game changer for Thea as well as the whole family. It meant fewer trips to the hospital. It meant a winter without getting sick. It meant her parents, Trisha and Jeff Danze, could take Thea and her younger sister, Lilly, to Disney World.

To Thea, going to Disney World meant “totally learning to ride my scooter. My scooter isn't like any other scooter,” she said in an interview. “The power lasts for the entire day.”

The little girl who once took chemotherapy so toxic that she had to be fed through a stomach tube was now able to ride her scooter all over the Magic Kingdom. “It was a *really* big deal,” she said.

Everything about Thea's progress is a really big deal.

This is a girl who has survived a stroke, 5 different courses of treatment, and more surgeries than she can remember. When she was 5, the shunt that controlled her hydrocephalus malfunctioned, and she had to learn to walk again. Motor and visual deficits persist. In May, the Danzes moved around the corner so that as Thea gets older, she will have a full bathroom on the first floor and stairs that are easier to navigate.

Thea is also the girl who lights up the room wherever she goes; she loves space and music and fire trucks. Since 2012, she has been the namesake and spokesperson for a foundation created to raise funds and awareness about pediatric

brain tumors. Called Thea's Star of Hope, the foundation supports development of therapies that will treat brain tumors without the toxic adverse effects that Thea has endured.¹

About 4600 children will receive a brain tumor diagnosis in 2018; 74% will survive and be among 28,000 children aged 19 and younger living with a brain tumor in the United States.² Survivors of brain tumors are a subset of this country's 419,000 survivors of childhood cancer,³ and as their ranks grow, the quality of their lives has gained investigators' interest. Survivorship guidelines from the National Comprehensive Cancer Network (NCCN) are still comparatively new, and the needs of long-term survivors of childhood cancer are not the same as those of adults. As noted in the NCCN's 2018 update for adolescents and young adults (including some guidance for survivors of childhood cancer), “most survivors have multiple treatment exposures, and therefore have multiple screening needs.”⁴

Trisha Danze sees the need for research funding across the spectrum—from treatment to family assistance.

“There's definitely a need for more funding for pediatric brain tumors and children's cancers in general,” she said during a visit with *Evidence-Based Oncology*[™] (EBO[™]), joined by both Thea and Lilly. “These kids go through a lot of treatment, and as a result, they have a lot of side effects that they have to live with for the rest of their lives.”

Apparently, FDA agrees. On July 23, as EBO[™] was going to press, Commissioner Scott Gottlieb, MD, followed through on a commitment to close a loophole in the Pediatric Research Equity Act, passed in 2003. Drug companies had been using the orphan drug exemption to treat small populations of adults with therapies to avoid research in children, but an FDA guidance said the agency will no longer grant these exemptions.⁵

Before switching to bevacizumab, Thea was receiving treatments that were far more toxic. Concern about what Thea and others like her might face down the road drives the foundation's work, and with good reason. The Childhood Cancer Survivor Study (CCSS), funded by the National Cancer Institute, began tracking

REDUCING ADVERSE EFFECTS



Board members and supporters of Thea's Star of Hope took part in a pregame ceremony at Trenton's Arm and Hammer Park on June 10, 2018, when the AA Yankees affiliate, the Trenton Thunder, played the Binghamton Rumble Ponies. Some proceeds went to the foundation, which funds research for less toxic therapies for children with brain tumors.

survivors in 1994 and reports that children treated for cancer can develop cardiac effects, mood and memory problems, secondary cancers, and psychosocial challenges long after treatment ends. In recent years, the study has focused on "late effects" of treatment and examined whether childhood cancers can be treated with less medication to reduce long-term effects.³

For Thea, the goal of the foundation is simple: "Personally, my favorite thing about Thea's Star of Hope is that it's like shooting laser guns at brain tumors until they get smaller and smaller and smaller, until *poof!* They disappear."

A Commitment to New Approaches

The "laser gun" description is not far off: The foundation is deeply committed to personalized medicine. Early on, the fund formed a relationship with the Children's Brain Tumor Consortium to promote data sharing and collaboration across institutions; in February 2016, Thea's Star of Hope was recognized as a funding source for a study published in *Nature Genetics*, led by Adam Resnick, PhD, director of the Center for Data Driven Discovery in Biomedicine at CHOP. That study involved pooling data from 249 cases across several institutions, including CHOP, that uncovered a 3-way mechanism in which a mutation drives tumor development.^{5,6} The results led to a new research commitment for Thea's Star of Hope.

The study in *Nature Genetics* helped scientists trying to understand an important problem in treating pediatric gliomas: Although there has been some success in understanding *BRAF* mutations that drive many tumors, there are opportunities for error. Select the wrong chemotherapy, and the tumor can grow. So Trisha and Jeff Danze and the foundation board were drawn to a study taking a different approach, the Pacific Pediatric Neuro-Oncology TAK-580 Trial.⁷ TAK-580 represents a new drug class, a type II *BRAF* inhibitor, which clinicaltrials.gov states would work by "locking the mutant *BRAF* molecule and the next molecule in the activation chain together," thus blocking the signal that tells the tumor cell to divide.⁸ In practical terms, the therapy would have the potential to target multiple mutations, eliminating the risks of selecting the

wrong therapy. Thea's Star of Hope has committed to raising \$100,000 for this trial through 2020.

Although there's lots of excitement on the therapy front, the foundation is also committed to programs that promote data sharing and family services. "We like to have other families involved with their kids and share their stories," Trisha Danze said. "Having a child with a serious medical issue affects the whole family."

As more survivors of childhood cancer live longer, the need for better aftercare services is becoming apparent. Major academic centers such as CHOP, the Cleveland Clinic, and the Dana-Farber Cancer Institute advertise services, but the CCSS still finds gaps in follow-up care. The study also concluded that survivors of pediatric cancer were 3 times more likely to develop a chronic condition and 8 times more likely to have a severe or life-threatening condition than a sibling group.^{3,9}

Raising Funds and Building Awareness

It's a rainy day in June, but the ballpark in Trenton, New Jersey, is filled with fans: Heisman Trophy winner turned minor league slugger Tim Lincecum is here, on hand with the Mets' Double-A affiliate to take on the Thunder, the Yankees' counterpart. But it's not just Lincecum who drew the crowd: Some of the game proceeds will benefit Thea's Star of Hope. One section is a who's who of Robbinsville, New Jersey, where the Danzes live. A short video highlighted foundation events that have become part of the community's fabric: a masquerade ball and an annual 5K complete with Thea's favorite, an inflatable fire truck. This spring, Trisha Danze was named the grand marshal of the community's St. Patrick's Day parade.

Many in Robbinsville know Thea's story: Everything was fine until she was 4 months old, when her wiggling eyes and screaming told her mother something was seriously wrong. A computed tomography scan revealed a large mass, and she underwent a series of surgeries to remove 50% of the tumor. Trisha and Jeff Danze learned the diagnosis: glioma. But the setbacks were not over. Within days, Thea suffered a stroke that would lead to years of speech and occupational therapy.

More than decade later, their world is forever changed. Care coordination may be a healthcare buzzword, but it's become Trisha Danze's full-time

job: She's the quarterback for Thea's medical and educational needs. On the medical side, that means managing Thea's physical therapy, psychosocial treatments, and nutrition regimen. Besides CHOP, Thea has spent considerable time at Children's Specialized Hospital addressing her physical challenges, especially after the setback when her shunt malfunctioned 6 years ago. On the education side, Trisha Danze must engage the school district on Thea's school placements and attend meetings on her individual education plan, or IEP. Trisha Danze also schedules Thea's MRIs and sends her to camp.

And she deals with the insurance company.

"Don't deny! Don't deny!" Trisha Danze said when asked what payers could do to ease the lives of families with children with cancer. "That's the biggest issue we see now with families," she said, explaining that patients who don't have time to spare often waste it going through step therapy until they get to the targeted therapy that would do the most good.

But she savors the victories: Trisha credits the CHOP Child Life staff for working with Thea to handle an MRI without sedation. Compared with 10 years ago, "Child Life has really expanded and become a much bigger part of children's care in the hospital, and that really makes a huge difference," Trisha Danze said. "Sometimes you just don't know what to say to your kid."

What is their vision for Thea's Star of Hope? Trisha Danze, Thea, and Lilly each gave a version of Lilly's answer:

"It will be helping kids." ♦

REFERENCES

1. Thea's Star of Hope. Thea's Star of Hope website. theasstarofhope.org/. Accessed July 8, 2018.
2. Quick brain tumor facts. National Brain Tumor Society website. braintumor.org/brain-tumor-information/brain-tumor-facts/. Accessed July 8, 2018.
3. Childhood cancer survivor study: an overview. National Cancer Institute website. cancer.gov/types/childhood-cancers/ccss. Updated August 29, 2017. Accessed July 8, 2018.
4. Clinical practice guidelines (NCCN guidelines). Adolescent and young adult oncology: version 2.2018. National Comprehensive Cancer Network website. nccn.org/professionals/physician_gls/pdf/aya.pdf. Updated October 11, 2017. Accessed July 17, 2018.
5. Department of Human Services. *Federal Register*. 2018;(83)145 FR 35655 gpo.gov/fdsys/pkg/FR-2018-07-27/pdf/2018-16027.pdf. Published and accessed July 27, 2018.
6. Bandopadhyay P, Ramkissoon LA, Jain P, et al. MYB-QKI rearrangements in angiogenic glioma drive tumorigenicity through a tripartite mechanism. *Nat Genet*. 2016;48(3):273-282. doi: 10.1038/ng.3500.
7. "Gene fusion" mutation uses three-way mechanism to drive childhood brain cancers [news release]. Philadelphia, PA: Healthcanal; February 27, 2016. healthcanal.com/cancers/70648-gene-fusion-mutation-uses-three-way-mechanism-to-drive-childhood-brain-cancers.html. Accessed July 25, 2018.
8. A phase I/II and target validation study of TAK-580 (MLN2480) for children with low-grade gliomas and other RAS/RAF/MEK/ERK pathway activated tumors. Pacific Pediatric Neuro-Oncology Consortium website. pnoc.us/clinical-trials/phase-iii-and-target-validation-study-tak-580-mln2480-children-low-grade-gliomas-and. Accessed July 25, 2018.
9. TAK-580 in gliomas and other tumors. clinicaltrials.gov/ct2/show/NCT03429803. Updated May 31, 2018. Accessed July 17, 2018.
10. Diller L, Chow EJ, Gurney JG, et al. Chronic disease in the Childhood Cancer Survivor Study cohort: a review of published findings. *J Clin Oncol*. 2009;27(14):2339-2355. doi: 10.1200/JCO.2008.21.1953.

CONFERENCE COVERAGE: NCCN POLICY SUMMIT 2018

Coverage by Mary Caffrey

Gottlieb Calls on Payers to Share Data to Aid Drug Innovation

THE FDA IS WORKING to modernize the clinical trial process and answer the right questions about today's innovative cancer drugs, but regulators need help from payers—or, more precisely, from their data, according to FDA Commissioner Scott Gottlieb, MD.

Gottlieb called for more data sharing during remarks at the National Comprehensive Cancer Network Oncology Policy Summit held June 25 in Washington, DC. The commissioner covered 4 policy areas he said were linked by “the need to modernize drug development to harness the full medical



GOTTLIEB

potential of this rapidly advancing science, while ensuring that innovation remains affordable for patients.”

He added that patients will not benefit from outdated regulatory frameworks that keep lifesaving drugs off the market, stretch out the process, and make drugs more expensive. Although the FDA does not have direct authority over drug costs, Gottlieb said, a different approach can take time and costs out of the approval process, as well as promote competition and encourage generics and biosimilar development. “If FDA-approved drugs are priced out of reach of patients, then the full benefits of innovation won't be realized,” he said.

He discussed:

- Steps the FDA is taking to modernize the clinical trial process in light of the rise of targeted therapies, which are given to select patients based on biomarkers and often bring more robust responses
- How to harness real-world data in regulatory approaches to answer questions about how patients respond to drugs over time
- How the FDA is working with payers and providers to “leverage” real-world evidence to answer payers' questions, such as whether a therapy keeps more patients out of the hospital
- Why this approach calls for payers to provide “more open access to the significant amount of data that they have”

Over the past 20 years, as both cancer therapies and survival rates have improved, more patients have been matched to drugs in trials based on “tumor biology,” Gottlieb said. This has allowed the FDA to approve drugs based on smaller trials with fewer patients and leapfrog from phase 1 studies directly to later phases. Oncology accounts for more breakthrough therapy designations than any other therapeutic area, including 50% of all designations granted since 2013.

“We had to ask ourselves some hard questions,” he said. “What should we do, for example, guided both by ethics and science, when a new drug in a heavily pretreated group of terminal cancer patients is in a phase 1 study, where it shows a dramatic response in more than half of these patients?” And, he asked, how are patients randomized in phase 2 based on that result?

Although some criticize the FDA's approach to approvals based on smaller groups of patients, “this criticism lacks historical and scientific context,” he said.

When cancer drugs were more toxic and less effective, the fact that they worked at all was the most relevant outcome, so overall survival was the most appropriate end point. “They were standards designed for an era that no longer exists,” he said.

The FDA has consulted extensively with stakeholders, including patient groups, and is now more interested in progression-free survival, tumor shrinkage, and the severity of adverse effects. It's not that these measures weren't relevant in the past, Gottlieb said: “It's just that the drugs were so toxic that these benefits generally were not seen as sufficient to justify the risks.” Today's drugs are far less toxic, and looking at how patients fare over longer periods is highly relevant. The FDA's changing approach “didn't evolve overnight,” Gottlieb said. “We didn't do it on a whim.”

The approach is working: Of 51 oncology accelerated approvals with post-marketing requirements and verified benefits, the average time from approval to verification is 3.4 years. Just 5 drugs have been pulled from the market for failing to confirm benefits.

In response to critics who say surrogate end points bring uncertainty about the eventual efficacy, Gottlieb said, “That's, in fact, the whole point.”

In some cases, trials would take far too long; without crossover trials, some patients would miss the opportunity for lifesaving treatment. “We would literally be asking patients to die so that we could achieve a lower *P* value,” he said.

To promote cost-saving solutions such as value-based contracting, Gottlieb called on payers to aid the process by sharing data that will guide FDA on how drugs work in different populations and over the long haul: “It's not enough to point fingers. We all need to work together.”

Payers who want to help the FDA ultimately drive down prices or show how therapies affect hospitalization rates must “put your data where your arguments are,” instead of charging huge sums for this information, Gottlieb said.

Real-world data do not replace the gold standard of randomized clinical trials but can fill in knowledge gaps. As a result, Gottlieb said, for the 2019 budget, the FDA seeks \$23 million to invest in advanced analytics and data analysis, which he said will give the agency the ability to do “near real-time” analysis of evidence from electronic health records for 10 million individuals.

During a question-and-answer period, Gottlieb said the FDA is working to help overcome impediments to using real-world data for value-based contracting by issuing a recent guidance on this topic. When asked if he's confident that the FDA will get the real-world evidence it needs to shift its approach, Gottlieb said that's the role of enforcement.

At the time of Gottlieb's speech, the FDA had just sent a letter to a manufacturer that has not fulfilled its postmarketing requirements. “The agency feels far more confident it will get the data,” he said. “The system is dependent on that.” ♦

Paying for Innovation in Cancer Care Means No Easy Answers

AS RON KLINE, MD, put it: If figuring out how to pay for innovation in cancer care was easy, someone would have already done it.

“We know it's hard. We know it's going to take a while,” said Kline, medical officer in the Patient Care Models Group for the Center for Medicare and Medicaid Innovation (CMMI) at CMS.



KLINE

Kline was on hand to discuss the Oncology Care Model (OCM), the 5-year effort to rethink cancer care delivery and cut costs in Medicare, during a discussion by the National Comprehensive Cancer Network (NCCN) on how to balance the revolution in cancer therapy with the need to pay for it.

During the session “Paying for Innovation,” part of NCCN's June 25, 2018, Policy Summit in Washington, DC, Kline explained that the OCM shouldn't be easy from the get-go—if it was, then CMMI would know it hadn't truly pushed the envelope. But CMMI wants practices to succeed, and early results show that 25% of practices cut costs 7%. “Sixty percent of practices decreased costs, compared with the baseline,” he said.

Guided by questions from moderator Cliff Goodman, PhD, of The Lewin Group, panelists discussed today's challenges in cancer care: the need to simultaneously overhaul delivery systems and learn to use—and bill for—some of most complex therapies and technologies ever conceived. Heading that list: chimeric antigen receptor (CAR) T-cell treatments, gene therapies that can take 2 to 4 weeks to manufacture for a specific patient, at a cost of up to \$475,000 just for the drugs.

But paying for innovation is more complicated than figuring out how to pay for CAR T-cell treatments or targeted therapies. It's also about helping patients who will live with cancer as a chronic condition, such as those with certain blood disorders.

