SPECIAL ISSUE: **PCOC 2019 MEETING RECAP**

AJMC®
THE AMERICAN JOURNAL OF MANAGED CARE®

25 YEARS
RESEARCH & LEADERSHIP

Evidence-Based ONCOLOGY™

FEBRUARY 2020
VOL. 26 • NO. 3

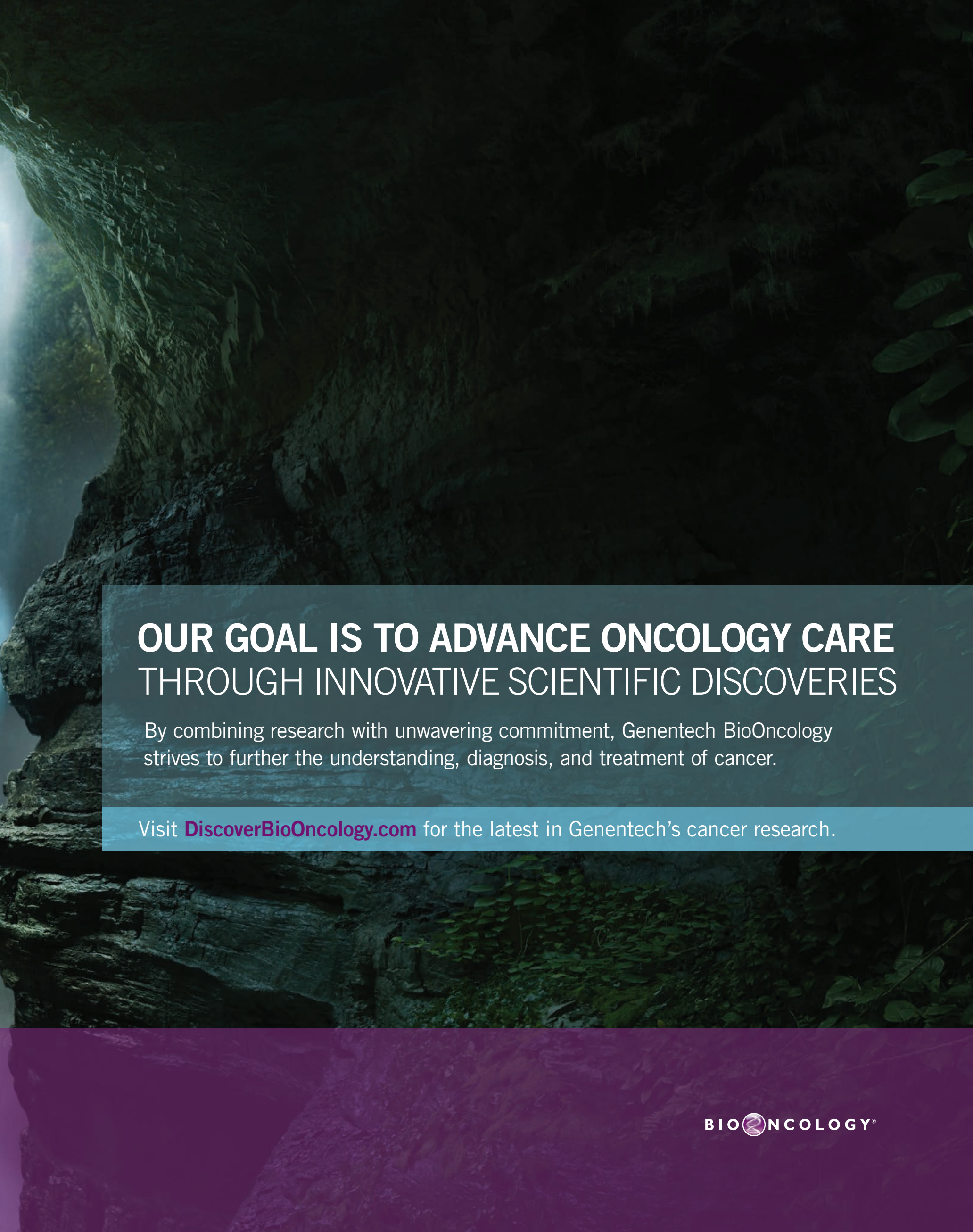
8TH ANNUAL PATIENT-CENTERED ONCOLOGY CARE® 2019 | NOV 8, 2019 | SOFITEL HOTEL, PHILADELPHIA, PA

HIGHLIGHTS FROM THE MEETING

AJMC® Managed Markets Network®
ACCC Association of Community Cancer Centers
AJMC® THE INSTITUTE FOR VALUE-BASED MEDICINE®
COA COMMUNITY ONCOLOGY ALLIANCE®

Genentech

A Member of the Roche Group


OUR GOAL IS TO ADVANCE ONCOLOGY CARE
THROUGH INNOVATIVE SCIENTIFIC DISCOVERIES
By combining research with unwavering commitment, Genentech BioOncology strives to further the understanding, diagnosis, and treatment of cancer.
Visit DiscoverBioOncology.com for the latest in Genentech's cancer research.
BIONCOLOGY®

FROM THE CHAIRMAN

Bringing Lessons From the OCM to the Next Phase of Reform

TIMING IS EVERYTHING. This was especially true on November 8, 2019, when faculty and stakeholders across cancer care gathered in Philadelphia, Pennsylvania, for Patient-Centered Oncology Care®. Days before *The American Journal of Managed Care®* held its signature meeting, the Center for Medicare & Medicaid Innovation announced plans for Oncology Care First (OCF), which will follow the Oncology Care Model (OCM) when that 5-year pilot concludes in 2021.

At its heart, Patient-Centered Oncology Care offers the rare opportunity for physicians and payers, pharmaceutical leaders and policy experts to gather in one place and learn from one another how cancer care can be better for patients.