“The advance of novel, innovative therapies has transformed treatment,” said Meghan Gutierrez, chief executive officer of the Lymphoma Research

Foundation. The combination of new treatments, diagnostic tests, and sequencing has produced more information about the disease. Patients have more opportunities than ever for better care, but for many, treatment will not be a one-time event. “Patients recognize they are likely to be in and out of care for the rest of their lives,” she said.



REDDY

Innovation isn’t just about approving new therapies, said Pavan Reddy, MD, FACP, of the Cancer Center of Kansas. Precision medicine means identifying treatments that are “tumor agnostic,” based on biomarkers, as well as research that tells clinicians when they can de-escalate or stop treatment, he said.

Reimbursement Drives Decisions

Patients are citing treatment costs as a factor in their medical decisions, according to Gutierrez. “Increasingly, patients are speaking to the economic burden across their lifetime,” she said. Therapies can extend life well beyond what was once imaginable, but with these advances come rising out-of-pocket costs.



FARNIA

Stephanie Farnia, MPH, director of health policy and strategic relations for the American Society for Blood and Marrow Transplantation, is a veteran of dealing with reimbursement challenges. Things such as delays in getting treatment codes, which allow physicians to bill properly, can be a barrier to lifesaving advances.

Panelist Stefanie Joho, a cancer survivor, lives with fatigue from the immunotherapy that saved her life, but, as Goodman noted, “some long-term impacts are unknown.”

In Joho’s case, that’s better than what she was facing when her sister, refusing to accept the grim prognosis that nothing could be done for Joho’s colon cancer, scoured the internet until she found an appropriate clinical trial. Other panelists conceded that some oncologists, especially in rural areas, don’t always refer patients for clinical trials. At this point, CAR T-cell therapies are unlikely to be delivered outside of a major academic medical center with expertise in transplants, said Caron A. Jacobson, MD, of the Dana Farber Cancer Institute/Brigham and Women’s Hospital in Boston, Massachusetts.

Kline, however, called this a copout. As a pediatric oncologist, he said, he finds that clinical trials for young patients “are the standard of care.”

Joho and others said they’d like to see more patients enroll in clinical trials, although they recognize barriers such as travel. Michael Ybarra, MD, representing the Pharmaceutical Research and Manufacturers of America, said that drugmakers are concerned about the ability of rural patients to gain access to trials, but factors such as hospital consolidations and benefit design also create access barriers. A major driver of consolidation in the health care industry has been the 340B program, which groups such as the Community Oncology Alliance say has been exploited beyond its original mission, to the detriment of community providers.

The Arrival of CAR T-Cell Therapy

The fact that administering CAR T-cell therapy demands special expertise and permission means that certain centers are likely to have several patients receiving the therapy, increasing that institution’s risk. This creates lots of discussion among leading oncologists and hospital executives, according to the panelists. Jacobson said she’s been “pleasantly surprised” at the speed with which CAR T-cell therapies have moved from FDA approval into general use, but it hasn’t been without its challenges. Patients outside of clinical trials may have less economic means and family support, and thus far, reimbursement with commercial payers is done through individual patient contracts, so there’s a heavy administrative burden.



JACOBSON

Even so, Jacobson said, for tisagenlecleucel (Kymriah)—the first CAR T-cell therapy approved for forms of pediatric leukemia—“you’re only charged if you respond in the first 30 days.” In pediatric patients, responses rates are 96%, she said, and although adult responses to CAR T-cell treatments are not quite that high, they are “still very impressive.”

CAR T-cell therapy is such a game changer that so far, CMMI is not including it in cost-of-care for OCM purposes, Kline said, because that would “overwhelm everything.”

Variables in the OCM

That said, Kline explained 2 factors in the OCM model—the novel therapy adjustment and the trend adjustment, which is based on regional cost factors—that allow practices to deal with externalities. But Goodman asked, “Are you confident that the novel therapy adjustment will accommodate all this new stuff?”



YBARRA

The adjustments are receiving attention within CMMI to make them work, Kline said. He acknowledged Goodman’s observation that so far, there’s virtually no update of 2-sided risk in OCM, but he said that practices are just now getting back early rounds of data to see how they are faring.

When asked for a 1-sentence summary of what’s next, Jacobson said, “It’s ultimately about solving the problem of reimbursement.” As CAR T-cell therapies are shown to work for more types of cancers, single-patient contracts won’t be sustainable, she said. The next step must be to pair innovation in technology with payment systems that can work out approvals “in real time,” she said.

Reddy sees the growing ranks of underinsured as a challenge, and Ybarra agreed that matching benefits designs to patient needs—to do something about huge out-of-pocket costs—is essential.

Said Kline, “It’s about putting the responsibility for the cost in the physician–patient relationship.” ♦

Narrow Networks in Cancer Care: Tough on Patients but Here to Stay

NARROW NETWORKS, WHICH LIMIT where patients can receive care, are holding down costs, but the price to patients with cancer and providers in lack of convenience can be high, according to panelists who discussed changes in care delivery at a policy summit of the National Comprehensive Cancer Network (NCCN), held June 25 in Washington, DC.

“The Evolving Healthcare Landscape: Implications for Access to Quality Cancer Care,” brought together leading oncologists, policy experts, and patient advocates to address the conundrum for today’s cancer patient: therapeutic advances bring more options than ever, but for many, barriers to the best treatments will be too high.



ALVARNAS

Joseph Alvarnas, MD, a hematologist/oncologist who serves as vice president of government affairs and senior medical director of employer strategy at City of Hope in Duarte, California, said that unlike many other parts of the country, his state has lots of health plans—but that doesn’t mean a patient will find adequate networks.

“The challenge here is [that] if the motivation is to deliver low-cost care, [health plans] can find a low-cost provider in every market,” said Alvarnas, who is also the editor-in-chief of *Evidence-Based Oncology*SM. Narrow networks can work if there is a commitment to quality, but when price is the only priority, that can pose a problem: “Their decisions are not based on ‘Where do I get the best care?’ but ‘Where do I get the lowest price?’”

Narrow networks have proliferated under the Affordable Care Act (ACA) because of lower-cost plans sold on the marketplace. In some cases, that has left leading academic medical centers and NCCN member health systems on the sidelines, because their costs are considered too high. Alyssa Schatz, MSW, policy director for NCCN, presented research to the group showing that most cancer centers are in some exchange networks but not all in their region. A few have not been placed in any exchange network, she said.

CONFERENCE COVERAGE: NCCN POLICY SUMMIT 2018

It's reached a point that the National Association of Insurance Commissioners, which creates policies and model legislation to help bring uniformity across state lines, needs to revisit the narrow network issue, said Jenny Carlson, associate vice president of government affairs at The Ohio State University's Wexner Medical Center.



COX

John Cox, DO, a medical oncologist at University of Texas Southwestern and Parkland Health and Hospital System, agreed that although the ACA brings coverage to many uninsured, it has its drawbacks. "On the 1 side, I love that our patients have a secure insurance contract. They have access to care," he said. But he's seen examples of patients who must travel long distances, often carrying their medical records, to use the lone specialist approved by their plan. "It just puts up tons of barriers," he said.

All this may be true, said Kavita Patel, MD, MS, FACP, a senior fellow at the Brookings Institution, but no one should expect narrow networks to go away any time soon. "Our narrow networks are an insurance company's high-value network," she said. They are considered a critical tool in controlling costs, so institutions that are left out must work with payers to show why they bring value and should be included.

Moderator Cliff Goodman, PhD, asked: If oncologists and patients with cancer must live with narrow networks, are there any consumer protections?

Both Joe Antos, PhD, of the American Enterprise Institute, and Elizabeth Franklin, LGSW, ACSW, executive director of the Cancer Policy Institute for the Cancer Support Community, said a key challenge for consumers is the complexity of insurance contracts. If healthcare experts have a hard time figuring out what's covered and what's not, they asked, how can patients navigate the system?



ANTOS

Most people still get coverage through their employer, Antos said, and a patient who receives a cancer diagnosis is "locked in" to whatever that plan provides and may not know how to avoid large out-of-pocket costs. "Patients don't know what to do," he said, "and doctors aren't very good at telling them."

Many health plans don't pay for social workers who could help a patient navigate the system, Franklin added.

Goodman asked whether CMS' push for more of cancer care in Medicare to be provided through alternative payment models, or APMs, would make a difference. In theory, when setting reimbursement, APMs take a patient's experience into account, not just cost.

A problem is that too many providers are simply trying to "game the system" for maximum reimbursement under the Merit-based Incentive Payment System, or MIPS, instead of aiming for excellence, Alvarnas said: "We should have transparency about what represents excellence, especially in cancer care."



PATEL

Patel noted that although the ACA contemplated APMs, they did not exist right after the law passed. MIPS is a tool to get doctors to experiment with taking on risk, because the transition to 2-sided risk in APMs cannot happen all at once. And in cancer care, this transition is happening just as the cost of immunotherapy is skyrocketing, giving doctors pause. She reminded the audience that the 2015 Medicare Access and CHIP Reauthorization Act, which set up MIPS and the ability of Medicare to pay doctors through

APMs, is "budget neutral," which suggests there will be winners and losers. That raises this question, Patel said: "What constitutes a loser?"

Carlson discussed experiments with Medicaid waivers, including the push by some states to add work or volunteerism requirements. She said this will be closely scrutinized in the courts. (Days after the summit, a federal judge blocked Kentucky's plan to add work requirements to Medicaid.¹) Schatz said the bureaucracy associated with Medicaid work rules is quite challenging.

An overlooked aspect of the ACA is that "it shifted resources, so there were winners and losers," Antos said. Some previously uninsured people gained access for the first time, but when too few healthy people signed up for coverage, some lower-middle-class families that were not eligible for subsidies "could no longer afford the coverage they used to have," he said.

The threat today is that the Trump administration's decision to eliminate the individual mandate through the recently enacted tax law will drive healthy people out of the risk pool. Patel, who worked on the ACA as a member of the Obama administration, said calls for harsher penalties for not enrolling went unheeded. The loss of the individual mandate is a much bigger threat to the healthcare system than association health plans (AHPs), she said.

Franklin sees the AHPs as a real problem. "What happens when a 30-year-old gets cancer?" she asked. For many, the diagnosis will reveal how little their plan actually covers.

The threat today is that the Trump administration's decision to eliminate the individual mandate through the recently enacted tax law will drive healthy people out of the risk pool. Kavita Patel, MD, MS, FACP, who worked on the Affordable Care Act as a member of the Obama administration, said calls for harsher penalties for not enrolling went unheeded.

In addition, buying cheap coverage will end up as barrier to accessing the lifesaving treatments that are reaching the market, such as chimeric antigen receptor (CAR) T-cell therapies. Anna Griffin of Kite Pharma, developer of the CAR T-cell treatment Yescarta, said, "We're not allowed to say 'cure,' because the data are still young," but researchers are starting to get results for people 2 years after treatment, "and it still looks really good."

"It's such a great time to be in cancer medicine," Cox said. But the downside is that for some patients, there's no access to bone marrow transplants—very few cancer centers can take on a charity transplant patient, he said.

Franklin is not encouraged by the prospect of telling patients, "This potentially is a cure, but not for you, because you're poor—or because you're not near a major cancer center."



GOODMAN

Goodman asked each panelist to predict what's ahead.

Alvarnas said he looks forward to "getting rid of the middlemen," referring to pharmacy benefit managers (PBMs); reining in pharmaceutical costs; and getting rid of wasteful procedures. He expressed excitement about the upcoming venture among Berkshire Hathaway, Amazon, and JPMorgan Chase, which could bring analytics to the cause in a more powerful way.²

In discussing the Trump administration's plan to hold down pharmaceutical costs, several panelists said the proposed merger of Medicare parts B and D will be much harder to achieve than most realize. Antos pointed out that Part D is very much driven by rebates, which have been a target of scorn among those who believe PBMs are largely responsible for pushing up prices. Antos said the extremely high costs of treatment will upset current financing models.

"I'm also concerned about patient safety," Franklin said. She would like to see patient experience data on drug labels. Carlson foresees a broader use of telemedicine and, she hopes, more streamlined coverage decisions.

Schatz said there's a great need for transparency of information so that consumers can make more informed choices.

Patel expects that by 2023, "50% of cancer care will be in some at-risk payment model."

"Patients are going to have some real options in cancer treatment—options that look different than they do today," according to Franklin. ♦

REFERENCES

1. Inserro A. Federal judge blocks Kentucky's Medicaid work requirements. *The American Journal of Managed Care*® website. ajmc.com/newsroom/federal-judge-blocks-kentuckys-medicaid-work-requirements. Published June 29, 2018. Accessed July 9, 2018.
2. Rosenberg J. Amazon, Berkshire Hathaway, JPMorgan Chase announce CEO of joint health company. *The American Journal of Managed Care*® website. ajmc.com/newsroom/amazon-berkshire-hathaway-jpmorgan-chase-announce-ceo-of-joint-health-company. Published June 20, 2018. Accessed July 9, 2018.



DeSAULNIER
Rep. Mark DeSaulnier,
D-California, represents
Contra Costa County in the
San Francisco Bay area.



POE
Rep. Ted Poe, R-Texas,
represents the Houston
suburbs.

Cancer Survivors Caucus Seeks to Find Common Ground in Congress

REP. MARK DESAULNIER, a California Democrat, has championed causes from reducing air pollution to fighting childhood obesity to improving gun safety.¹ Rep. Ted Poe, a Texas Republican, is still called “Judge” from his years handing down sentences, such as ordering thieves to carry signs outside stores where they stole merchandise.²

A political odd couple? For sure. But they also share a bond that guides their work in Congress: Both are leukemia survivors.

In 2017, DeSaulnier, who represents Contra Costa County in the San Francisco Bay Area, and Poe, whose district covers the Houston suburbs, formed the Congressional Cancer Survivors Caucus, a bipartisan group that is calling attention to the need for more research and removing the stigma that still lingers over cancer. Formed when the Trump administration was weighing a \$5.8 billion budget cut to the National Institutes Health,³ the caucus advocates for issues that cross party lines. The group also hears from leading scientists so members can learn firsthand what’s happening in the world of research.

“We have the best medical knowledge in the world. If people cannot have access to that knowledge, then we’re missing the whole point of having it. We have to figure out a way so that people can have [access]. That is something we have to strive for.”

—Rep. Ted Poe, R-Texas

On June 25, 2018, DeSaulnier and Poe appeared at the National Comprehensive Cancer Network Policy Summit, where they discussed legislation they introduced in March: the Cancer Care Planning and Communications Act (HR 5160), which would allow doctors to bill Medicare for the time spent developing cancer care plans and coordinating services.⁴ Care planning and management are part of CMS’ Oncology Care Model (OCM), a 5-year initiative aimed at improving care and reducing costs, but not all practices are part of the OCM.⁵

Living well after cancer should not be a controversial topic, in their view. “It’s a nonpartisan issue that is really important,” Poe said. “You hear all the rhetoric. You hear all the fussing and fighting and feuding. This is not one of those issues.”

“It’s a quality-of-life issue, and Congress should be involved in quality-of-life issues,” DeSaulnier said. After 30 years as a public official, he sees fighting cancer as something that can allow Congress to get past its divisions and make a difference—by promoting better technology and ensuring that people with preexisting conditions can get care. “In the wealthiest country in the world, Americans should be assured that preexisting conditions are covered,” he said.

DeSaulnier and Poe agree on the need for more research, education about causes of cancer, and screening to identify

people at risk. Prevention, Poe said, is much cheaper than being treated. “Take smoking,” he said. “[Back] when we had black-and-white TV, people smoked and thought nothing of it.... There was smoking in jails, in the Astrodome.”

As a judge, Poe convinced the Harris County commissioners to eliminate smoking from all county buildings, including the courthouse and the jail. “You would have thought the world had come to an end,” he said.

Today, no one questions the need to keep smoking out of public spaces, DeSaulnier said.

Poe had high praise for the treatment he received at The University of Texas MD Anderson Cancer Center in Houston, noting that access to care for all patients is key. “We have the best medical knowledge in the world. If people cannot have access to that knowledge, then we’re missing the whole point of having it,” he said. “We have to figure out a way so that people can have [access]. That is something we have to strive for.”

DeSaulnier, 66, and Poe, 69, received their diagnoses about a year apart. DeSaulnier found out he had chronic lymphocytic leukemia in 2015, during his first year in Congress. He went through treatment quietly and didn’t share the news until May 2016, when he announced he would seek a second term.⁶ For Poe, the diagnosis of leukemia came in 2016, more than 10 years after he was elected to Congress in 2004. Although his treatment has gone well and he said he’s in good health, he decided not to seek reelection this year.⁷

The focus on survivorship, DeSaulnier said, has emerged because living with cancer is now more like having a chronic disease. “We have these treatments that are capable of keeping you alive longer,” he said, but this can create new challenges, such as living with a weakened immune system.

Finding solutions means following the science, DeSaulnier said: “We are at the most elevated point in our existence. We both agree—must look at prevention, at intervention, and deployment of evidence-based research so that people will be better off.” ♦

REFERENCES

1. Congressman Mark DeSaulnier website. desaulnier.house.gov/. Accessed July 18, 2018.
2. Biography. U.S. Congressman Ted Poe website. poe.house.gov/biography. Accessed July 18, 2018.
3. Tolan C. Bay Area congressman’s cancer survivors caucus raises attention on research funding. *The Mercury News*. Published April 30, 2017. Updated May 1, 2017. mercurynews.com/2017/04/30/mark-desaulnier-cancer-survivors-caucus-research-funding/. Accessed July 18, 2018.
4. Cancer Care Planning and Communications Act of 2018, HR 5160, 115th Cong, 2nd Sess (2018).
5. Oncology Care Model. CMS website. innovation.cms.gov/initiatives/oncology-care. Updated July 20, 2017. Accessed April 11, 2018.
6. Wire SD. U.S. Rep. Mark DeSaulnier says blood cancer won’t keep him from seeking another term. *Los Angeles Times*. Published May 6, 2016. latimes.com/politics/la-pol-ca-desaulnier-cancer-20160506-snap-story.html. Published May 6, 2016. Accessed July 18, 2018.
7. Lima C. Texas Republican Ted Poe won’t seek reelection in 2018. *POLITICO* website. politico.com/story/2017/11/07/ted-poe-texas-congress-2018-244668. Published November 7, 2017. Accessed July 18, 2018.

curetoday

Reflections on Eight Years of Survivorship
curetoday.com/link/109

Reporting by Alison Rodriguez and Jaime Rosenberg

Feedback on the Direction, Challenges of the OCM

THE ONCOLOGY CARE MODEL (OCM), CMS' bundled payment program for oncology, is a 5-year model that began 2 years ago,¹ and early experiences have revealed areas for improvement, as well as just how hard it can be for practices to perform well.

During a webcast, Bruce Feinberg, DO, of Cardinal Health Specialty Solutions, moderated a conversation with Bruce Gould, MD, of Northwest Georgia Oncology Centers (NGOC), and Mark Liu, of Mount Sinai Health System, regarding the implications of feedback to the model, so far.

This discussion was part of an OCM webcast series by *The American Journal of Managed Care*.²

Most practices participating in the OCM are sophisticated practices that deliver quality care and have a background with alternative payment models. NGOC has had years of experience already through UnitedHealthcare's episodes of care program and the COME HOME program, developed by Barbara McAneny, MD, and Innovative Oncology Business Solutions.³

Participating in both of these programs prior to the OCM gave NGOC the confidence that it could meet many of the practice transformations required for OCM participation. However, Liu noted, Mount Sinai spent a lot of time the first year on building the infrastructure and educating employees to get in the right mind-set.

The challenge is that newer therapies are increasingly expensive, which can negatively affect practices trying to meet a target price. During 2012-2015, a patient diagnosed with breast cancer and placed on aromatase inhibitors had relatively low costs. The episode was priced at about \$5000 for 6 months. But now, cyclin-dependent kinase (CDK) 4/6 inhibitors, which nearly double progression-free survival, are priced at roughly \$50,000 for 6 months, which "blows away" the target price.

Although NGOC might have had the infrastructure mostly in place, it—like most other participating practices—struggled with the "onerous" reporting requirements, Gould said. The practice also had difficulties compiling data for the 13-point care plan of the Institute of Medicine (IOM), which is mandatory for all OCM participants.⁴ "A lot of the information that's required for that 13-point IOM plan is not in the [electronic medical record], where we can push a button and just have it spit out," he explained.

Liu echoed the challenges Gould faced at NGOC, adding that, when it came time to presenting the information to CMS, Sinai realized that most of it didn't live in a structured field. As a result, Sinai studied the clinical documentation to see if it could redo how information was being captured in a way that didn't greatly affect the care team.

Looking at the first results of the program, Feinberg noted that drug costs were higher among OCM participants than nonparticipants. Because the participants represent some of the most sophisticated in the country, he wondered if those higher costs come as a result of these practices being more up to date on the latest treatments and early adopters of them.

Gould agreed that the assessment was likely accurate. NGOC gets experience with newer drugs before they're on the market, which means the practices are comfortable using them and adopt them "right out of the gate," he said.



The challenge is that newer therapies are increasingly expensive, which can negatively affect practices trying to meet a target price. For example, during 2012-2015, a patient diagnosed with breast cancer and placed on aromatase inhibitors had relatively low costs. The episode was priced at about \$5000 for 6 months, Gould said. But now, cyclin-dependent kinase (CDK) 4/6 inhibitors, which nearly double progression-free survival, are priced at roughly \$50,000 for 6 months. "And that, of course, blows away the target price," he said.

Although there is a novel therapy adjustment, Liu said that Sinai expected CMS to provide more of an adjustment than it actually did. Sinai hoped that the adjustment would offset the vast majority of the amount it was over the target price, but that was not the case.

Both Liu and Gould admitted that their practices were in the red as of the first reconciliation reports, released in February. Gould said the challenge was that NGOC was being compared against itself, so the bar was a lot higher.

"We've got probably the most sophisticated practice in the country with the most experience doing this work [in the red], which is fascinating and scary at the same time," Feinberg said.

Both Liu and Gould agreed that even if they would like to see some aspects changed and adjusted, the OCM is headed in the right direction. "Value-based care is here to stay," Liu said, and the OCM has allowed practices of all shapes and sizes to work together.

Gould added that he has been glad to see CMS get into the value-based care arena. NGOC and other practices participating in the OCM are working hard to provide feedback to improve the program and make it sustainable.

"At the end of the day, I think it's imperative upon physicians to really not only use good clinical judgment but [also] be good financial stewards of the healthcare dollar so that we're able to afford these new, expensive treatments," Gould said. ♦

REFERENCES

1. Oncology Care Model. CMS website. [cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2016-Fact-sheets-items/2016-06-29.html](https://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2016-Fact-sheets-items/2016-06-29.html). Published June 29, 2016. Accessed January 7, 2018.
2. Implementing alternative payment models for improved population health: experiences from the OCM. *The American Journal of Managed Care* website. ajmc.com/interactive-tools/experiences-from-the-ocm. Accessed July 9, 2018.
3. Innovative Oncology Business Solutions. The COME HOME model. COME HOME program website. come-homeprogram.com/index.php/come-home-practices/. Accessed July 9, 2018.
4. Fargnoli B, Holleran R, Kolodziej M. Why oncologists need technology to succeed in alternative payment models. *Am J Manag Care*. 2017;23(SP5):SP196-SP198.

Experts Suggest Prioritizing Price and Benefit, Allowing Negotiations for Targeted Cancer Drugs

IN THE UNITED STATES, spending on cancer drugs continues to substantially increase, and targeted cancer drugs contribute significantly to this growth. Experts recently proposed 3 steps to promote targeted cancer drugs that yield clinical benefits and also reduce overall price growth.

“The distorted pricing of marginally effective drugs risks crowding out the capacity of the US health system to pay for highly effective cancer drugs or other therapies of public health importance, potentially jeopardizing valuable innovation and escalating out-of-pocket expenses,” the authors said. “The combination of high prices and marginal effectiveness is unsustainable.”

First, the report suggested that the FDA should develop guidance on minimum clinically meaningful effect sizes for cancer drugs. This would explain past FDA guidance and establish a consensus-driven definition of minimum clinically meaningful effect sizes. To achieve this, multidisciplinary advisory councils of scientists, oncologists, patient advocates, and industry representatives should work together.

The authors noted that clinical experts have already supported this principal: The American Society of Clinical Oncology endorsed a minimum absolute improvement of 3 to 6 months in overall survival over best available treatment for drug trials among metastatic disease patients.

“The distorted pricing of marginally effective drugs risks crowding out the capacity of the US health system to pay for highly effective cancer drugs or other therapies of public health importance, potentially jeopardizing valuable innovation and escalating out-of-pocket expenses.”

“Guidance could separately address cases in which, despite little or no change in median overall survival or hazard ratios, small proportions of patients experience large gains and the challenge of estimating benefits when pivotal trials involve head-to-head comparisons against active controls, thereby potentially underestimating the overall efficacy of novel agents,” the authors wrote. “By defining norms, the FDA would encourage manufacturers to design trials that demonstrate clinically meaningful benefits.”

The next step the experts proposed stated that Medicare should negotiate for targeted cancer drugs. Specifically, it was suggested that Congress could direct CMS to conduct a demonstration project. In this project, Medicare should negotiate the prices of targeted cancer drugs paid for by parts B and D, and it is authorized to apply limited formulary tools to marginally effective targeted cancer drugs.

The last recommended step to promote targeted cancer drugs and reduce overall price growth was that guidelines should prioritize drugs by benefit and price. The authors explained that evidence-based guidelines are best suited to complete this, and such guidelines should distinguish marginally effective drugs from highly effective drugs, as well as promote price transparency by reporting the estimated monthly price of cancer drugs.

“Successfully implementing steps to limit the use of high-priced, marginally effective drugs will be difficult; patients with life-threatening diseases may expect access to drugs despite their high costs and limited benefits,” the report concluded. “Nevertheless, the ultimate beneficiaries of these changes will be patients, who deserve the substantial efficacy, reduced toxicity, and enhanced value that were the original promise of targeted cancer drugs.” ♦

REFERENCE

Bekelman JE, Joffe S. Three steps toward a more sustainable path for targeted cancer drugs. *JAMA*. 2018;319(21):2167-2168. doi: 10.1001/jama.2018.3414.

Study Suggests HPV Test More Accurate Than Pap Smear for Cervical Cancer Screening

WHEN IT COMES TO cervical cancer screening, most women receive a cytology-based Papanicolaou (Pap) smear, in which cells are scraped from the back of the cervix. However, human papillomavirus (HPV)-based testing may be a more accurate way to screen for cervical cancer, new study results suggest.¹

Despite the widespread use of Pap smears, it was estimated that 12,820 women in the United States would develop, and 4210 would die from, cervical cancer in 2017. Because more than 99% of all cervical cancers are associated with HPV, testing for the infection has been touted as an alternative for cervical cancer screening. Previous research has indicated that HPV testing alone or combined with a Pap smear is linked to increased detection of precancerous lesions in the first screening round, followed by a reduction in lesions.

However, major organizations, such as the American Society of Clinical Oncology, have called for clinical trials involving HPV testing alone for more than 1 round of screening to further inform the implementation of the screening.

To determine the efficacy of primary HPV testing alone, researchers conducted the 4-year HPV For Cervical Cancer (HPV FOCAL) screening trial of women aged 25 to 65 years. Women were recruited from January 2008 through May 2012 and followed through December 2016.

A total of 19,009 women were randomized to receive either HPV testing (intervention group) or a Pap smear (control group). Women with negative Pap smear results received a second Pap smear after 24 months. After 48 months, both groups received HPV screening and a Pap smear.

Consistent with prior studies, more cases of abnormal cells in the cervix, known as cervical intraepithelial neoplasia (CIN), grade 3 or worse (CIN3+), were detected in the intervention group compared with the control group in the first round of screening. By 48 months, there were significantly fewer cases of CIN2+ and CIN3+ detected among all age groups in the intervention group.

The researchers observed that women who were HPV-negative at baseline were significantly less likely to have CIN2+ or CIN3+ at 48 months compared with those who had negative Pap smear results at baseline. “These results have demonstrated that primary HPV testing detects cervical neoplasia earlier and more accurately than cytology,” they wrote.

However, by the end of follow-up (72 months), incidence was similar across both groups.

The researchers also noted concerns regarding lower CIN2+ specificity with HPV testing, leading to higher rates of positive screens and therefore more colonoscopies and biopsies, which could cause unintended harm for women and increased costs if the tests prove unnecessary.

In 2017, the US Preventive Services Task Force made a draft recommendation that women 30 years or older receive just 1 screening method—a Pap smear or an HPV test—instead of cotesting.² Chris Zahn, MD, vice president of practice for the American College of Obstetricians and Gynecologists, said in an email that studies like the HPV FOCAL trial can lead to a change in the guidelines.

Even if guidelines do change for women 30 years or older, the Pap smear is still important for women age 21 to 29, according to Kathleen Schmeler, MD, a gynecologic oncologist at The University of Texas MD Anderson Cancer Center. She told National Public Radio that she believes that the age group can't rely on HPV testing because the majority will contract HPV at some point, and in many cases, it goes away on its own.³

However, if the virus persists until women are in their 30s, it becomes a problem, Schmeler said. “If you tested everyone for HPV in their 20s, they are almost all going to be positive, but there's going to be all of this intervention that's not needed,” she said. ♦

Reporting by Surabhi Dangi-Garimella, PhD; Kelly Davio; Samantha DiGrande; and Laura Jozst

REFERENCES

- Ogilvie G, Niekerk D, Krajden M, et al. Effect of screening with primary cervical HPV testing vs cytology testing on high-grade cervical intraepithelial neoplasia at 48 months: the HPV FOCAL randomized clinical trial [published online July 3, 2018]. *JAMA*. doi: 10.1001/jama.2018.7464.
- US Preventive Services Task Force. Draft recommendation statement. cervical cancer: screening. USPSTF website. uspreventiveservicestaskforce.org/Page/Document/draft-recommendation-statement/cervical-cancer-screening2. Published September 2017. Accessed July 9, 2018.
- Watson SK. For women over 30, there may be a better choice than the Pap smear. National Public Radio website. npr.org/sections/health-shots/2018/07/03/625696664/for-women-over-30-there-may-be-a-better-choice-than-the-pap-smear. Published July 3, 2018. Accessed July 9, 2018.

Senate Judiciary Committee Votes to Advance CREATES Act

THE SENATE JUDICIARY COMMITTEE voted 16 to 5 on June 14, 2018, to report the Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act to the Senate floor.

Under the CREATES Act,¹ a generic or biosimilar developer can bring a civil action against an innovator drug company that refuses to make available enough samples of a product for testing. It also allows the FDA to approve alternative Risk Evaluation and Mitigation Strategy programs if a generic or biosimilar developer and the innovator company are unable to arrive at a single shared system.

The legislation, sponsored by Sen. Patrick Leahy, D-Vermont, was first introduced in a different version in 2016 and, since then, has enjoyed broad bipartisan support. However, the bill languished without a vote as it faced opposition from pharmaceutical companies. *The Hill* reported in April 2018² that the Pharmaceutical Research and Manufacturers of America spent approximately \$10 million on lobbying efforts—including efforts to halt progress of the CREATES Act—in the first quarter of this year.

Among the bill's most vocal supporters³ is former Rep. Henry Waxman, D-California, who cosponsored (with Senator Orrin Hatch, R-Utah) the legal foundation for the US generics drug market: the Drug Price Competition and Patent Term Restoration Act of 1984, referred to colloquially as Hatch-Waxman.

Despite Waxman's support, 1 of the 5 senators to vote against reporting the CREATES Act to the floor was Hatch. Before the vote, Hatch noted his "keen interest in ensuring that we have a well-functioning generics industry" and added that, although the CREATES Act has a "laudable goal," its monetary caps on damages that generic and biosimilar development companies can seek are, in his view, high enough to incentivize "nonmeritorious litigation."

Hatch added that he will be sponsoring an amendment to the bill designed to limit the challenges that generic and biosimilar developers can bring against innovator product sponsors. His amendment would force a challenger to choose between bringing a Hatch-Waxman suit or seeking an inter partes review proceeding; a company could not pursue both avenues to challenge a drug patent. The provisions of the amendment would also apply to postgrant review proceedings and biosimilar litigation, he said. ♦

REFERENCES

- CREATES Act of 2017, S 974, 115th Cong, 1st Sess (2017).
- Hellmann J. PhRMA spends record amount on lobbying amid drug pricing fights. *The Hill* website. thehill.com/policy/healthcare/384176-phrma-spends-record-amount-on-lobbying-amid-drug-pricing-fights. Published April 20, 2018. Accessed June 14, 2018.
- Davio K. Renewed push for CREATES Act as budget deadline looms. The Center for Biosimilars® website. centerforbiosimilars.com/news/renewed-push-for-creates-act-as-budget-deadline-looms. Published February 5, 2018. Accessed June 14, 2018.

BrainChild-01 Will Evaluate CAR T Cells in Pediatric CNS Tumors

INVESTIGATORS AT SEATTLE CHILDREN'S Hospital have initiated enrollment in the BrainChild-01 trial, which is designed to test chimeric antigen receptor (CAR) T-cell therapy in children and young adults with relapsed/refractory brain and central nervous system (CNS) tumors. Intriguingly, the modified CAR T cells will not be infused intravenously—rather, they will be injected either directly at the site of tumor resection or into the ventricular system of the CNS.¹

According to the National Brain Tumor Society, about 28,000 US children are living with a brain tumor, and 4610² cases of childhood and adolescent primary malignant and nonmalignant brain and CNS tumors are expected to be diagnosed in 2018. Brain tumors surpass leukemia as the leading cause of cancer-related deaths among children and adolescents.