Leaders from academic medicine and community oncology alike had been waiting to hear what would follow the OCM. Participants have invested heavily to succeed in this alternative payment model, which is rooted in Medicare but sought to involve commercial payers. By all accounts, the OCM forced improvements in the quality of care, and few would abandon the use of navigators or same-day appointments. But there was plenty that the OCM didn't get right, especially when it came to paying for innovative therapies. Drug costs, said one PCOC participant, are "the elephant in the room."

The OCF addresses drug costs somewhat. For example, novel therapy adjustments would be made by cancer type, not as a group. Our meeting marked the first time many stakeholders could compare notes on this change, among others. During networking breaks, the questions came fast: What does the OCF get right? Where will it need more work? What other information do we need?

Thanks to a forward-looking agenda and outstanding faculty, there was much to learn:

- Our session on patient-reported outcomes (PROs) and quality metrics offered an opportunity to discuss the proposal for practices to gather feedback through electronic PROs.
- Jeffrey Patton, MD, of Tennessee Oncology and OneOncology, outlined what payers should do to support community practices and why it's in their interest to do so.
- Attendees heard former FDA Commissioner Scott Gottlieb, MD, outline how the agency will make greater use of real-world evidence.
- Joshua Ofman, MD, MSHS, described the lifesaving potential of a new test to diagnose cancer early and how this could hold down healthcare costs. A separate panel discussed the importance of paying for diagnostic testing in the era of precision medicine.

At its heart, PCOC offers the rare opportunity for physicians, payers, pharmaceutical leaders, and policy experts to gather in 1 place and learn from each other how cancer care can be better for patients. We've seen how practices have become more patient-focused and evolved since we convened this meeting in 2012. For all its flaws, the OCM has been a catalyst for doing things differently, for patients to spend less time waiting, and for delivering care that is more personalized and consistent with patient values. We were proud to be the first stop for conversations on what will come next, and we look forward to driving the discussion throughout 2020. ◆

Sincerely,
Mike Hennessy, Sr
Chairman and Founder

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.

AJMC®
THE AMERICAN JOURNAL OF MANAGED CARE®

www.ajmc.com/about/ebo
EBOncology

SPECIAL ISSUE /PCOC
FEBRUARY 2020
VOLUME 26, ISSUE 3

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

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.

Above left, former FDA Commissioner Scott Gottlieb, MD, discusses use of real-world evidence in the regulatory process. Above right, Jeffrey Patton, MD, of Tennessee Oncology and OneOncology outlines examples of innovation at the community practice level in cancer care.

PHOTOS © KERRY MCINTYRE

BRUKINSA
IS NOW APPROVED

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage

Fatal and serious hemorrhagic events have occurred in patients with hematological malignancies treated with BRUKINSA monotherapy. Grade 3 or higher bleeding events including intracranial and gastrointestinal hemorrhage, hematuria and hemothorax have been reported in 2% of patients treated with BRUKINSA monotherapy. Bleeding events of any grade, including purpura and petechiae, occurred in 50% of patients treated with BRUKINSA monotherapy.

Bleeding events have occurred in patients with and without concomitant antiplatelet or anticoagulation therapy. Co-administration of BRUKINSA with antiplatelet or anticoagulant medications may further increase the risk of hemorrhage.

Monitor for signs and symptoms of bleeding. Discontinue BRUKINSA if intracranial hemorrhage of any grade occurs. Consider the benefit-risk of withholding BRUKINSA for 3-7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

Infections

Fatal and serious infections (including bacterial, viral, or fungal) and opportunistic infections have occurred in patients with hematological malignancies treated with BRUKINSA monotherapy. Grade 3 or higher infections occurred in 23% of patients treated with BRUKINSA monotherapy. The most common Grade 3 or higher infection was pneumonia. Infections due to hepatitis B virus (HBV) reactivation have occurred.

Consider prophylaxis for herpes simplex virus, pneumocystis jiroveci pneumonia and other infections according to standard of care in patients who are at increased risk for infections. Monitor and evaluate patients for fever or other signs and symptoms of infection and treat appropriately.

Cytopenias

Grade 3 or 4 cytopenias, including neutropenia (27%), thrombocytopenia (10%) and anemia (8%) based on laboratory measurements, were reported in patients treated with BRUKINSA monotherapy.

Monitor complete blood counts during treatment and treat using growth factor or transfusions, as needed.

Second Primary Malignancies

Second primary malignancies, including non-skin carcinoma, have occurred in 9% of patients treated with BRUKINSA monotherapy. The most frequent second primary malignancy was skin cancer (basal cell carcinoma and squamous cell carcinoma of skin), reported in 6% of patients. Advise patients to use sun protection.

Cardiac Arrhythmias

Atrial fibrillation and atrial flutter have occurred in 2% of patients treated with BRUKINSA monotherapy. Patients with cardiac risk factors, hypertension, and acute infections may be at increased risk. Grade 3 or higher events were reported in 0.6% of patients treated with BRUKINSA monotherapy. Monitor signs and symptoms for atrial fibrillation and atrial flutter and manage as appropriate.

Brukinsa™
zanubrutinib 80 mg capsules

BRUKINSA™ (zanubrutinib) IS A KINASE INHIBITOR INDICATED FOR THE TREATMENT OF ADULT PATIENTS WITH MANTLE CELL LYMPHOMA (MCL) WHO HAVE RECEIVED AT LEAST ONE PRIOR THERAPY.