Direct infusion of CAR T cells into the resected tumor cavity in the brain is also being evaluated in adult patients. Speaking at the recent annual meeting³ of the American Society of Clinical Oncology, Amy B. Heimberger, MD, a professor in the Department of Neurosurgery at The University of Texas MD Anderson Cancer Center, told the audience that the process helps overcome the lack of T-cell infiltration in the tumor. Multiple intracranial infusions of interleukin-13 receptor $\alpha 2$ CAR T cells in the resected tumor cavity of a patient with recurrent multifocal glioblastoma, as well as in the ventricular system, resulted in a regression of intracranial and spinal tumors in that patient. The response was sustained for 7.5 months.

The phase 1 BrainChild-01 study expects to recruit 26 patients with recurrent or refractory *HER2*-positive CNS tumors. The participants will be treated with autologous CD4 and CD8 T cells transduced to express a *HER2*-specific CAR and a truncated human epidermal growth factor receptor polypeptide, or EGFRt. Children with *HER2*-positive tumors that have relapsed or are refractory to prior treatment and who meet the trial's inclusion criteria⁴ will undergo apheresis.⁵ The collected T cells will then be genetically modified to target *HER2* gene-expressing tumor cells, and the modified cells will be administered through an indwelling catheter in 2 phases:

- A weekly dose for 3 weeks, followed by a week off and an examination period
- Weekly dose for 3 weeks

Following evaluation of treatment impact, including magnetic resonance imaging, patients can receive 6 more courses of infusion if there are T cells available and patients have not had adverse effects.

Primary outcomes that the study plans to measure include safety and feasibility of administering the CAR T-cell infusion directly into the tumor cavity.

Secondary objectives include examining the distribution of CAR T cells in the cerebrospinal fluid, their diffusion into the bloodstream, and, if possible, monitoring *HER2* gene expression in the tumors at diagnosis versus at recurrence.

BrainChild-01, as the trial is named, will initially leave out patients diagnosed with diffuse intrinsic pontine gliomas, or DIPG tumors, highly aggressive tumors found at the base of the brain. However, Seattle Children's Hospital plans to include children needing treatment for DIPG tumors in future BrainChild trials. ♦

REFERENCES

- T-Cell immunotherapy for brain and central nervous system tumors. Seattle Children's Hospital website. seattlechildrens.org/clinics-programs/cancer/research-and-clinical-trials/t-cell-therapy-brain-cns/. Published June 2018. Accessed July 5, 2018.
- Quick brain tumor facts. National Brain Tumor Society website. braintumor.org/brain-tumor-information/brain-tumor-facts/. Accessed July 5, 2018.
- Dangi-Garimella S. Identifying rational immunotherapy combinations for glioblastoma: a progress report. *The American Journal of Managed Care*® website. ajmc.com/conferences/asco-2018/identifying-rational-immunotherapy-combinations-for-glioblastoma-a-progress-report?p=2. Published June 2, 2018. Accessed July 5, 2018.
- HER2*-Specific CAR T Cell Locoregional Immunotherapy for *HER2*-Positive Recurrent/Refractory Pediatric CNS Tumors. clinicaltrials.gov/ct2/show/NCT03500991?term=BrainChild-01&rank=1. Updated June 20, 2018. Accessed July 5, 2018.
- Dangi-Garimella S. Q&A with Dr Jae Park on the promise of CAR-T cells in cancer care. *The American Journal of Managed Care*® website. ajmc.com/journals/evidence-based-oncology/2017/february-2017/q-a-with-dr-jae-park-on-the-promise-of-car-t-cells-in-cancer-care/. Published February 16, 2017. Accessed July 5, 2018.

Research Highlights Long-Term Survival and Health-Related QoL in Patients With Newly Diagnosed MM

RESEARCH PRESENTED AT THE 2018 American Society of Clinical Oncology Annual Meeting identified predictors of long-term survival and health-related quality of life in patients with newly diagnosed multiple myeloma (MM).

The first abstract used data from the registry, a multicenter prospective observational cohort study in the United States designed to examine diagnostic and treatment patterns, clinical outcomes, and quality of life in patients with newly diagnosed MM, in order to identify characteristics associated with overall survival of 6 years or greater versus death at less than 6 years.¹

As of February 2017, the median follow-up was 65.4 months. Baseline characteristics associated with overall survival of 6 years or greater included age (being 70 years old or younger); Eastern Cooperative Oncology Group Performance Status of grade 0 or 1 (being fully active or being restricted in physically strenuous activity but ambulatory); lower International Staging System stage, which is used to prognosticate MM severity; and lack of history of diabetes.

In addition, the investigators found that patients who had an overall survival of 6 years or longer also had higher rates of triplet treatment, stem cell transplant, and maintenance therapy (with or without stem cell transplant), as well as higher response rates.

The second abstract focused on patients with newly diagnosed MM who are ineligible for stem cell transplantation (SCT) as part of ALCYONE, an ongoing multicenter, open-label, phase 3 trial.² Participants are not eligible for high-dose chemotherapy with SCT because of their age (65 years or older) or coexisting conditions. The trial has shown³ significant progression-free survival (PFS) with patients treated with daratumumab, bortezomib, melphalan, and prednisone (D-VMP) compared with patients receiving bortezomib, melphalan, and prednisone alone (VMP).

“Measuring patient-reported outcomes (PROs) alongside disease progression provides the patient perspective on quality of survival and the value of health-related quality of life (HRQoL) for treatment decisions,” the authors of the abstract explained.

Patients completed the European Organization for Research and Treatment of Cancer Questionnaire (EORTC QLQ-C30) and the EuroQoL Questionnaire at baseline and every 3 months during treatment. A total of 350 patients were receiving D-VMP, and 356 received VMP. The investigators found better HRQoL in patients in the D-VMP arm, plus 59.7% of patients receiving D-VMP reported meaningful improvement in global health status, as measured by EORTC QLQ-C30, compared with 52% of patients receiving VMP.

“Improvements in HRQoL were consistent with the clinical benefit showing superior PFS of D-VMP over VMP alone,” the authors concluded. ♦

REFERENCES

1. Gasparetto C, Rifkin RM, Terebello HW, et al. Predictors of long-term survival in newly diagnosed multiple myeloma (NDMM) patients (pts) enrolled in the Connect MM Registry. Presented at: 2018 American Society of Clinical Oncology Annual Meeting; June 1-5, 2018; Chicago, IL. Abstract 8037. abstracts.asco.org/214/AbstView_214_214549.html.
2. Gries K, Fastenau J, Chen Y, et al. Health-related quality of life in patients with newly diagnosed multiple myeloma who are ineligible for stem cell transplantation: results from the ALCYONE trial. Presented at: 2018 American Society of Clinical Oncology Annual Meeting; June 1-5, 2018; Chicago, IL. Abstract 8042. ascopubs.org/doi/abs/10.1200/JCO.2018.36.15_suppl.8042.
3. Joszt L. Daratumumab approved as frontline treatment in newly diagnosed multiple myeloma. *The American Journal of Managed Care* website. ajmc.com/newsroom/daratumumab-approved-as-frontline-treatment-in-newly-diagnosed-multiple-myeloma. Published May 8, 2018. Accessed July 6, 2018.

Glasdegib Receives Priority Review Based on Results That Show Nearly Doubled OS in AML

IMPRESSIVE PHASE 2 STUDY results prompted the FDA to grant priority review designation to Glasdegib, an investigational oral smoothened inhibitor for treating adult patients with previously untreated acute myeloid leukemia (AML) in combination with low-dose chemotherapy (cytarabine).

Findings from the randomized phase 2 trial showed a 49.9% reduction in the risk of death for patients treated with glasdegib plus cytarabine compared with patients treated with cytarabine alone. The Prescription Drug User Fee Act goal date for the FDA's decision is in December 2018.

“Patients with acute myeloid leukemia who are ineligible for intensive chemotherapy are in critical need of new treatment options to improve their overall survival,” Mace Rothenberg, MD, chief development officer of oncology at Pfizer Global Product Development, said in a statement.¹

“The Hedgehog pathway is a compelling target in cancer research because of the ability to target and disrupt the root of the cancer; that is, the cancer-originating cell.”

—Jorge Cortes, MD,
The University of Texas MD Anderson Cancer Center

In the phase 2 BRIGHT 1003 study, a randomized, open-label, multicenter trial, 88 patients received 100 mg daily of glasdegib with 20 mg of cytarabine twice daily, and 44 patients received cytarabine alone. The median overall survival (OS) was 8.8 months for patients treated with glasdegib, whereas the patients on cytarabine alone had a median OS of 4.9 months.

The phase 2 trial results were originally presented at the 58th American Society of Hematology Annual Meeting and Exposition. After the findings were reported, Jorge Cortes, MD, an investigator in the trial and deputy chair and professor of medicine in the Department of Leukemia at The University of Texas MD Anderson Cancer Center, explained that glasdegib works by disrupting the Hedgehog pathway, which is thought to play a role in the development of multiple types of cancer.

“The Hedgehog pathway is a compelling target in cancer research because of the ability to target and disrupt the root of the cancer; that is, the cancer-originating cell,” Cortes said in a statement in December 2016.² “As the first smoothened inhibitor to demonstrate clinical benefit in patients with AML and high-risk MDS [myelodysplastic syndrome] who were ineligible for intensive chemotherapy, these results with glasdegib provide hope that interfering with this pathway may lead to potential new treatment options for blood cancers that may improve patient outcomes.”

The most common serious adverse effects were febrile neutropenia (29% of patients in the glasdegib arm vs 20% in the cytarabine alone arm) and pneumonia (21% vs 17%). ♦

REFERENCES

1. US FDA grants priority review for Pfizer's new drug application for glasdegib in patients with previously untreated acute myeloid leukemia [press release]. New York, NY: Pfizer; June 27, 2018. press.pfizer.com/press-release/us-fda-grants-priority-review-pfizers-new-drug-application-glasdegib-patients-previous. Accessed July 9, 2018.
2. New phase 2 results show investigational compound glasdegib improved overall survival in acute myeloid leukemia and high-risk myelodysplastic syndrome [press release]. New York, NY: Pfizer; December 3, 2016. pfizer.com/news/press-release/press-release-detail/new_phase_2_results_show_investigational_compound_glasdegib_improved_overall_survival_in_acute_myeloid_leukemia_and_high_risk_myelodysplastic_syndrome. Accessed July 9, 2018.

PTAB Denies Samsung Bioepis' Request for IPR on Herceptin Patent

THE UNITED STATES PATENT Trial and Appeal Board (PTAB) has denied biosimilar developer Samsung Bioepis' request for inter partes review (IPR) of a patent that Genentech holds covering reference trastuzumab (Herceptin).¹

This is not the first time that the board has denied a claim for review of US patent 7,846,441. Previously, Hospira, owned by Pfizer, and Celltrion petitioned PTAB to review the Genentech patent in January 2017. The PTAB initially denied that request but reversed the decision after finding that Hospira had shown that each of the patent's claims were likely invalid.

Celltrion filed its own challenge in March 2017, in which the PTAB had instituted an IPR, and Hospira subsequently joined.

Samsung Bioepis had stated that Genentech's claim was obvious, based in part on a research paper, which also was cited in both prior claims from Celltrion and Hospira.

Although the outcome favored Genentech, the pharma company is taking steps to further protect its drug from competitors and recently indicated plans to seek injunctions to stop Samsung Bioepis from selling its biosimilar trastuzumab in Europe.

In the board's denial of Samsung Bioepis' request for an IPR proceeding, it explained that the company's evidence brought nothing new to the table. The previously cited research paper was cited in an additional reference provided by Samsung Bioepis, and that reference was cited by yet another. "In other words, Bioepis' arguments on the newly asserted references are substantially the same as those in the earlier cases," said the board.

According to Genentech, that particular paper was also considered in the prosecution of the patent. "Thus, after considering the totality of the circumstances, we agree with [Genentech] that it is appropriate for us to exercise our discretion to deny the petition under 35 USC § 325(d)," the board stated.

Although the outcome favored Genentech, the pharma company is taking steps to further protect its drug from competitors and recently indicated plans² to seek injunctions to stop Samsung Bioepis from selling its biosimilar trastuzumab in Europe.

Genentech has requested US District Judge Robert Sweet to order Samsung Bioepis' counsel, White & Case LLP, to share parts of its abbreviated biologics license application to examine certain chemical properties of the proposed trastuzumab biosimilar.

According to White & Case, Genentech is not entitled to receive this information from the European Medicines Agency and is "fishing" for grounds to challenge the biosimilar. The judge has yet to rule. ♦

REFERENCES

1. Bultman M. PTAB rejects Samsung challenge to Herceptin patent. Law 360 website. law360.com/lifesciences/articles/1054712/ptab-rejects-samsung-challenge-to-herceptin-patent?nl_pk=5d0ac488-f0bb-4d08-9a99-0117196d0e19&utm_source=newsletter&utm_medium=email&utm_campaign=lifesciences. Published June 18, 2018. Accessed June 19, 2018.
2. Newsham J. Genentech wants White & Case to share Samsung drug info. Law 360 website. law360.com/articles/1051153/genentech-wants-white-case-to-share-samsung-drug-info. Published June 6, 2018. Accessed June 19, 2018.

Progress Continues for Celltrion on Trastuzumab and Subcutaneous Infliximab Biosimilars

AFTER RECEIVING COMPLETE RESPONSE letters (CRLs) in April 2018 for 2 proposed biosimilars,¹ Korean drug maker Celltrion announced² that it resubmitted its biologics license application (BLA) for CT-P6, a trastuzumab molecule referencing Herceptin. In May, the company resubmitted its BLA for CT-P10, a rituximab biosimilar referencing Rituxan.

According to a statement on Celltrion's website, the FDA requested supplementary information about both products when it issued the CRLs, and the company worked closely with regulators to address issues identified in a February 2018 FDA warning letter related to manufacturing processes. In its announcement about trastuzumab's resubmission, Celltrion indicated that the FDA had notified the company of its reinspection schedule, and both molecules could potentially be approved by the end of 2018.

Separately, Celltrion announced new data for its proposed subcutaneous formulation of its flagship biosimilar, CT-P13 (sold in the United States as Inflectra and in the European Union as Reimsima). During the European League Against Rheumatism's Annual European Congress of Rheumatology, held in June in Amsterdam, the Netherlands, investigators reported that the company's subcutaneous CT-P13, which can be self-administered, had similar efficacy and generally similar safety to the currently approved intravenous (IV) CT-P13 up to week 30 in patients with rheumatoid arthritis (RA).³

Right now, patients with inflammatory disease have no subcutaneous infliximab options; a self-administered option could offer greater flexibility in treatment plans.

In a study of 48 patients with RA, who were assigned to receive either IV infliximab or subcutaneous injections of 90, 120, or 180 mg of infliximab, disease improvement (assessed in terms of disease activity score in a count of 28 joints and the American College of Rheumatology's criteria for 20% improvement) was comparable across all 4 treatment groups.

Two patients experienced hypersensitivity reactions, 1 of whom tested positive for antidrug antibodies at week 6.

In June, Celltrion reported positive results from a phase 1 study of its subcutaneous formulation of the biosimilar in patients with Crohn disease.⁴ In that study, patients who received IV therapy and those who received subcutaneous doses of 120, 180, and 240 mg showed similar improvement in terms of Crohn Disease Activity Index score.

Currently, patients with inflammatory diseases have no subcutaneous infliximab options; a self-administered option, if eventually approved, could offer greater flexibility in their treatment plans. ♦

REFERENCES

1. Davio K. FDA rejects Celltrion's rituximab and trastuzumab biosimilars. The Center for Biosimilars® website. centerforbiosimilars.com/news/fda-rejects-celltrions-rituximab-and-trastuzumab-biosimilars. Published April 5, 2018. Accessed June 18, 2018.
2. Celltrion completes resubmission to FDA for proposed trastuzumab biosimilar [press release]. Incheon, South Korea: Celltrion; June 18, 2018. businesswire.com/news/home/20180617005036/en/Celltrion-Completes-Resubmission-FDA-Proposed-Trastuzumab-Biosimilar. Accessed June 18, 2018.
3. Westhovens R, Yoo DH, Jaworski J, et al. Novel formulation of CT-P13 for subcutaneous administration in patients with rheumatoid arthritis: initial results from a phase i/iii randomised controlled trial. Presented at: the European League Against Rheumatism's Annual European Congress of Rheumatology; June 13-16, 2018; Amsterdam, the Netherlands. Abstract THU0191.
4. Davio K. Celltrion reports positive phase 1 results for subcutaneous inflectra in CD. The Center for Biosimilars® website. centerforbiosimilars.com/news/celltrion-reports-positive-phase-1-results-for-subcutaneous-inflectra-in-cd. Published June 5, 2018. Accessed June 18, 2018.

YES CAR T IS HERE

YESCARTA®, THE FIRST CAR T THERAPY FOR CERTAIN TYPES OF RELAPSED OR REFRACTORY LARGE B-CELL LYMPHOMA

The following data reflect results from the ZUMA-1 pivotal trial*¹

// PROVEN EFFICACY

51%

Patients achieved a best response of complete remission (CR) (52/101)

NR

Response duration was not reached at a median follow-up of 7.9 months in patients who achieved CR

// CYTOKINE RELEASE SYNDROME

13% 94%

Grade ≥ 3 incidence Overall incidence

// NEUROLOGIC TOXICITIES

31% 87%

Grade ≥ 3 incidence Overall incidence

// RAPID & RELIABLE MANUFACTURING

17 DAYS

Median turnaround time[†]

99%

Manufacturing success of CAR T cells engineered and expanded ex vivo

VISIT YESCARTAHCP.COM/CENTERS TO FIND A LIST OF AUTHORIZED TREATMENT CENTERS

*ZUMA-1 was an open-label, single-arm study in 101 adult patients who received YESCARTA® therapy. Patients received lymphodepleting chemotherapy prior to a single infusion of YESCARTA® at a target dose of 2×10^6 viable CAR T cells/kg body weight (maximum of 2×10^8 viable CAR T cells). Patients had refractory disease to their most recent therapy, or had relapsed within 1 year after autologous hematopoietic stem cell transplantation.

[†]The median time from leukapheresis to product delivery.

INDICATION

YESCARTA® is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Limitation of Use: YESCARTA® is not indicated for the treatment of patients with primary central nervous system lymphoma.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: CYTOKINE RELEASE SYNDROME AND NEUROLOGIC TOXICITIES

- **Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving YESCARTA®. Do not administer YESCARTA® to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.**
- **Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving YESCARTA®, including concurrently with CRS or after CRS resolution. Monitor for neurologic toxicities after treatment with YESCARTA®. Provide supportive care and/or corticosteroids as needed.**
- **YESCARTA® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA® REMS.**

Important Safety Information continued on adjacent page.

IMPORTANT SAFETY INFORMATION (continued)

CYTOKINE RELEASE SYNDROME (CRS): CRS occurred in 94% of patients, including 13% with \geq Grade 3. Among patients who died after receiving YESCARTA[®], 4 had ongoing CRS at death. The median time to onset was 2 days (range: 1-12 days) and median duration was 7 days (range: 2-58 days). Key manifestations include fever (78%), hypotension (41%), tachycardia (28%), hypoxia (22%), and chills (20%). Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), cardiac arrest, cardiac failure, renal insufficiency, capillary leak syndrome, hypotension, hypoxia, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome. Ensure that 2 doses of tocilizumab are available prior to infusion of YESCARTA[®]. Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for 4 weeks after infusion. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time. At the first sign of CRS, institute treatment with supportive care, tocilizumab or tocilizumab and corticosteroids as indicated.

NEUROLOGIC TOXICITIES: Neurologic toxicities occurred in 87% of patients. Ninety-eight percent of all neurologic toxicities occurred within the first 8 weeks, with a median time to onset of 4 days (range: 1-43 days) and a median duration of 17 days. Grade 3 or higher occurred in 31% of patients. The most common neurologic toxicities included encephalopathy (57%), headache (44%), tremor (31%), dizziness (21%), aphasia (18%), delirium (17%), insomnia (9%) and anxiety (9%). Prolonged encephalopathy lasting up to 173 days was noted. Serious events including leukoencephalopathy and seizures occurred with YESCARTA[®]. Fatal and serious cases of cerebral edema have occurred in patients treated with YESCARTA[®]. Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of neurologic toxicities. Monitor patients for signs or symptoms of neurologic toxicities for 4 weeks after infusion and treat promptly.

YESCARTA[®] REMS: Because of the risk of CRS and neurologic toxicities, YESCARTA[®] is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA[®] REMS. The required components of the YESCARTA[®] REMS are: Healthcare facilities that dispense and administer YESCARTA[®] must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab, and ensure that a minimum of 2 doses of tocilizumab are available for each patient for infusion within 2 hours after YESCARTA[®] infusion, if needed for treatment of CRS. Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense or administer YESCARTA[®] are trained about the management of CRS and neurologic toxicities. Further information is available at www.YESCARTAREMS.com or 1-844-454-KITE (5483).

HYPERSENSITIVITY REACTIONS: Allergic reactions may occur. Serious hypersensitivity reactions including anaphylaxis may be due to dimethyl sulfoxide (DMSO) or residual gentamicin in YESCARTA[®].

SERIOUS INFECTIONS: Severe or life-threatening infections occurred. Infections (all grades) occurred in 38% of patients, and in 23% with \geq Grade 3. Grade 3 or higher infections with an unspecified pathogen occurred in 16% of patients, bacterial infections in 9%, and viral infections in 4%. YESCARTA[®] should not be administered to patients with clinically significant active systemic infections. Monitor patients for signs and symptoms of infection before and after YESCARTA[®] infusion and treat appropriately. Administer prophylactic anti-microbials according to local guidelines. Febrile neutropenia was observed in 36% of patients and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad spectrum antibiotics, fluids and other supportive care as medically indicated. Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, can occur in patients treated with drugs directed against B cells. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing.

PROLONGED CYTOPENIAS: Patients may exhibit cytopenias for several weeks following lymphodepleting chemotherapy and YESCARTA[®] infusion. Grade 3 or higher cytopenias not resolved by Day 30 following YESCARTA[®] infusion occurred in 28% of patients and included thrombocytopenia (18%), neutropenia (15%), and anemia (3%). Monitor blood counts after YESCARTA[®] infusion.

HYPOGAMMAGLOBULINEMIA: B-cell aplasia and hypogammaglobulinemia can occur. Hypogammaglobulinemia occurred in 15% of patients. Monitor immunoglobulin levels after treatment and manage using infection precautions, antibiotic prophylaxis and immunoglobulin replacement. The safety of immunization with live viral vaccines during or following YESCARTA[®] treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during YESCARTA[®] treatment, and until immune recovery following treatment.

SECONDARY MALIGNANCIES: Patients may develop secondary malignancies. Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Kite at 1-844-454-KITE (5483) to obtain instructions on patient samples to collect for testing.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: Due to the potential for neurologic events, including altered mental status or seizures, patients are at risk for altered or decreased consciousness or coordination in the 8 weeks following YESCARTA[®] infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, during this initial period.

ADVERSE REACTIONS: The most common adverse reactions (incidence \geq 20%) include CRS, fever, hypotension, encephalopathy, tachycardia, fatigue, headache, decreased appetite, chills, diarrhea, febrile neutropenia, infections-pathogen unspecified, nausea, hypoxia, tremor, cough, vomiting, dizziness, constipation, and cardiac arrhythmias.

Please see Brief Summary of Prescribing Information, including **BOXED WARNING**, on the following pages.

BRIEF SUMMARY OF PRESCRIBING INFORMATION FOR YESCARTA®
(axicabtagene ciloleucel) suspension for intravenous infusion

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

<p>WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITIES</p> <ul style="list-style-type: none"> • Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving YESCARTA. Do not administer YESCARTA to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids [see Dosage and Administration (2.2, 2.3), Warnings and Precautions (5.1)]. • Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving YESCARTA, including concurrently with CRS or after CRS resolution. Monitor for neurologic toxicities after treatment with YESCARTA. Provide supportive care and/or corticosteroids, as needed [see Dosage and Administration (2.2, 2.3), Warnings and Precautions (5.2)]. • YESCARTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA REMS [see Warnings and Precautions (5.3)].

1 INDICATIONS AND USAGE

YESCARTA is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Limitation of Use: YESCARTA is not indicated for the treatment of patients with primary central nervous system lymphoma.

2 DOSAGE AND ADMINISTRATION

2.2 Administration: YESCARTA is for autologous use only. The patient's identity must match the patient identifiers on the YESCARTA cassette and infusion bag. Do not infuse YESCARTA if the information on the patient-specific label does not match the intended patient [see Dosage and Administration(2.2.3)].

Preparing Patient for YESCARTA Infusion: Confirm availability of YESCARTA prior to starting the lymphodepleting regimen. **Pre-treatment:** Administer a lymphodepleting chemotherapy regimen of cyclophosphamide 500 mg/m² intravenously and fludarabine 30 mg/m² intravenously on the fifth, fourth, and third day before infusion of YESCARTA. **Premedication:** Administer acetaminophen 650 mg PO and diphenhydramine 12.5 mg intravenously or PO approximately 1 hour before YESCARTA infusion. Avoid prophylactic use of systemic corticosteroids, as it may interfere with the activity of YESCARTA.

Preparation of YESCARTA for Infusion: Coordinate the timing of YESCARTA thaw and infusion. Confirm the infusion time in advance, and adjust the start time of YESCARTA thaw such that it will be available for infusion when the patient is ready. Confirm patient identity: Prior to YESCARTA preparation, match the patient's identity with the patient identifiers on the YESCARTA cassette. Do not remove the YESCARTA product bag from the cassette if the information on the patient-specific label does not match the intended patient. Once patient identification is confirmed, remove the YESCARTA product bag from the cassette and check that the patient information on the cassette label matches the bag label. Inspect the product bag for any breaches of container integrity such as breaks or cracks before thawing. If the bag is compromised, follow the local guidelines (or call Kite at 1-844-454-KITE). Place the infusion bag inside a second sterile bag per local guidelines. Thaw YESCARTA at approximately 37°C using either a water bath or dry thaw method until there is no visible ice in the infusion bag. Gently mix the contents of the bag to disperse clumps of cellular material. If visible cell clumps remain continue to gently mix the contents of the bag. Small clumps of cellular material should disperse with gentle manual mixing. Do not wash, spin down, and/or re-suspend YESCARTA in new media prior to infusion. Once thawed, YESCARTA may be stored at room temperature (20°C to 25°C) for up to 3 hours.

Administration: For autologous use only. Ensure that tocilizumab and emergency equipment are available prior to infusion and during the recovery period. Do NOT use a leukodepleting filter. Central venous access is recommended for the infusion of YESCARTA. Confirm the patient's identity matches the patient identifiers on the YESCARTA product bag. Prime the tubing with normal saline prior to infusion. Infuse the entire contents of the YESCARTA bag within 30 minutes by either gravity or a peristaltic pump. YESCARTA is stable at room temperature for up to 3 hours after thaw. Gently agitate the product bag during YESCARTA infusion to prevent cell clumping. After the entire content of the product bag is infused, rinse the tubing with normal saline at the same infusion rate to ensure all product is delivered. YESCARTA contains human blood cells that are genetically modified with replication incompetent retroviral vector. Follow universal precautions and local biosafety guidelines for handling and disposal to avoid potential transmission of infectious diseases.

Monitoring: Administer YESCARTA at a certified healthcare facility. Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of CRS and neurologic toxicities. Instruct patients to remain within proximity of the certified healthcare facility for at least 4 weeks following infusion.

2.3 Management of Severe Adverse Reactions

Cytokine Release Syndrome (CRS): Identify CRS based on clinical presentation [see Warnings and Precautions (5.1)]. Evaluate for and treat other causes of fever, hypoxia, and hypotension. If CRS is suspected, manage according to the recommendations in Table 1. Patients who experience Grade 2 or higher CRS (e.g., hypotension, not responsive to fluids, or hypoxia requiring supplemental oxygenation) should be monitored with continuous cardiac telemetry and pulse oximetry. For patients experiencing severe CRS, consider performing an echocardiogram to assess cardiac function. For severe or life-threatening CRS, consider intensive care supportive therapy.

Table 1. CRS Grading and Management Guidance

CRS Grade (a)	Tocilizumab	Corticosteroids
Grade 1 Symptoms require symptomatic treatment only (e.g., fever, nausea, fatigue, headache, myalgia, malaise).	N/A	N/A
Grade 2 Symptoms require and respond to moderate intervention. Oxygen requirement less than 40% FiO ₂ or hypotension responsive to fluids or low-dose of one vasopressor or Grade 2 organ toxicity (b).	Administer tocilizumab (c) 8 mg/kg intravenously over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.	Manage per Grade 3 if no improvement within 24 hours after starting tocilizumab.

Table 1. CRS Grading and Management Guidance (continued)

CRS Grade (a)	Tocilizumab	Corticosteroids
Grade 3 Symptoms require and respond to aggressive intervention. Oxygen requirement greater than or equal to 40% FiO ₂ or hypotension requiring high-dose or multiple vasopressors or Grade 3 organ toxicity or Grade 4 transaminitis.	Per Grade 2	Administer methylprednisolone 1 mg/kg intravenously twice daily or equivalent dexamethasone (e.g., 10 mg intravenously every 6 hours). Continue corticosteroids use until the event is Grade 1 or less, then taper over 3 days.
Grade 4 Life-threatening symptoms. Requirements for ventilator support, continuous veno-venous hemodialysis (CVVHD) or Grade 4 organ toxicity (excluding transaminitis).	Per Grade 2	Administer methylprednisolone 1000 mg intravenously per day for 3 days; if improves, then manage as above.

(a) Lee et al 2014, (b) Refer to Table 2 for management of neurologic toxicity, (c) Refer to tocilizumab Prescribing Information for details

Neurologic Toxicity: Monitor patients for signs and symptoms of neurologic toxicities (Table 2). Rule out other causes of neurologic symptoms. Patients who experience Grade 2 or higher neurologic toxicities should be monitored with continuous cardiac telemetry and pulse oximetry. Provide intensive care supportive therapy for severe or life threatening neurologic toxicities. Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis for any Grade 2 or higher neurologic toxicities.

Table 2. Neurologic Toxicity Grading and Management Guidance

Grading Assessment	Concurrent CRS	No Concurrent CRS
Grade 2	Administer tocilizumab per Table 1 for management of Grade 2 CRS. If no improvement within 24 hours after starting tocilizumab, administer dexamethasone 10 mg intravenously every 6 hours if not already taking other corticosteroids. Continue dexamethasone use until the event is Grade 1 or less, then taper over 3 days.	Administer dexamethasone 10 mg intravenously every 6 hours. Continue dexamethasone use until the event is Grade 1 or less, then taper over 3 days.
	Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.	
Grade 3	Administer tocilizumab per Table 1 for management of Grade 2 CRS. In addition, administer dexamethasone 10 mg intravenously with the first dose of tocilizumab and repeat dose every 6 hours. Continue dexamethasone use until the event is Grade 1 or less, then taper over 3 days.	Administer dexamethasone 10 mg intravenously every 6 hours. Continue dexamethasone use until the event is Grade 1 or less, then taper over 3 days.
	Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.	
Grade 4	Administer tocilizumab per Table 1 for management of Grade 2 CRS. Administer methylprednisolone 1000 mg intravenously per day with first dose of tocilizumab and continue methylprednisolone 1000 mg intravenously per day for 2 more days; if improves, then manage as above.	Administer methylprednisolone 1000 mg intravenously per day for 3 days; if improves, then manage as above.
	Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.	

4 CONTRAINDICATIONS: None.

5 WARNINGS AND PRECAUTIONS

5.1 Cytokine Release Syndrome (CRS): CRS, including fatal or life-threatening reactions, occurred following treatment with YESCARTA. In Study 1, CRS occurred in 94% (101/108) of patients receiving YESCARTA, including ≥ Grade 3 (Lee grading system) CRS in 13% (14/108) of patients. Among patients who died after receiving YESCARTA, four had ongoing CRS events at the time of death. The median time to onset was 2 days (range: 1 to 12 days) and the median duration of CRS was 7 days (range: 2 to 58 days). Key manifestations of CRS include fever (78%), hypotension (41%), tachycardia (28%), hypoxia (22%), and chills (20%). Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), cardiac arrest, cardiac failure, renal insufficiency, capillary leak syndrome, hypotension, hypoxia, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS) [see Adverse Reactions (6)]. Ensure that 2 doses of tocilizumab are available prior to infusion of YESCARTA. Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for 4 weeks after infusion. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time [see Patient Counseling Information (17)]. At the first sign of CRS, institute treatment with supportive care, tocilizumab or tocilizumab and corticosteroids as indicated [See Dosage and Administration (2.3)].

5.2 Neurologic Toxicities: Neurologic toxicities, that were fatal or life-threatening, occurred following treatment with YESCARTA. Neurologic toxicities occurred in 87% of patients. Ninety-eight percent of all neurologic toxicities occurred within the first 8 weeks of YESCARTA infusion, with a median time to onset of 4 days (range: 1 to 43 days). The median duration of neurologic toxicities was 17 days. Grade 3 or higher neurologic toxicities occurred in 31% of patients. The most common neurologic toxicities included encephalopathy (57%), headache (44%), tremor (31%), dizziness (21%), aphasia (18%), delirium (17%), insomnia (9%) and anxiety (9%). Prolonged encephalopathy lasting up to 173 days was noted. Serious events including leukoencephalopathy and seizures occurred with YESCARTA. Fatal and serious cases of cerebral edema have occurred in patients treated with YESCARTA. Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of neurologic toxicities. Monitor

patients for signs or symptoms of neurologic toxicities for 4 weeks after infusion and treat promptly [see *Management of Severe Adverse Reactions (2.3; Neurologic Toxicities)*].