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Learn more at BRUKINSA.com

Embryo-Fetal Toxicity

Based on findings in animals, BRUKINSA can cause fetal harm when administered to a pregnant woman. Administration of zanubrutinib to pregnant rats during the period of organogenesis caused embryo-fetal toxicity including malformations at exposures that were 5 times higher than those reported in patients at the recommended dose of 160 mg twice daily. Advise women to avoid becoming pregnant while taking BRUKINSA and for at least 1 week after the last dose. Advise men to avoid fathering a child during treatment and for at least 1 week after the last dose.

If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

ADVERSE REACTIONS

The most common adverse reactions in > 10% of patients who received BRUKINSA were decreased neutrophil count (53%), decreased platelet count (39%), upper respiratory tract infection (38%), decreased white blood cell count (30%), decreased hemoglobin (29%), rash (25%), bruising (23%), diarrhea (20%), cough (20%), musculoskeletal pain (19%), pneumonia (18%), urinary tract infection (13%), hematuria (12%), fatigue (11%), constipation (11%), and hemorrhage (10%).

DRUG INTERACTIONS

CYP3A Inhibitors: When BRUKINSA is co-administered with a strong CYP3A inhibitor, reduce BRUKINSA dose to 80 mg once daily. For coadministration with a moderate CYP3A inhibitor, reduce BRUKINSA dose to 80 mg twice daily.

CYP3A Inducers: Avoid coadministration with moderate or strong CYP3A inducers.

SPECIFIC POPULATIONS

Hepatic Impairment: The recommended dose of BRUKINSA for patients with severe hepatic impairment is 80 mg orally twice daily.

INDICATION

BRUKINSA is a kinase inhibitor indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

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

BeiGene

BRIEF SUMMARY OF PRESCRIBING INFORMATION
FOR BRUKINSA™ (zanubrutinib)
SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

BRUKINSA is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

This indication is approved under accelerated approval based on overall response rate *[see Clinical Studies (14.1)]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

4 CONTRAINDICATIONS: None.

5 WARNINGS AND PRECAUTIONS

5.1 Hemorrhage

Fatal and serious hemorrhagic events have occurred in patients with hematological malignancies treated with BRUKINSA monotherapy. Grade 3 or higher bleeding events including intracranial and gastrointestinal hemorrhage, hematuria, and hemothorax have been reported in 2% of patients treated with BRUKINSA monotherapy. Bleeding events of any grade, including purpura and petechiae, occurred in 50% of patients treated with BRUKINSA monotherapy.

Bleeding events have occurred in patients with and without concomitant antiplatelet or anticoagulation therapy. Co-administration of BRUKINSA with antiplatelet or anticoagulant medications may further increase the risk of hemorrhage.

Monitor for signs and symptoms of bleeding. Discontinue BRUKINSA if intracranial hemorrhage of any grade occurs. Consider the benefit-risk of withholding BRUKINSA for 3-7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

5.2 Infections

Fatal and serious infections (including bacterial, viral, or fungal) and opportunistic infections have occurred in patients with hematological malignancies treated with BRUKINSA monotherapy. Grade 3 or higher infections occurred in 23% of patients treated with BRUKINSA monotherapy. The most common Grade 3 or higher infection was pneumonia. Infections due to hepatitis B virus (HBV) reactivation have occurred.

Consider prophylaxis for herpes simplex virus, pneumocystis jiroveci pneumonia, and other infections according to standard of care in patients who are at increased risk for infections. Monitor and evaluate patients for fever or other signs and symptoms of infection and treat appropriately.

5.3 Cytopenias

Grade 3 or 4 cytopenias, including neutropenia (27%), thrombocytopenia (10%), and anemia (8%) based on laboratory measurements, were reported in patients treated with BRUKINSA monotherapy.

Monitor complete blood counts during treatment and treat using growth factor or transfusions, as needed.

5.4 Second Primary Malignancies

Second primary malignancies, including non-skin carcinoma, have occurred in 9% of patients treated with BRUKINSA monotherapy. The most frequent second primary malignancy was skin cancer (basal cell carcinoma and squamous cell carcinoma of skin), reported in 6% of patients. Advise patients to use sun protection.

5.5 Cardiac Arrhythmias

Atrial fibrillation and atrial flutter have occurred in 2% of patients treated with BRUKINSA monotherapy. Patients with cardiac risk factors, hypertension, and acute infections may be at increased risk. Grade 3 or higher events were reported in 0.6% of patients treated with BRUKINSA monotherapy. Monitor signs and symptoms for atrial fibrillation and atrial flutter and manage as appropriate.

5.6 Embryo-Fetal Toxicity

Based on findings in animals, BRUKINSA can cause fetal harm when administered to a pregnant woman. Administration of zanubrutinib to pregnant rats during the period of organogenesis caused embryo-fetal toxicity, including malformations at exposures that were 5 times higher than those reported in patients at the recommended dose of 160 mg twice daily. Advise women to avoid becoming pregnant while taking BRUKINSA and for at least 1 week after the last dose. Advise men to avoid fathering a child during treatment and for at least 1 week after the last dose. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus *[see Use in Specific Populations (8.1)]*.

6 ADVERSE REACTIONS

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

- Hemorrhage *[see Warnings and Precautions (5.1)]*
- Infections *[see Warnings and Precautions (5.2)]*
- Cytopenias *[see Warnings and Precautions (5.3)]*
- Second Primary Malignancies *[see Warnings and Precautions (5.4)]*
- Cardiac Arrhythmias *[see Warnings and Precautions (5.5)]*

6.1 Clinical Trials Experience

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

The data in the WARNINGS AND PRECAUTIONS reflect exposure to BRUKINSA as a single agent at 160 mg twice daily in 524 patients in clinical trials BGB-3111-AU-003, BGB-3111-206, BGB-3111-205, BGB-3111-210, and BGB-3111-1002 and to BRUKINSA at 320 mg once daily in 105 patients in trials BGB-3111-AU-003 and BGB-3111-1002. Among 629 patients receiving BRUKINSA, 79% were exposed for 6 months or longer and 61% were exposed for greater than one year.

In this pooled safety population, the most common adverse reactions in > 10% of patients who received BRUKINSA were neutrophil count decreased (53%), platelet count decreased (39%), upper respiratory tract infection (38%), white blood cell count decreased (30%), hemoglobin decreased (29%), rash (25%), bruising (23%), diarrhea (20%), cough (20%), musculoskeletal pain (19%), pneumonia (18%), urinary tract infection (13%), hematuria (12%), fatigue (11%), constipation (11%), and hemorrhage (10%).

Mantle Cell Lymphoma (MCL)

The safety of BRUKINSA was evaluated in 118 patients with MCL who received at least one prior therapy in two single-arm clinical trials, BGB-3111-206 [NCT03206970] and BGB-3111-AU-003 [NCT02343120] *[see Clinical Studies (14.1)]*. The median age of patients who received BRUKINSA in studies BGB-3111-206 and BGB-3111-AU-003 was 62 years (range: 34 to 86), 75% were male, 75% were Asian, 21% were White, and 94% had an ECOG performance status of 0 to 1. Patients had a median of 2 prior lines of therapy (range: 1 to 4). The BGB-3111-206 trial required a platelet count ≥ 75 x 10^9/L and an absolute neutrophil count ≥ 1 x 10^9/L independent of growth factor support, hepatic enzymes ≤ 2.5 x upper limit of normal, total bilirubin ≤ 1.5 x ULN. The BGB-3111-AU-003 trial required a platelet count ≥ 50 x 10^9/L and an absolute neutrophil count ≥ 1 x 10^9/L independent of growth factor support, hepatic enzymes ≤ 3 x upper limit of normal, total bilirubin ≤ 1.5 x ULN. Both trials required a CLcr ≥ 30 mL/min. Both trials excluded patients with prior allogeneic hematopoietic stem cell transplant, exposure to a BTK inhibitor, known infection with HIV, and serologic evidence of active hepatitis B or hepatitis C infection and patients requiring strong CYP3A inhibitors or strong CYP3A inducers. Patients received BRUKINSA 160 mg twice daily or 320 mg once daily. Among patients receiving BRUKINSA, 79% were exposed for 6 months or longer and 68% were exposed for greater than one year.

Fatal events within 30 days of the last dose of BRUKINSA occurred in 8 (7%) of 118 patients with MCL. Fatal cases included pneumonia in 2 patients and cerebral hemorrhage in one patient.

Serious adverse reactions were reported in 36 patients (31%). The most frequent serious adverse reactions that occurred were pneumonia (11%) and hemorrhage (5%).

Of the 118 patients with MCL treated with BRUKINSA, 8 (7%) patients discontinued treatment due to adverse reactions in the trials. The most frequent adverse reaction leading to treatment discontinuation was pneumonia (3.4%). One (0.8%) patient experienced an adverse reaction leading to dose reduction (hepatitis B).

Table 3 summarizes the adverse reactions in BGB-3111-206 and BGB-3111-AU-003.

Table 3: Adverse Reactions (≥ 10%) in Patients Receiving BRUKINSA in BGB-3111-206 and BGB-3111-AU-003 Trials

Body System	Adverse Reaction	Percent of Patients (N=118)	
		All Grades %	Grade 3 or Higher %
Blood and lymphatic system disorders	Neutropenia and Neutrophil count decreased	38	15
	Thrombocytopenia and Platelet count decreased	27	5
	Leukopenia and White blood count decreased	25	5
	Anemia and Hemoglobin decreased	14	8
Infections and infestations	Upper respiratory tract infection¶	39	0
	Pneumonia§	15	10^
	Urinary tract infection	11	0.8
Skin and subcutaneous tissue disorders	Rashǁ	36	0
	Bruising*	14	0
Gastrointestinal disorders	Diarrhea	23	0.8
	Constipation	13	0
Vascular disorders	Hypertension	12	3.4
	Hemorrhage†	11	3.4^
Musculoskeletal and connective tissue disorders	Musculoskeletal pain‡	14	3.4
Metabolism and nutrition disorders	Hypokalemia	14	1.7
Respiratory, thoracic and mediastinal disorders	Cough	12	0

^ Includes fatal adverse reaction
* Bruising includes all related terms containing bruise, bruising, contusion, ecchymosis
† Hemorrhage includes all related terms containing hemorrhage, hematoma
‡ Musculoskeletal pain includes musculoskeletal pain, musculoskeletal discomfort, myalgia, back pain, arthralgia, arthritis
§ Pneumonia includes pneumonia, pneumonia fungal, pneumonia cryptococcal, pneumonia streptococcal, atypical pneumonia, lung infection, lower respiratory tract infection, lower respiratory tract infection bacterial, lower respiratory tract infection viral
ǁ Rash includes all related terms containing rash
¶ Upper respiratory tract infection includes upper respiratory tract infection, upper respiratory tract infection viral

Other clinically significant adverse reactions that occurred in < 10% of patients with mantle cell lymphoma include major hemorrhage (defined as ≥ Grade 3 hemorrhage or CNS hemorrhage of any grade) (5%), hyperuricemia (6%) and headache (4.2%).

Table 4: Selected Laboratory Abnormalities* (> 20%) in Patients with MCL in Studies BGB-3111-206 and BGB-3111-AU-003

Laboratory Parameter	Percent of Patients (N=118)	
	All Grades (%)	Grade 3 or 4 (%)
Neutrophils decreased	45	20
Platelets decreased	40	7
Hemoglobin decreased	27	6
Lymphocytosis†	41	16
Chemistry abnormalities		
Blood uric acid increased	29	2.6
ALT increased	28	0.9
Bilirubin increased	24	0.9

* Based on laboratory measurements.
† Asymptomatic lymphocytosis is a known effect of BTK inhibition.