5.3 YESCARTA REMS: Because of the risk of CRS and neurologic toxicities, YESCARTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA REMS [see *Boxed Warning and Warnings and Precautions (5.1 and 5.2)*]. The required components of the YESCARTA REMS are:

- Healthcare facilities that dispense and administer YESCARTA must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab, and ensure that a minimum of two doses of tocilizumab are available for each patient for infusion within 2 hours after YESCARTA infusion, if needed for treatment of CRS.
- Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense or administer YESCARTA are trained about the management of CRS and neurologic toxicities.

Further information is available at www.YescartaREMS.com or 1-844-454-KITE (5483).

5.4 Hypersensitivity Reactions: Allergic reactions may occur with the infusion of YESCARTA. Serious hypersensitivity reactions including anaphylaxis, may be due to dimethyl sulfoxide (DMSO) or residual gentamicin in YESCARTA.

5.5 Serious Infections: Severe or life-threatening infections occurred in patients after YESCARTA infusion. In Study 1, infections (all grades) occurred in 38% of patients. Grade 3 or higher infections occurred in 23% of patients. Grade 3 or higher infections with an unspecified pathogen occurred in 16% of patients, bacterial infections in 9%, and viral infections in 4%. YESCARTA should not be administered to patients with clinically significant active systemic infections. Monitor patients for signs and symptoms of infection before and after YESCARTA infusion and treat appropriately. Administer prophylactic anti-microbials according to local guidelines. Febrile neutropenia was observed in 36% of patients after YESCARTA infusion and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad spectrum antibiotics, fluids and other supportive care as medically indicated. *Viral Reactivation:* Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, can occur in patients treated with drugs directed against B cells. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing.

5.6 Prolonged Cytopenias: Patients may exhibit cytopenias for several weeks following lymphodepleting chemotherapy and YESCARTA infusion. In Study 1, Grade 3 or higher cytopenias not resolved by Day 30 following YESCARTA infusion occurred in 28% of patients and included thrombocytopenia (18%), neutropenia (15%), and anemia (3%). Monitor blood counts after YESCARTA infusion.

5.7 Hypogammaglobulinemia: B-cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment with YESCARTA. In Study 1, hypogammaglobulinemia occurred in 15% of patients. Monitor immunoglobulin levels after treatment with YESCARTA and manage using infection precautions, antibiotic prophylaxis and immunoglobulin replacement. The safety of immunization with live viral vaccines during or following YESCARTA treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during YESCARTA treatment, and until immune recovery following treatment with YESCARTA.

5.8 Secondary Malignancies: Patients treated with YESCARTA may develop secondary malignancies. Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Kite at 1-844-454-KITE (5483) to obtain instructions on patient samples to collect for testing.

5.9 Effects on Ability to Drive and Use Machines: Due to the potential for neurologic events, including altered mental status or seizures, patients receiving YESCARTA are at risk for altered or decreased consciousness or coordination in the 8 weeks following YESCARTA infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, during this initial period.

6 ADVERSE REACTIONS: The following adverse reactions are described in Warnings and Precautions: Cytokine Release Syndrome, Neurologic Toxicities, Hypersensitivity Reactions, Serious Infections, Prolonged Cytopenias, Hypogammaglobulinemia.

6.1 Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The safety data described in this section reflect exposure to YESCARTA in the clinical trial (Study 1) in which 108 patients with relapsed/refractory B-cell NHL received CAR-positive T cells based on a recommended dose which was weight-based [see *Clinical Trials (14)*]. Patients with a history of CNS disorders (such as seizures or cerebrovascular ischemia) or autoimmune disease requiring systemic immunosuppression were ineligible. The median duration of follow up was 8.7 months. The median age of the study population was 58 years (range: 23 to 76 years); 68% were men. The baseline ECOG performance status was 43% with ECOG 0, and 57% with ECOG 1. The most common adverse reactions (incidence \geq 20%) include CRS, fever, hypotension, encephalopathy, tachycardia, fatigue, headache, decreased appetite, chills, diarrhea, febrile neutropenia, infections-pathogen unspecified, nausea, hypoxia, tremor, cough, vomiting, dizziness, constipation, and cardiac arrhythmias. Serious adverse reactions occurred in 52% of patients. The most common serious adverse reactions ($>$ 2%) include encephalopathy, fever, lung infection, febrile neutropenia, cardiac arrhythmia, cardiac failure, urinary tract infection, renal insufficiency, aphasia, cardiac arrest, *Clostridium difficile* infection, delirium, hypotension, and hypoxia. The most common (\geq 10%) Grade 3 or higher reactions include febrile neutropenia, fever, CRS, encephalopathy, infections-pathogen unspecified, hypotension, hypoxia, and lung infections. Forty-five percent (49/108) of patients received tocilizumab after infusion of YESCARTA.

Summary of Adverse Reactions Observed in at Least 10% of the Patients Treated with YESCARTA in Study 1

Adverse Reaction		Any Grade (%)	Grades 3 or Higher (%)
Cardiac disorders	Tachycardia	57	2
	Arrhythmia	23	7
Gastrointestinal disorders	Diarrhea	38	4
	Nausea	34	0
	Vomiting	26	1
	Constipation	23	0
	Abdominal pain	14	1
	Dry mouth	11	0
General disorders and administration site conditions	Fever	86	16
	Fatigue	46	3
	Chills	40	0
	Edema	19	1
Immune system disorders	Cytokine release syndrome	94	13
	Hypogammaglobulinemia	15	0
Infections and infestations	Infections-pathogen unspecified	26	16
	Viral infections	16	4
	Bacterial infections	13	9
Investigations	Decreased appetite	44	2
	Weight decreased	16	0
	Dehydration	11	3

Summary of Adverse Reactions Observed in at Least 10% of the Patients Treated with YESCARTA in Study 1 (continued)

Adverse Reaction		Any Grade (%)	Grades 3 or Higher (%)
Musculoskeletal and connective tissue disorders	Motor dysfunction	19	1
	Pain in extremity	17	2
	Back pain	15	1
	Muscle pain	14	1
	Arthralgia	10	0
Nervous system disorders	Encephalopathy	57	29
	Headache	45	1
	Tremor	31	2
	Dizziness	21	1
	Aphasia	18	6
Psychiatric disorders	Delirium	17	6
Respiratory, thoracic and mediastinal disorders	Hypoxia	32	11
	Cough	30	0
	Dyspnea	19	3
	Pleural effusion	13	2
Renal and urinary disorders	Renal insufficiency	12	5
Vascular disorders	Hypotension	57	15
	Hypertension	15	6
	Thrombosis	10	1

The following events were also counted in the incidence of CRS: tachycardia, arrhythmia, fever, chills, hypoxemia, renal insufficiency, and hypotension. For a complete list of events that contributed to the incidence of certain adverse reactions, please see footnote below Table 3 in Section 6.1 of the Full Prescribing Information.

Other clinically important adverse reactions that occurred in less than 10% of patients treated with YESCARTA include the following: blood and lymphatic system disorders: coagulopathy (2%); cardiac disorders: cardiac failure (6%) and cardiac arrest (4%); immune system disorders: hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS) (1%), hypersensitivity (1%); infections and infestations disorders: fungal infections (5%); nervous system disorders: ataxia (6%), seizure (4%), dyscalculia (2%), and myoclonus (2%); respiratory, thoracic and mediastinal disorders: pulmonary edema (9%); skin and subcutaneous tissue disorders: rash (9%); vascular disorders: capillary leak syndrome (3%).

Grade 3 or 4 Laboratory Abnormalities Occurring in \geq 10% of Patients in Study 1 Following Treatment with YESCARTA based on CTCAE (N=108)

Lymphopenia 100%, Leukopenia 96%, Neutropenia 93%, Anemia 66%, Thrombocytopenia 58%, Hypophosphatemia 50%, Hyponatremia 19%, Uric acid increased 13%, Direct Bilirubin increased 13%, Hypokalemia 10%, Alanine Aminotransferase increased 10%.

6.2 Immunogenicity: YESCARTA has the potential to induce anti-product antibodies. The immunogenicity of YESCARTA has been evaluated using an enzyme-linked immunosorbent assay (ELISA) for the detection of binding antibodies against FMC63, the originating antibody of the anti-CD19 CAR. Three patients tested positive for pre-dose anti-FMC63 antibodies at baseline and Months 1, 3, or 6 in Study 1. There is no evidence that the kinetics of initial expansion and persistence of YESCARTA, or the safety or effectiveness of YESCARTA, was altered in these patients.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy: Risk Summary: There are no available data with YESCARTA use in pregnant women. No animal reproductive and developmental toxicity studies have been conducted with YESCARTA to assess whether it can cause fetal harm when administered to a pregnant woman. It is not known if YESCARTA has the potential to be transferred to the fetus. Based on the mechanism of action, if the transduced cells cross the placenta, they may cause fetal toxicity, including B-cell lymphocytopenia. Therefore, YESCARTA is not recommended for women who are pregnant, and pregnancy after YESCARTA infusion should be discussed with the treating physician. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% - 4% and 15% - 20%, respectively.

8.2 Lactation: Risk Summary: There is no information regarding the presence of YESCARTA in human milk, the effect on the breastfed infant, and the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for YESCARTA and any potential adverse effects on the breastfed infant from YESCARTA or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential: Pregnancy Testing: Pregnancy status of females with reproductive potential should be verified. Sexually-active females of reproductive potential should have a pregnancy test prior to starting treatment with YESCARTA. *Contraception:* See the prescribing information for fludarabine and cyclophosphamide for information on the need for effective contraception in patients who receive the lymphodepleting chemotherapy. There are insufficient exposure data to provide a recommendation concerning duration of contraception following treatment with YESCARTA. *Infertility:* There are no data on the effect of YESCARTA on fertility.

8.4 Pediatric Use: The safety and efficacy of YESCARTA have not been established in pediatric patients.

8.5 Geriatric Use: Clinical trials of YESCARTA did not include sufficient numbers of patients aged 65 years and older to determine whether they respond differently or have different safety outcomes as compared to younger patients.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide). Ensure that patients understand the risk of manufacturing failure (1% in clinical trial). In case of a manufacturing failure, a second manufacturing of YESCARTA may be attempted. In addition, while the patient awaits the product, additional chemotherapy (not the lymphodepletion) may be necessary and may increase the risk of adverse events during the pre-infusion period. Advise patients to seek immediate attention for any of the following: Cytokine Release Syndrome, Neurologic Toxicities, Serious Infections, Prolonged Cytopenia [see *Warnings and Precautions (5.1, 5.2, 5.3, 5.5) and Adverse Reactions (6)* for more information and signs and symptoms]. Advise patients for the need to: Refrain from driving or operating heavy or potentially dangerous machinery after YESCARTA infusion until at least 8 weeks after infusion [see *Warnings and Precautions (5.2)*]. Have periodic monitoring of blood counts. Contact Kite at 1-844-454-KITE (5483) if they are diagnosed with a secondary malignancy [see *Warnings and Precautions (5.8)*].

Manufactured by, Packed by, Distributed by: Kite Pharma, Inc., Santa Monica, CA 90404

US License No 2064

YESCARTA and KITE are trademarks of Kite Pharma, Inc.

© 2018 Kite Pharma | PRC-00428 03/2018

AJMC[®]TV interviews let you catch up on what's new and important about changes in healthcare, with insights from key decision makers—from the clinician, to the health plan leader, to the regulator. When every minute in your day matters, AJMC[®]TV interviews keep you informed. Access the video clips at ajmc.com/interviews.

Produced by Mary Caffrey, Samantha DiGrande, and Jaime Rosenberg

**Denalee O'Malley, PhD, LSW, Instructor,
Department of Family Medicine and
Community Health, Research Division, Rutgers
Robert Wood Johnson Medical School, New
Brunswick, New Jersey**



How can primary care doctors and oncologists collaborate to ensure that premenopausal patients with breast cancer have the necessary support to address the unique concerns of relationships, work, parenting, and other caregiving issues in a younger generation?

It's important for the primary care physicians to get a report from the primary oncology team with both the treatments that patients have received and the anticipated late and long-term effects, as well as a surveillance plan. That's currently called a cancer survivorship plan, and so as a part of that plan, [it designates] who's going to be responsible for the different aspects of a patient's care. For younger [survivors of] breast cancer, in particular, if there are anticipated changes in menopausal status, that would be helpful for primary care physicians to know. Also, who is going to be...the point person for symptoms management—so if something comes up, does the patient know who to call and how to get their needs met? [That] is important for the navigational experience for the patient.

In your research, have you discovered trends that indicate which patients fare better after active cancer treatment has been completed?

In my own research, what I focus on often is the experience of [patients with] cancer [who] have comorbid conditions. Also, I've done some work with longer-term survivors, and with longer-term survivors, [those] patients who have perceived to have had to make a financial sacrifice during the acute treatment experience can have longer-term experiences of distress, psychological distress. So I think the impact [on] finances at the acute phase can have a really enduring effect on someone's experience over the long term.

What gaps do caregivers and patients face when trying to access and understand health information during treatment and post treatment? How can oncologists and primary care physicians ensure that health literacy issues are resolved so that patients are informed about their options?

This is a really tricky issue because [as] treatments become more and more complicated, it...can be very time consuming and complex to communicate treatment options but also risk in a way that people understand that. I think it's really important to assess what a patient understands about their illness. Also, what they understand about the goals of their treatment: Is everyone on the same page [regarding] the actual goal of the treatment? And what are the practicalities: Do they understand what they need in that environment to manage that? Do they have the practical issues covered financially to be able to get the resources they need to manage the day-to-day issues getting to and from treatment? I think that not only do we need to assess it from a health literacy perspective, but [we] also [need to help] patients make sense of what this means to them in their world. Do they accommodate it without help, and do they need help, and are there people on the healthcare team who can assist them so that they can have the optimal treatment outcome?

Are payers doing enough to ensure that survivors of cancer receive appropriate follow-up care, and, if not, what needs to change?

I think that currently the evidence in survivorship is evolving as the population of [survivors of] cancer is growing. I think that as more information is developed about risk stratifications, which patients have the most complex long-term sequelae. Payers can really incentivize providers coordinating that care and providing that care in a way that's efficient but also effective. I think that is improving the information evidence over time, and I think payers can incentivize putting that evidence into practice. ♦

**Don Dizon, MD, FACP, Director of Women's
Cancers, Lifespan Cancer Institute; Clinical
Director, Gynecologic Medical Oncology and
Director of Medical Oncology, Rhode Island
Hospital in Providence**



How has care for the sexual health needs of patients changed over the years?

The care for sexual health needs for patients unfortunately has not changed that much over the years. Part of it is [because] I don't think oncologists are necessarily trained or comfortable discussing sexual health with their patients. There is a movement now in select centers where sexual health services specific to patients with cancer have started to gain footing. Certainly, in my own experience, I have started several sexual health programs in my own institutions. More recently, I've started working on what I call the oncology sexual health first responders clinic at the Lifespan Cancer Institute.

But what it takes is really some passionate provider to take up this area and say, "I will be the person to help my patients." Without it, it's hard to develop these services nationwide. But to meet these needs of patients no matter where they are, there are some very good resources—both in written form as well as online—that patients can access independent of their oncologist visits or independent, I should say, of the lack of discussion within their cancer centers. I do still believe that these are essential issues that need to be discussed to help improve survivorship, whether it's a patient who's living without any evidence of cancer or for patients still living with active disease. You should not have to give up your sexual health because of cancer. My hope is that going forward, these issues will be more readily available and addressed by cancer centers.

Are there services that payers are not covering that could improve quality of life for women after breast cancer? If so, what are they?

There are certainly some services that are not typically covered today by insurance, particularly for that group of women who had breast cancer. If you look at that group, those women who are premenopausal, because our therapies, probably now more than in the last 5 years, are geared toward estrogen deprivation, women actively menstruating at the time of breast cancer are being put into treatment-induced ovarian failure and accelerated menopause. [Some] of these consequences are significant changes in vaginal health and the experience of sexual function as well as intimacy. Things insurance companies can do a better job of [providing] are consultative services, particularly for survivorship needs in a sexual health program.

There are certainly some emerging modalities that are available but are not covered services, such as vaginal laser therapies, which have been shown to be effective for postmenopausal patients, as well as some medications. The ones I'm thinking of that do have use in very selective situations might be things like PDE-5 [phosphodiesterase-5] inhibitors, for those women who are experiencing sexual dysfunction after cancer but are also on an antidepressant, for example. So yes, there are some medications, some procedures, and some techniques that could be covered more broadly as well as sexual health visits—and I'm hoping we're going to see more covered than not-covered services in the future. ♦

Leonard B. Saltz, MD, Executive Director of Clinical Value and Sustainability, Head of Colorectal Oncology Section, Memorial Sloan Kettering Cancer Center



How do you decide when a patient should receive next-generation sequencing (NGS) testing?