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on BRUKINSA

Table 5: Drug Interactions that Affect Zanubrutinib

Moderate and Strong CYP3A Inhibitors	
Clinical Impact	• Co-administration with a moderate or strong CYP3A inhibitor increases zanubrutinib C_{max} and AUC *[see Clinical Pharmacology (12.3)]* which may increase the risk of BRUKINSA toxicities.
Prevention or management	• Reduce BRUKINSA dosage when co-administered with moderate or strong CYP3A inhibitors *[see Dosage and Administration (2.3)]*.
Moderate and Strong CYP3A Inducers	
Clinical Impact	• Co-administration with a moderate or strong CYP3A inducer decreases zanubrutinib C_{max} and AUC *[see Clinical Pharmacology (12.3)]* which may reduce BRUKINSA efficacy.
Prevention or management	• Avoid co-administration of BRUKINSA with moderate or strong CYP3A inducers *[see Dosage and Administration (2.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings in animals, BRUKINSA can cause fetal harm when administered to pregnant women. There are no available data on BRUKINSA use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of zanubrutinib to pregnant rats during the period of organogenesis was associated with fetal heart malformation at approximately 5-fold human exposures *(see Data)*. Women should be advised to avoid pregnancy while taking BRUKINSA. If BRUKINSA is used during pregnancy, or if the patient becomes pregnant while taking BRUKINSA, the patient should be apprised of the potential hazard to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Embryo-fetal development toxicity studies were conducted in both rats and rabbits. Zanubrutinib was administered orally to pregnant rats during the period of organogenesis at doses of 30, 75, and 150 mg/kg/day. Malformations in the heart (2- or 3-chambered hearts) were noted at all dose levels in the absence of maternal toxicity. The dose of 30 mg/kg/day is approximately 5 times the exposure (AUC) in patients receiving the recommended dose of 160 mg twice daily.

Administration of zanubrutinib to pregnant rabbits during the period of organogenesis at 30, 70, and 150 mg/kg/day resulted in post-implantation loss at the highest dose. The dose of 150 mg/kg is approximately 32 times the exposure (AUC) in patients at the recommended dose and was associated with maternal toxicity.

In a pre- and post-natal developmental toxicity study, zanubrutinib was administered orally to rats at doses of 30, 75, and 150 mg/kg/day from implantation through weaning. The offspring from the middle and high dose groups had decreased body weights preweaning, and all dose groups had adverse ocular findings (e.g. cataract, protruding eye). The dose of 30 mg/kg/day is approximately 5 times the AUC in patients receiving the recommended dose.

8.2 Lactation

Risk Summary

There are no data on the presence of zanubrutinib or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions from BRUKINSA in a breastfed child, advise lactating women not to breastfeed during treatment with BRUKINSA and for at least two weeks following the last dose.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential prior to initiating BRUKINSA therapy.

Contraception

Females

BRUKINSA can cause embryo-fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)]*. Advise female patients of reproductive potential to use effective contraception during treatment with BRUKINSA and for at least 1 week following the last dose of BRUKINSA. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus.

Males

Advise men to avoid fathering a child while receiving BRUKINSA and for at least 1 week following the last dose of BRUKINSA.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Of the 641 patients in clinical studies with BRUKINSA, 49% were ≥ 65 years of age, while 16% were ≥ 75 years of age. No overall differences in safety or effectiveness were observed between younger and older patients.

8.6 Renal Impairment

No dosage modification is recommended in patients with mild to moderate renal impairment (CLcr ≥ 30 mL/min, estimated by Cockcroft-Gault). Monitor for BRUKINSA adverse reactions in patients with severe renal impairment (CLcr < 30 mL/min) or on dialysis *[see Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment

Dosage modification of BRUKINSA is recommended in patients with severe hepatic impairment *[see Dosage and Administration (2.2)]*. The safety of BRUKINSA has not been evaluated in patients with severe hepatic impairment. No dosage modification is recommended in patients with mild to moderate hepatic impairment. Monitor for BRUKINSA adverse reactions in patients with hepatic impairment *[see Clinical Pharmacology (12.3)]*.

Distributed and Marketed by:
BeiGene USA, Inc.
San Mateo, CA 94403

AGENDA

FRIDAY, NOVEMBER 8, 2019

7:45 to 8:15 AM	**REGISTRATION AND BREAKFAST**
8:15 to 8:45 AM	**Welcome and Keynote Presentation** Joshua Ofman, MD
8:45 to 9:25 AM	**CAR-T Therapy Updates: Reimbursement, Policy, and Patient Access** John W. Sweetenham, MD, FRCP, FACP, FASCO Shannon L. Maude, MD, PhD Erika Miller, JD
9:25 to 10:05 AM	**Innovation in Oncology Care and Treatment** Jennifer Atkins Sonia Oskouei, PharmD Bo Gamble Judith Bachman, RN, BSN, MSN, CNAA
10:05 to 10:25 AM	**BREAK**
10:25 to 11:05 AM	**Making an Impact through Experience** Rebecca Kaul, MBA
11:05 to 11:45 AM	**Personalized Medicine and Value-Based Care** James Almas, MD Edward Abrahams, PhD Bryan Loy, MD, MBA
11:45 to 12:15 PM	**Healthcare Innovation in the Political Economy** Scott Gottlieb, MD
12:15 to 1:00 PM	**BREAK FOR LUNCH**
1:00 to 1:15 PM	**Seema S. Sonnad Emerging Leader in Managed Care Research Award**
1:15 to 1:45 PM	**How Community Oncology is Disrupting the Marketplace and Improving Patient-Centered Care** Jeffrey F. Patton, MD
1:45 to 2:25 PM	**Patient-Reported Outcomes and Quality Metrics** Stephen B. Edge, MD, FACS, FASCO Collette Pitzen, RN, BSN, CPHQ Amila Patel, PharmD, BCOP Nate Gosse, PhD
2:25 to 2:45 PM	**BREAK**
2:45 to 3:25 PM	**Future of Oncology Advanced Payment Models** Steven D`Amato, RPh, BSPharm Lalan Wilfong, MD Jeffrey Odell Rani Khetarpal
3:25 to 4:15 PM	**Oncology Networks: Collaboration for Value-Based Care** Erich Mounce, MSHA Sibel Blau, MD Terrill Jordan, JD, LL.M Brad Prechtl, MBA
4:15 to 4:25 PM	**Closing Remarks and Adjournment** Joseph Alvarnas, MD Kashyap Patel, MD

FACULTY

CHAIRMAN

Joseph Alvarnas, MD
Vice President of Government Affairs and Senior Medical Director for Employer Strategy
Associate Clinical Professor, Department of Hematology & Hematopoietic Cell Transplantation
City of Hope
Duarte, CA

Joseph Alvarnas, MD, attended medical school at the University of California, San Francisco. He completed internal medicine training and fellowships in hematology and hematopoietic cell transplantation at Stanford University Medical Center. He helped found the City of Hope–Banner Bone Marrow Transplant Program and later served as director of the Hematopoietic Stem Cell Processing Laboratory and chair of the Quality Committee for the transplant program. Today, he is an associate clinical professor in the Department of Hematology and Hematopoietic Cell Transplantation at City of Hope, where he also serves as the institution's vice president of Government Affairs and senior medical director for Employer Strategy. Dr Alvarnas is the national cochair for 2 Blood and Marrow Transplant Clinical Trials Network clinical trials studying stem cell transplantation in patients infected with HIV. He serves on the American Society of Hematology (ASH) Committee on Practice and as an ASH liaison to the Committee on Quality. He is editor-in-chief of *Evidence-Based Oncology*™, a publication of *The American Journal of Managed Care*®.

CHAIRMAN

Kashyap Patel, MD
CEO
Carolina Blood and Cancer Care Associates
Rock Hill, SC

Kashyap Patel, MD, is the CEO of Carolina Blood and Cancer Care Associates, based in Rock Hill, South Carolina. Dr Patel is a board-certified hematologist and oncologist who is the current vice president of the Community Oncology Alliance and a trustee of the Association of Community Cancer Centers. He is recognized as one of the nation's experts in implementing value-based payment models in the community oncology practice through local partnerships and an emphasis on palliative care. A graduate of St. Xavier's College, Dr Patel received his medical degree at Thomas Jefferson University. He serves as an independent contractor for Palmetto GBA and a medical director for the International Oncology Network.

Inmaculada Hernandez, PharmD, PhD, accepts the Seema Sonnad Emerging Leader in Managed Care Research Award. Joining her from left are Henry Glick, PhD, husband of the late Seema Sonnad, PhD, along with Michael Chernew, PhD, and A. Mark Fendrick MD, the co-editors in chief of *The American Journal of Managed Care*®.

EVENT PHOTO © KERRY MCINTYRE

FEATURED FACULTY

Scott Gottlieb, MD
Featured Speaker of AJMC's Patient-Centered Oncology Care Meeting
Former Commissioner of the US Food and Drug Administration (FDA)

KEYNOTE SPEAKER

Joshua Ofman, MD, MSHS
Chief of Corporate Strategy & External Affairs
Grail, Inc
Menlo Park, CA

FACULTY

Edward Abrahams, PhD
President
Personalized Medicine Coalition
Washington, DC

James Almas, MD
Vice President and National Medical Director of Clinical Effectiveness
LabCorp
Burlington, NC

Jennifer Atkins
Vice President, Network Solutions
Blue Cross Blue Shield Association
Chicago, IL

Judith Bachman, RN, BSN, MSN, CNAA
Chief Operating Officer
Fox Chase Cancer Center
Philadelphia, PA

Sibel Blau, MD
Medical Oncology Provider
Northwest Medical Specialties, PLLC
Puyallup, WA

Steven D`Amato, R.Ph, BSPharm
Executive Director
New England Cancer Specialists
Portland, ME

Stephen B. Edge, MD, FACS, FASCO
Vice President, Healthcare Outcomes and Policy
Professor of Oncology
Roswell Park Comprehensive Cancer Center
Professor of Surgery
University of Buffalo and Jacobs School of Medicine
Buffalo, NY

Robert (Bo) Gamble
Director of Strategic Practice Initiatives
Community Oncology Alliance
Virginia Beach, VA

Nate Gosse, PhD
Vice President of Product Management
McKesson
Philadelphia, PA

Terrill Jordan, JD, LL.M
President and Chief Executive Officer
Regional Cancer Care Associates
Hackensack, NJ

Rebecca Kaul, MBA
Vice President and Chief Innovation Officer
MD Anderson Cancer Center
Houston, TX

Rani Khetarpal
Vice President
New Century Health
Brea, CA

Bryan Loy, MD, MBA
Corporate Medical Director Oncology, Laboratory, and Personalized Medicine
Humana
Louisville, KY

Shannon L. Maude, MD, PhD
Assistant Professor of Pediatrics, Division of Oncology
The Children's Hospital of Philadelphia
Medical Director, Center for Cellular Immunotherapies
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, PA