That's not as straightforward of a question as you might think, and I think that's a question for which the answer is evolving. At Memorial Sloan Kettering, we've had a longstanding interest in this approach. We have an in-house assay that we've been leveraging both to try and help individual patients as well as to understand the biology of tumors. So, perhaps our practice is somewhat different than what can be expected to be out there in general practice.

Now that there is at least 1 assay commercially available that's FDA approved, and a number [that are] FDA authorized, I think we're going to see an increased use of the technology, and our challenge is going to be to figure out when and how. I would argue that we don't really know how to use it for early-stage disease, and I don't think that's the right place to do it.

I think that at the initiation of treatment for metastatic disease would be the most value-added time to think about using NGS to try and understand what our options are. It's important to take a look at what's covered because not only does the assay itself cost money, but the results of the assay are going to cost money.

Right now, as I read the approval, it's covered as kind of a 1-shot deal. It's not a sequential process. So, I think getting that information early on in the strategizing of how you're going to approach the patient with metastatic disease makes the most sense.

If a patient is tested and there is no available targeted therapy for them to be matched with, can the patient still benefit from the test?

Of course, the easiest thing is if we find a mutational profile that tells us there's a high probability of benefit from a current commercially available drug. That's perhaps the best-case scenario. The next would be if we see something that suggests an investigational approach if there is availability of that investigational approach. Now that would require that there be a clinical trial, that the clinical trial have openings, and that the patient be well enough to be treated on that trial.

One of the things I worry about is patients are imbuing this concept of precision oncology with almost magical ability, and there's a bit of magical thinking going on in terms of what it might offer. Everybody wants to believe that they'll have seen 4 or 5 doctors [who] tell them there really isn't more to be done, that hospice care is appropriate, and that the next one is going to do some precision medicine and cure them.

That's not going to happen in the overwhelming majority of people, and the question of whether it happens at all is really suspect. It depends on how sick the individual is. Once a person gets to the point where they're too sick for clinical trials, they're often too sick to tolerate or benefit from therapies, and that's something that we have to bear in mind.

What role does NGS currently play in advancing precision medicine?

Precision medicine is a term that we're still working on defining, and to some degree, these NGS assays are what most people have in mind when we talk about precision medicine. One of the points I tried to make in the session we had this afternoon is that we're not talking about the precision use of accepted targets. We're talking about trying to use NGS to open a new therapeutic option for a patient [who] otherwise might not have it.

What we're finding, and what the data I went through this afternoon show, is that, unfortunately, that happens in a very small minority of patients. So, as we work to move this field forward, we have to keep a certain balance between optimism and realism and help patients understand that this is not going to help everyone. In fact, it's not going to help a very substantial percentage of patients. Arguably, the substantial majority. There's a limited number of people for whom it's going to be helpful, and that's going to be very useful.

I think it's also going to become more important as we start to see some therapies become available that are highly effective with a very rare target, and it's not going to be practical, I don't believe, to go searching for multiple targets separately when we're looking for the needle-in-the-haystack kind of patient.

But if we can assemble an NGS assay that looks for a lot of different rare possibilities, that may be a more practical way to bring those therapies to patients. ♦

Hope Rugo, MD, Director of the Breast Oncology Clinical Trials Program at the University of California at San Francisco



Do you plan to prescribe Mylan's biosimilar trastuzumab to patients? Would you switch patients from the reference product to the biosimilar, or just begin new patients on the biosimilar, and will payer coverage decisions affect provider and patient choices?

There's always a big question about whether or not you would—OK, now the biosimilar is available, are you going to use it in your patients? In everybody? Are you going to switch patients who are on the originator to a biosimilar?

I think that there are a number of issues that we need to understand. In the [United States], that's very much driven by insurers and what insurers are going to mandate. For example, with biosimilars for the filgrastim, the insurers, very quickly, many of them said, "You have to use the biosimilar because it's cheaper." And then what happens is, the institution—I work at an academic institution—changes over wholesale to say, "OK, that's what we're going to give people," so [that] you don't have to worry about what the insurance said beforehand.

So that's 1 thing that I think often happens, and with the trastuzumab—and we also switch people because, you know, supportive care it comes and goes, right? With the trastuzumab biosimilars, I think it's going to depend on the price points and what the insurers and institutions say about if there is a real cost savings, and then they will want us to switch over to the biosimilars, which I am very happy to do.

I think these are agents which are biosimilar, so I don't have a problem switching over. And I don't have a problem switching a patient either, I just took a patient off trastuzumab who has been on it for 17 years and has no evidence of disease. We had a big conversation about stopping the trastuzumab and I said, "I really would've stopped you at 10 years, but you said no," and she's moving away now. But that's a patient where you may have a patient on it for so many years; if you could have a drug that's 20% or 30% less, that's a huge savings over time, so it's possible that those people who are on forever-maintenance trastuzumab in the metastatic setting, that that will be a situation where patients are switching or switched.

I don't think that I would switch anybody that was in the neo-adjuvant or adjuvant setting on short-term exposure to the drug. It's going to be an interesting time to see what happens. ♦

Survivorship Care Throughout the Cancer Journey

Don Champlain, MHA, RN, and Lucio Gordan, MD

CONTINUED FROM COVER



CHAMPLAIN
Don Champlain, MHA, RN, is the associate director of care management for Florida Cancer Specialists.



GORDAN
Lucio Gordan, MD, is head of Quality and Medical Informatics with Florida Cancer Specialists.

The diagnosis phase includes the commitment to education about the disease and the latest treatment options available. This is also where we begin preparing patients for the future phases of survivorship, which include instruction about available resources and how to use them for the best possible outcomes.

One tool under development for patient education is a customized animated video about chemotherapy and its potential adverse effects. The video supplements face-to-face education with a nurse and physician, along with standardized and vetted written materials. Easy access to internet information sources means patient and families may be exposed to significant amounts of unrefined data, which may lead to confusion and anxiety about treatment plans. This video allows the patient to go back and review the physician and nurse instructions received during their initial education. Often, some family members do not live close to the patient, so the video allows them to share in the patient's education, which better enables them to assist from a distance. The personal care manager can also use this as a teaching tool during active treatment.

Patients frequently share feelings of fear and anxiety at the time of their diagnosis. Giving appropriate attention to details during the diagnosis period of survivorship allows them to manage these emotions and prepare for the physical aspects of treatment, as well as, ultimately, post treatment.

Allowing each patient to achieve success during this phase requires the services and collaboration of many team members, who provide the appropriate tools for this short but very important stage of survivorship.

Care Managers Are Key

The next phase begins with active treatment of the disease and can include intravenous and oral therapy, surgery, or radiation. Patients are assigned a team that includes the oncologist, care manager, pharmacist, clinic nurse, and nutritionist, among others.

A key factor in this phase is the assignment of a care manager. The care managers are experienced, oncology-certified registered nurses (RNs) who become liaisons for the patients during their active phase of treatment.

The goals of care management include managing the patient's physical, psychosocial, and emotional needs. Our approach is patient-centered and holistic in nature, as we want to manage aspects of health of the whole patient and not just the physical symptoms of the disease.

One of the keys to success is the proactivity of the care managers. The nurses contact the patients based on the prescribed regimens and risk scores. For example, treatment regimens that are more emetogenic in nature will have closer follow-up by RN care managers. Standard operating procedures developed by our nurses, pharmacists, physicians, and advanced practice practitioners provide the information backbone, triggering when to contact the patients to reeducate them on how to manage any issue if or when it arises. We base the risk scores on multiple areas: the treatment regimen, patient's performance status, and comorbidities. The care managers are experts in triage and, with the assistance of the treating team, manage patient symptoms very successfully, improving the overall experience and outcomes. Symptom management is guided by standard operating procedures.

One tool that makes this phase successful is the creation of an individualized care plan, which is based on the patient and his or her goals for treatment and eventual outcome and implemented by the care team. The care plan is created by team members and reviewed with the patient by the physician and care manager.

During this active phase, patients are also aided by 24/7 on-call nursing support. We use oncology-certified RNs to provide this service. Physicians are available for support as needed. This service has been shown to decrease the number of unnecessary emergency department (ED) visits, as well as hospitalizations.

Proper nutrition is a priority for survivorship patients at Florida Cancer Specialists during the active phase of treatment and beyond. We recognize the need for adequate nutrition to prepare patients for the treatments that lie ahead. We know that nutritionally sound patients have improved outcomes, and our physicians have committed the resources to make this a reality for our patients. Oncology-certified, specially trained nutritionists assist our patients during this phase of their journey, providing local resources to help meet individual nutritional needs. Study findings show the value of providing appropriate nutrition; a recent pilot project involving Medicare patients discharged from the hospital saved a health system \$3.87 for every \$1 spent on meals.³

Surveillance Leads to Savings

Although we often focus on the physical and emotional benefits of this phase of survivorship program, other positive aspects occur due to the increased attention. We have found that with appropriate surveillance of patients during and after treatment, ED visits and hospitalizations decrease. Within the first year of implementation of care management services, 1 insurer realized a 34% reduction in hospital days. We have also realized a 16% decrease in the number of hospital days for our Medicare population. We found that patients who go to the ED are frequently admitted, often resulting in a 3- to 5-day hospital stay. This adds up to large costs to society.

Finally, we reach what might be the most important phase of survivorship—life after cancer treatment. To begin with, the patient is assigned a personal survivorship coordinator, who creates an individualized plan of care to help the patient navigate the care to be delivered after the completion of treatment. Common issues in this phase include the ability to obtain healthcare coverage, follow-up treatment, late effects of treatment, secondary cancers, and quality of life. The coordinator is responsible for assisting with the patient's physical, emotional, and psychosocial issues, as well. A primary goal in this phase is to help the patient find their new normal after cancer treatment. It often surprises patients that they will never be exactly as they were before cancer. We assist them on this journey of discovering who they are after cancer.

During this phase, we educate the patient about the importance of follow-up care. Very often in the first year, follow-up appointments are scheduled every 3 months. With some diagnoses, specific scans and labs are ordered per national guidelines. The survivorship coordinator will not only help the patient schedule these tests but also encourage making the appointments to ensure improved outcomes.

With the assistance of the physician and care team, the survivorship coordinator will address late-term adverse effects.

OncLive

What Can We Learn from Extreme Survivors of Breast Cancer?
onclive.com/link/3263

CLINICAL PRACTICE

Unfortunately, in some cases, the patient's cancer will recur, and this continued relationship with the survivorship coordinator allows them to get scheduled with their original oncologist and care manager and more quickly begin the next stage of treatment.

We also maintain a focus on nutrition post treatment. The nutritionists assist the patient with a meal plan designed to meet their specific needs after completing active treatment. This is especially important because many people assume that all cancer patients need to gain weight after treatment, but sometimes the opposite is true. The plan of care must include the proper nutrition education that meets the patient's unique needs, based on their particular type of cancer post treatment.

At Florida Cancer Specialists, we created this final phase to match the active phase of survivorship as closely as possible. We offer the same

services, including the 24/7 on call, to give patients a sense of security, although they are no longer being seen as frequently as they were during their active phase. This is where the survivorship program fills a much-needed gap in care. We slowly help patients regain control of their health and life after cancer treatment by being available, but we give the patient the responsibility to call if they need assistance.

Through years of experience, we have found that survivorship benefits all patients, regardless of age, gender, financial status, or cultural background. Survivorship is an important part of a patient's cancer journey. All phases are important and signify a different step along the path to completion of treatment and life beyond. As medical professionals continue to progress in the treatment, the number of survivors will continue to grow, as will the need for quality survivorship programs to support them. ♦

AUTHOR INFORMATION

Don Champlain, MHA, RN, is director of Care Management at Florida Cancer Specialists. He is accountable for all aspects of care management and oversees the Nutrition, Social Work, and Central Triage departments. A registered nurse, he has a master's of science in Health Care Administration from Oklahoma State University.

Lucio N. Gordan, MD, is head of Quality and Medical Informatics for Florida Cancer Specialists. He is board certified in medical oncology, hematology, and internal medicine and practices in the Gainesville Cancer Center. A graduate of State University of Londrina College of Medicine in Brazil, he completed residency at the University of Iowa and a fellowship in hematology and medical oncology at the University of Florida in Gainesville.

REFERENCES

1. National Cancer Institute. NCI dictionary of cancer terms. NCI website. cancer.gov/publications/dictionaries/cancer-terms/def/survivorship. Published May 15, 2015. Accessed July 13, 2018.
2. Miller KD, Siegel RL, Lin CC, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin.* 2016;66(4):271-289. doi: 10.3322/caac.21349.
3. Martin SL, Connelly N, Parsons C, Blackstone K. Simply delivered meals: a tale of collaboration. *Am J Manag Care.* 2018;24(6):301-304.



AJMC® | THE CENTER FOR BIOSIMILARS®

Health economics experts. Managed care professionals. Key clinical specialists.

Join the Center for Biosimilars® network to gain access to industry leading insights and engage with your peers.

BIOSIMILARS PEER EXCHANGE



PEER EXCHANGE™

Our Peer Exchange™ program provides a multistakeholder perspective on important issues that providers, pharmacists, payers, and patients grapple with as they step into the world of biosimilars.



NEWS

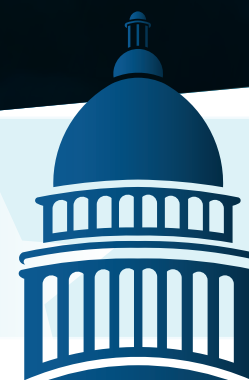
We provide the most up-to-date clinical, regulatory, business, and policy news in the rapidly changing world of biosimilars.



CONFERENCE COVERAGE

From clinical developments to policy concerns, we provide coverage of the top conferences on biologics and biosimilars.

The Center for Biosimilars® was cited in the United States Senate testimony on prices and out-of-pocket costs for rheumatoid arthritis drugs. The resource also discusses the current landscape for advanced healthcare management.



Join the Center for Biosimilars® network at centerforbiosimilars.com

Healthcare Costs and Access for Young Adult Cancer Survivors: A Snapshot Post ACA

Michelle S. Landwehr, MPH; Samantha E. Watson, MBA; and Maia Dolphin-Krute, BFA

CONTINUED FROM COVER



LANDWEHR

Michelle S. Landwehr, MPH, is the chief operating officer of The Samfund.



WATSON

Samantha E. Watson, MBA, is the founder of The Samfund and a 2-time cancer survivor.



DOLPHIN-KRUTE

Maia Dolphin-Krute, BFA, is the grants assistant at The Samfund.

In 2016, we published a retrospective analysis² of the financial impact of cancer on young adults, looking at data just up to 2013, before the Affordable Care Act (ACA) took full effect. The law made it possible for some applicants to purchase coverage through the marketplace, with the first plans taking effect January 1, 2014. At that time, given the uncertainty of the ACA's future, we decided to analyze a snapshot of our applicant population's medical expenses and overall medical and credit card debt both before and after the ACA went into effect. We also looked at grant recipients' access to health care post ACA to determine the law's impact on this population thus far.

Methods

The Samfund looked at applicant data from 2007 to 2017 to identify differences that may be apparent pre and post ACA. Grant applicants—who today must be aged 21 to 39 years (until 2013, the eligible age range was 17-35), finished with active treatment, and US residents—were asked a series of in-depth questions about their finances. Of the applicants, 361 who sought assistance between 2007 and 2013, as well as 873 who sought help from 2014 to 2017, consented to have their data analyzed. Those who receive funding were subsequently asked to complete an onboarding survey that covered access to care and psychosocial measures. Follow-up surveys at 6, 12, and 24 months post funding contain similar measures; of note, recipients were asked, “During the past 6 months, did you have access to needed health care, including doctor visits, prescription medication, or diagnostic tests?” If the response was negative, respondents were prompted to answer how various factors, including adequate insurance, affected their ability to access this care. (This survey is still in use.)

Quantitative Results

As seen in **Table 1**, the highest percentage of applicants from 2014 to 2017 (44.2%) received coverage through an employer-sponsored plan (through either through their own job or a spouse's). The next largest percentage, 32.7%, are covered via a public plan (primarily Medicaid), and 13.2% are covered through a private plan or a plan obtained through the marketplace. Just 2.6% report having no coverage. When asked whether their premiums are deducted from their paycheck, 44.5% indicated yes, whereas 55.5% indicated no. The mean pretax premium deduction among 2014-2017 applicants with insurance coverage was \$143.00, and the mean monthly out-of-pocket premium cost (for those who did not have premiums taken out of a paycheck) was \$303.12. The mean age of all applicants and recipients is 30, and nearly 75% of recipients identify as female (applicants are not asked about their gender identity).

We began asking about type of health insurance coverage post ACA, in 2014, so we have no earlier data to compare for type of coverage or monthly premium costs. However, as seen in **Table 2**, we did examine mean monthly medical expenses, overall medical debt, and overall credit card debt before and after ACA (as a general indicator of financial health). Although 2014-2017 grant applicants reported equivalent average monthly medical expenses (likely because we did not ask about health insurance costs separately prior to ACA,

TABLE 1. Types of Health Insurance Coverage (2014-2017)

Plan Type	Percentage
Parent plan	4.4
Employer plan (self or spouse)	44.2
Private plan or marketplace	13.2
Public plan	32.7
COBRA	1.1
Student health plan	0.4
Multiple plans	0.8
Other	0.6
No coverage	2.6

Number of respondents = 835

NOTE: COBRA indicates Consolidated Omnibus Budget Reconciliation Act of 1985 which required employers to allow certain former employees, their spouses, and their eligible dependent children to remain in group health plans.

Source: Consolidated Omnibus Budget Reconciliation Act of 1985, HR 3128 (1985). congress.gov/bill/99th-congress/house-bill/3128. Accessed July 20, 2018.

and applicants included premiums as part of their monthly medical expenses), they reported higher overall medical debt and higher credit card debt. Of note, from applicant essays, we often see that that medical debt has been paid on credit cards to avoid collections (although credit cards are also used for travel, treatment, and living expenses).

In recent cohorts of onboarding and follow-up surveys (N = 363 surveys, 245 recipients from 2015 onward), our recipients have reported that they have high access to healthcare even at baseline; in our most recent 2 cohorts of recipients, 95% reported access to the healthcare they needed in the past 6 months. At follow-up, the results were similarly high—90% to 92% of recipients reported similar access. Of those who did not feel they had adequate access to healthcare in the last 6 months, between 75% and 100% reported that lack of health insurance contributed at least somewhat to this situation.

Qualitative Results

Qualitatively, reports of YAs' experiences securing coverage post ACA are still very mixed though seem to skew toward the positive. Some recipients report that they are able to get the coverage they need, whereas others feel they have been given the runaround when trying to get on a plan. For some, the ACA has made all the difference with respect to their treatment. Some examples:

“Because of the ACA, I was able to stay on my step-father’s insurance for 3 years longer than I otherwise would have been able to, which covered my cancer treatment. The ACA was a true lifesaver.” — Lauren M.

Others had horror stories of having to switch facilities midway through treatment, with some abandoning their medical teams due to loss of coverage.

“I relapsed in November 2015, and I had a PPO [preferred provider organization] insurance plan at

Targeted Therapies

New Treatment Paradigm Required for Breast Cancer in Young Women
targetedonc.com/link/222

COST PERSPECTIVE

TABLE 2. Mean and Median Financial Indicators (2007-2013, 2014-2017)

	N	2007-2013		N	2014-2017	
		Mean	Median		Mean	Median
Outstanding medical debt	361	\$3755.76	\$0.00	870	\$5092.44	\$692.00
Monthly medical payments	361	\$231.15	\$60.00	862	\$225.60	\$80.00
Total credit card debt ¹	361	\$2919.44	\$0.00	873	\$5475.03	\$2000.00
Monthly health insurance premium deduction	N/A	N/A	N/A	331	\$243.49	\$170.00
Monthly out-of-pocket premium costs	N/A	N/A	N/A	141	\$303.12	\$287.00

N/A, not applicable.

¹P < .001

the time through the ACA marketplace. I started my treatment in [Hospital 1] at the time, and the plan was to do a stem cell transplant. At the start of 2016, all marketplace plans no longer [offered] PPO plans, so I was forced to get an HMO [health maintenance organization] plan, which made that hospital out-of-network for me....Fortunately, they came up with a compromise to give me a grandfathered plan so I [could] continue my transplant at [Hospital 1], but it delayed my treatment for 2 weeks....After my transplant, they didn't tell me that they made my hospital out-of-network for me again. [I'd] already done scans and tests that were billed out-of-network, and I ended up with a bill of around \$40,000." — Carlo L.

Another recipient commented on the inconsistencies in the marketplace:

"It all depends on the state you live in! My fiancée used it to get healthcare, which was free for her income range. Depending on how your state responded to [ACA], you may end up getting a great deal, or get nothing at all."

For others, even with coverage, it seems that the process never runs smoothly:

"I have used healthcare from the marketplace for the past 2 years. It has been a tremendous help for me. I wouldn't have had any way to afford to see doctors without it. The prices on the plans have fluctuated exponentially each year, causing me to have to switch insurance plans and all my doctors 1 of those years, which was frustrating—but nonetheless, I am able to see doctors and get tests done, which has been crucial to my peace of mind."

Discussion

Although many cancer survivors in the general population may face challenges when seeking health insurance coverage and health care, they are often exacerbated for young adults due to their relative inexperience with the health insurance market, as well as what can be a confusing marketplace site. Though not statistically significant, the mean amount of overall medical debt

increased substantially in the post-ACA group, suggesting a possible overall increase in medical cost burden for YAs. Additionally, we have found that YAs in particular may be more likely to choose a plan with the lowest monthly premium without fully understanding the total costs for the year. As a result, they often choose plans that cost more than they had anticipated (due to high deductibles) and/or offer paltry coverage that affects access to follow-up care. Samfund grant recipients commonly report difficulties in accessing adequate in-network care under their insurance plan or the need to switch healthcare

Young adults in particular may be more likely to choose a plan with the lowest monthly premium without fully understanding the total costs for the year. As a result, they often choose plans that cost more than they anticipated (due to high deductibles) and/or offer paltry coverage that affects access to follow-up care.

providers during treatment due to changes in their coverage, as described above.

Though recipients broadly reported adequate access to health insurance coverage despite the aforementioned logistical challenges, in a pre-ACA study with a broader target population, between 33% and 48% of YAs were forgoing necessary follow-up care, regardless of health insurance status.³ Clearly, further analysis in the post-ACA era is needed to better assess the relationship between health insurance coverage and follow-up care.

Study Limitations

Though we consider it worthwhile to examine our applicant and recipient data, we do recognize several inherent limitations: namely, that we did not track health insurance coverage or specific premium or out-of-pocket costs prior to 2014 and

that applicants who approach the Samfund for funding are facing extreme financial hardship, so they may not be representative of the YA population as a whole. We are also looking at relatively small cohorts for follow-up data and may suffer from response bias—those recipients faring better overall may be more likely to complete follow-up surveys. Lastly, we do receive repeat applicants, but because their financial situations may have changed over time, we included them in this preliminary analysis.

Conclusions

From this snapshot of YAs contending with financial toxicity, we see 2 stories emerging: 1 of high access to care, and a second of overall increased costs post treatment. More research involving a comparison of coverage and cost burdens in YAs is warranted. Some of these challenges can be remedied with education; to that end, The Samfund, in partnership with Triage Cancer, launched CancerFinances.org to provide guidance around issues common to young adults with a cancer history. The health insurance module was the first topic introduced and remains a great resource for individuals seeking information about their health insurance options before selecting a plan. Although coverage may be improving/increasing, at least for now, there is still much work to be done to mitigate the debilitating financial aftereffects of cancer in the young adult population. ♦

AUTHOR INFORMATION

Michelle S. Landwehr, MPH, is the chief operating officer of The Samfund and has been involved with the organization since its inception. She oversees all program and evaluation activities and is grateful for the opportunity to work with the young adult survivor community. She holds a bachelor's degree from Brandeis University in Waltham, Massachusetts, and a master of public health from Columbia University.

Samantha E. Watson, MBA, is a 2-time young adult cancer survivor. She received a diagnosis of Ewing sarcoma in December 1999 and of secondary myelodysplastic syndrome in April 2001. She cofounded The Samfund in 2003 after recognizing a void in programs and services tailored specifically for young adult cancer survivors after treatment. She is proud to be an active member of the cancer community and an advocate for young adult survivors throughout the country. She holds a bachelor's degree from Brandeis University in Waltham, Massachusetts, and a master of business administration in mission-driven management from the Heller School for Social Policy and Management at Brandeis.

Maia Dolphin-Krute, BFA, is the grants assistant at The Samfund and helps applicants through every step of the process. As a chronically ill young adult, she is happy to support other young adults and The Samfund community. She is a graduate of Tufts University and the School of the Museum of Fine Arts in Boston, Massachusetts, and is the author of 2 recent books on illness and disability studies.

FUNDING SOURCES: None

CORRESPONDING AUTHOR:

Michelle Landwehr
The Samfund
89 South St, Ste LL02
Boston, MA 02111
michelle@thesamfund.org

REFERENCES

- Zafar SY, Peppercorn JM, Schrag D, et al. The financial toxicity of cancer treatment: a pilot study assessing out-of-pocket expenses and the insured cancer patient's experience. *Oncologist*. 2013;18(4):381-390. doi:10.1634/theoncologist.2012-0279.
- Landwehr MS, Watson SE, Macpherson CE, Novak KA, Johnson RH. The cost of cancer: a retrospective analysis of the financial impact of cancer on young adults. *Cancer Med*. 2016;5(5):863-870. doi:10.1002/cam4.657.
- Beaupin LM, Boldt A, Amato K. Come back: identifying targets to engage young adult survivors who have been lost to follow-up. *J Clin Oncol* 2018;36(7):29-29. doi: 10.1200/JCO.2018.36.7_suppl.29.

CareMore's Togetherness Program Addresses a Symptom of Living With Chronic Illness: Loneliness

Robin Caruso, MSW, LCSW

CONTINUED FROM COVER



CARUSO
Robin Caruso, MSW, LCSW, is the chief togetherness officer for CareMore Health.

And make no mistake, loneliness can be lethal. Investigators at the University of California, San Francisco, who analyzed government data,² reported that seniors suffering from loneliness have a 45% increased risk of mortality. Because loneliness weakens the body's defense systems, it inhibits the ability of those who are lonely—particularly the elderly—to fend off cancer and other serious illnesses.

A study at Brigham Young University in Provo, Utah, suggests that social isolation poses as much a threat to longevity as obesity does.³

CareMore Health, an Anthem company, has been actively focusing on the impact of loneliness on the health of senior patients for the past year. The company launched the Togetherness Program in May 2017. The program is a first-in-industry approach to targeting loneliness as a health condition that can be diagnosed and treated through community-based interventions and close engagement with patients.

To diagnose loneliness, a provider might ask a patient, "Who would you call if you had a great day or if you had a bad day?" Sadly, many elderly patients do not have that "someone" to call to say, "I went out for a walk today; my pain is better today." Or "It was a rough night; I didn't sleep well, and I had trouble breathing."

For patients dealing with chronic illnesses, a lack of social support and feelings of loneliness can sabotage recovery. CareMore's clinical program fills this void. It incorporates a loneliness survey into an extensive initial health assessment protocol and assesses for loneliness at other health checkpoints.

Since the program launched last year, approximately 700 seniors have enrolled. Participants receive interventions that include weekly phone calls from Togetherness Connectors—full-time CareMore employees hired to manage the program—in addition to CareMore employees who volunteer to be phone pals. Patients also receive home visits from social workers, who help connect them to community-based organizations and other available CareMore Health programs.

One program, the Nifty After Fifty gym, offers a physical exercise program tailored to older adults, many of whom are battling at least 1 chronic illness. However, it's more than a fitness center; it also serves as a social connection point for a population facing increasing health issues and limited mobility, which reduce the opportunity to meet peers and socialize. We are always heartened to retell the story of 2 widowed individuals who met at a Nifty After Fifty gathering, began dating, and eventually married at the center.

Another noteworthy success story involves a CareMore patient named John, who was struggling with loneliness and chronic illness. A 69-year-old man with bladder cancer and diabetes, John enrolled in the CareMore Togetherness program last June after a discussion with Dr Jain. He shared that he was in a poor relationship with his wife and had a strained relationship with his children. He felt alone.

Through the program, John received support from a social worker who helped him develop coping skills and tools to help reduce his depression. However, his condition continued to worsen. After John learned that surgery was ruled out due to his deteriorated health, the Togetherness Program social worker continued to support him and his family, guiding them to reconcile their differences and focus on John's health. This, in turn, helped John better deal with his prognosis. With the newfound support of his family and his improved emotional state, John compiled a bucket list and is now pursuing dreams he had long put off.

The case of another CareMore patient illustrates how loneliness compounds the stress and helplessness so many seniors with chronic disease face. During a lecture at a recent conference, Marjorie shared her own story about the pain of loneliness. "I have been dealing with chronic disease most of my adult life," she said. "My friends don't understand why I can't go out and do things with them. I feel so lonely and left out of things in life."

The CareMore Togetherness team and phone pals hear this same message often. Over half of patients report that their barrier to leaving their home is due to medical issues. "If it were not for my medical appointments," Marjorie said with a dash of self-deprecating humor, "I would have no social life at all."

One of the discoveries in the first year of the Togetherness Program is that it's not just the patients with chronic illnesses who need our attention. Up to 70% of those caring for older, frail, and chronically ill patients say they, too, have experienced symptoms of depression.

In fact, a significant percentage of CareMore senior patients have taken on the responsibility as caregiver for sick family members. As they confront the deteriorating condition of their loved ones, combined with their own health issues, they begin exhibiting signs of depression. Their concerns over fiscal resources further compound the situation.

A vital objective of the Togetherness Program is to assess isolated patients' concerns and barriers to overcoming loneliness—and to compassionately explore available options to guide them to an improved outlook. With increased attention to these previously unserved needs, CareMore's Togetherness Program helps heal these patients.

Although initial outcomes data are still being analyzed, early results show that the program's participants have increased engagement with CareMore's Nifty After Fifty gym by 53%; their outpatient emergency room use has declined by 5%; and, despite a higher disease burden, acute hospital admissions are 11% lower per thousand.

CareMore's Togetherness Program is confronting the loneliness epidemic the best way we know how—through consistent personal interaction. Whether patients are dealing with serious chronic illnesses such as cancer, recent loss, or general feelings of disconnection from society, the Togetherness approach is the same: Listen to patients, and ensure they know that someone is always there for them. ♦

AUTHOR INFORMATION

Robin Caruso, MSW, LCSW, is a licensed clinical social worker who joined CareMore in 2011. In 2017, she took a leading role in CareMore's effort to combat loneliness among seniors as the health plan's first chief togetherness officer. A graduate of Oral Roberts University, she received her master in social work from the University of Southern California.

REFERENCES

1. CareMore's 'be in the Circle: Be Connected' campaign tackles unmet challenge of senior loneliness [press release]. Cerritos, CA: CareMore; May 8, 2017. businesswire.com/news/home/20170508005351/en. Accessed July 20, 2018.
2. Perissinotto CM, Cenzer IS, Covinsky KE. Loneliness in older persons: a predictor of functional decline and death. *JAMA Intern Med*. 2012;172(14):1078-1083. doi: 10.1001/archinternmed.2012.1993.
3. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspect Psychol Sci*. 2015;10(2):227-237. doi: 10.1177/1745691614568352.

PCOC¹⁸

— PATIENT-CENTERED —
ONCOLOGY CARE[®]

SAVE THE DATE

November 16, 2018
Sofitel Philadelphia

Join your peers for a full-day experience with industry-leading experts to collaborate on patient-centric value-based care.

KEYNOTE SPEAKER

Barbara L. McAneny, MD
President
American Medical Association

AGENDA

- Lessons Learned From OCM Data Reporting
- Advancing Oncology Value-Based Payment Models
- Case Study: Integration Across the Oncology Setting for Quality Reporting
- Innovation in Clinical Pathways Design and Implementation
- CART and Gene Therapy Treatment and Management: A Provider and Patient Perspective
- Pharmacy Role in the Patient Care Pathway and Management of Oral Therapies
- Future of Oncology Care

For more information, please visit
ajmc.com/PCOC18

SUPPORT FROM EVERY ANGLE.



PATIENTS FACE ENOUGH CHALLENGES. WE GET THAT.

That's why we created Amgen Assist 360™—so patients and their caregivers have a single place to go to find the support, tools, and resources they need.*



AMGEN REIMBURSEMENT COUNSELORS

Call an Amgen Reimbursement Counselor anytime or schedule a visit with a Field Reimbursement Specialist right at your office.



BENEFIT VERIFICATION

Our secure system makes it easy to electronically submit, store, and retrieve benefit verifications for all your patients currently on an Amgen product.



AMGEN NURSE AMBASSADORS†

Amgen Nurse Ambassadors offer your patients a single point of contact to help them find important resources,* which could include referrals to independent charitable organizations that may provide counseling and community resources.

*Resources include referrals to independent nonprofit patient assistance programs. Eligibility for resources provided by independent nonprofit patient assistance programs is based on the nonprofits' criteria. Amgen has no control over these programs and provides referrals as a courtesy only.

†Amgen Nurse Ambassadors are only available to patients that are prescribed certain products. Nurse Ambassadors are there to support, not replace, your treatment plan and do not provide medical advice or case management services. Patients should always consult their healthcare provider regarding medical decisions or treatment concerns.

ENROLL YOUR ELIGIBLE PATIENTS TODAY.

VISIT AMGENASSIST360.COM/ENROLL
OR CALL 888-4ASSIST (888-427-7478).

MONDAY-FRIDAY, 9 AM TO 8 PM ET



AMGEN ASSIST 360 is a trademarks of Amgen Inc.
©2018 Amgen Inc. All rights reserved. USA-OCF-061889 02-18