Erika Miller, JD
Senior Vice President & Counsel
CRD Associates
Washington, DC

Erich Mounce
Chief Operating Officer
OneOncology
Memphis, TN

Jeffrey Odell
Provider Collaboration Programs Director
Payment Innovation Team
Anthem
Richmond, VA

Sonia T. Oskouei, PharmD, BCMAS, DPLA
Vice President, Innovation and Solution Development
Applied Sciences
Premier Inc.
Charlotte, NC

Amila Patel, PharmD, BCOP
Director of Clinical Product & Content, Clinical Oncology
Flatiron Health
New York, NY

Jeffrey F. Patton, MD
President of Physician Services, OneOncology
Chief Executive Officer, Tennessee Oncology
Nashville, TN

Collette Pitzen, RN, BSN, CPHQ
Clinical Measure Developer
MN Community Measurement
Minneapolis, MN

Brad Pretchl, MBA
Chief Executive Officer
Florida Cancer Specialists
American Oncology Network
Fort Myers, FL

John W Sweetenham, MD, FRCP, FACP, FASCO
Professor of Medicine
Associate Director of Clinical Affairs
Harold C Simmons Comprehensive Cancer Center
UT Southwestern

Lalan Wilfong, MD
Executive Vice President, Value-Based Care and Quality Programs
Texas Oncology
Dallas, TX

Using Technology to Intervene Earlier in Cancer and Improve Survival Rates

Laura Joszt

MOST CANCERS ARE DIAGNOSED in the later stages, but if this disease could be diagnosed earlier and with greater accuracy, patient outcomes could be much better, said Joshua Ofman, MD, MSHS, chief of corporate strategy and external affairs, Grail, Inc.

"I know that nothing can keep you up at night like the concerns people have about cancer," Ofman said, as he began his keynote address during Patient-Centered Oncology Care, the annual multistakeholder gathering presented by *The American Journal of Managed Care*® in Philadelphia, Pennsylvania.

Although there are effective screening methods for some cancers, most are not screened for at all, and the process is inefficient: screening for one type of cancer at a time. Furthermore, screening rates are "suboptimal," Ofman said. As a result, most cancers are diagnosed in later stages, when outcomes are poorer. Finding cancer in later stages means the cost of care will be dramatically higher, too.

On the flip side, however, there are concerns that when cancers are diagnosed early, there can be overdiagnosis or cancers diagnosed that might not cause harm. Ofman pointed to controversies over recommendations for mammography and prostate-specific antigen testing.

According to the data Ofman presented, approximately 2000 Americans die each day due to cancer. By 2020, cancer care is projected to cost more than $150 billion dollars.

"So, we have got to transition our current healthcare system away from a 'break it and fix it' healthcare system and toward a healthcare system that focuses on prevention and early detection," he said. "And if we don't do that, these numbers are not going to change."

New technologies are the key to focusing on early detection. Sequencing the human genome and reading the code of DNA is allowing the healthcare system to find mutations and changes, but we are not yet at a place where we can distinguish cancer from noncancer just based on mutations, Ofman explained.

The next step in technology has been the convergence of machine learning and artificial intelligence. This technology is allowing Grail to look into blood to identify fragments of DNA that degrading cancer cells release. However, healthy cells also degrade and release fragments. Any test of these cell fragments would have to be able to discriminate a cancer cell from a noncancer cell with high specificity in order to create few false positives. And that test would have to be able to tell clinicians what tissue it was from to localize the cancer.

In a study, Grail examined the methylation patterns in DNA. Methylation patterns change the activity of a DNA segment and tell cells what cells to become and what tissue to go to. Grail also looked at RNA, mutations, and DNA code in order to determine the best way to detect cancer.

© KERRY MCINTYRE

Joshua Ofman, MD, MSHS, of Grail, Inc., explains the human and cost implications of intercepting cancer early.

The Circulating Cell-Free Genome Atlas Study included more than 15,000 participants with and without cancer and compared how efficient the technologies were at detecting cancer, how many false-positive test results there were, and how well they could identify where the cancer was localized.

The study revealed that DNA methylation was the best method, and adding on any of the other methods, such as mutations, did not improve the test. Then, Grail trained a machine learning algorithm to detect the cancer and determine its location.

The test can diagnose or find more than 24 different types of cancer, but Ofman presented on a subset of the 12 deadliest cancers that account for about 70% of cancer mortality. The test detected cancer across these 12 cancers with 76% sensitivity and the false-positive rate was below 1%. In comparison, the false-positive rate for mammography is 10%. The test was also able to accurately localize the cancer in more than 90% of cases.

The low false-positive rate is important, as the test identifies early-stage cancers. Ofman presented data that showed patients whose cancers were diagnosed by the Grail test had a worse mortality rate, which appears to mean that the Grail test is diagnosing harmful and lethal cancers.

"And that's really important for an early-detection test, because as you know, one of the biggest concerns with cancer detection right now is that we're finding too many false positives," Ofman said. "And we're finding early cancers that probably don't need to be treated as aggressively as they're being treated. So, we can be fairly confident based on these early data that the cancers the Grail test is finding required treatment, which is exactly what you want to know."

What does this test mean for overall public health? If everyone in the United States from age 50 to 79 were eligible for screening and they were all given the Grail test, or a test like it, almost half a million cancers would be identified, and many of these cancers would not have been identified without this test because there is no capability to detect the cancer that early.

If the same population went through current screenings, such as mammography for breast cancer, Cologuard (Exact Sciences Corporation, Madison, WI) for colon cancer, or low-dose computed tomography for lung cancer, the tests would diagnose 150,000 cancers but produce about 9 million false positives. Adding the Grail test to the current screening assessments would find 3 times as many cancers but only add 1 million false positives.

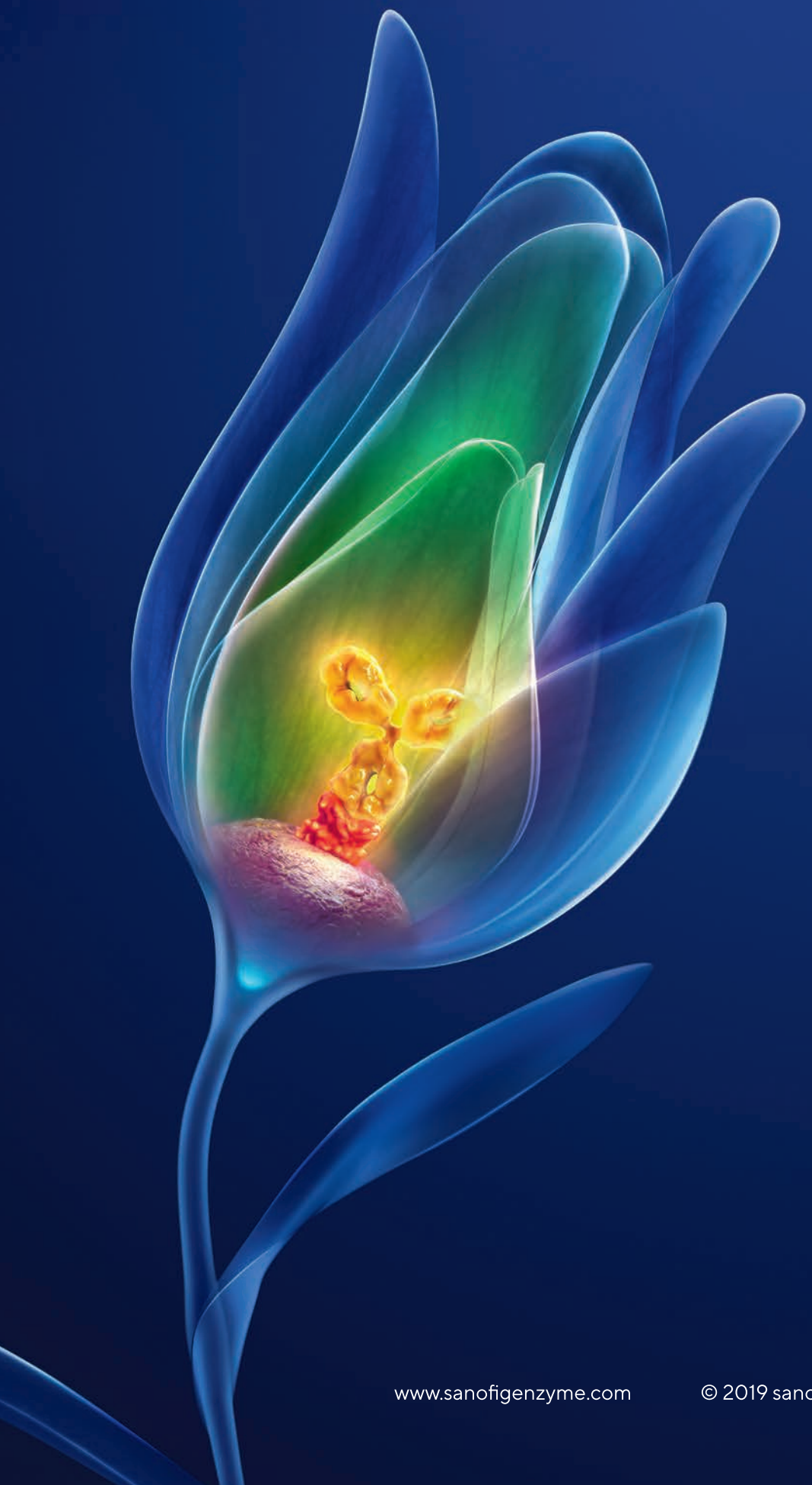
Grail also looked at how its test could intercept cancers at an earlier stage and what impact this finding would have. Looking at the participant data of those likely to die in the next 5 years from cancer, Grail found it could intercept at an earlier stage for 68% of cancers. This interception would flip the current distribution of diagnosis, which is mostly happening at stage III or stage IV. This test has the potential to reduce the cancer mortality rate by 37%.

"This is all a projection, and it's early modeling, and there's much more to come, but this paints the magnitude of the opportunity that we're staring into, to focus on early detection," Ofman said. ◆

The outlook

for patients with multiple myeloma

is still unfolding.



Development in the anti-CD38 class needs to continue.

Multiple myeloma remains incurable despite recent therapeutic advances. There's still a significant need for new treatment options. At Sanofi Genzyme, we're working to ensure patients can look ahead with newfound hope.

Their fight is our fight.

See what's unfolding at
CommittedtoMM.com

SANOFI GENZYME

www.sanofigenzyme.com

SAUS.ISX.19.08.4489

The Fast Pace of CAR T-Cell Innovation Caused an Array of Treatment Challenges

Laura Joszt

MAUDE

Shannon L. Maude, MD, PhD, assistant professor of pediatrics, Division of Oncology, Children's Hospital of Philadelphia

SWEETENHAM

John W. Sweetenham, MD, FRCP, FACP, FASCO, professor of medicine, associate director, Clinical Affairs, Harold C. Simmons Comprehensive Cancer Center, UT Southwestern

MILLER

Erika Miller, JD, senior vice president, CRD Associates

EVIDENCE SHOWS THAT chimeric antigen receptor (CAR) T-cell therapies are effective, but their price tags are high, raising concerns about how many patients will receive treatment. During a discussion at *The American Journal of Managed Care*®'s Patient-Centered Oncology Care® meeting in Philadelphia, panelists outlined the efficacy of the 2 FDA-approved therapies, Medicare reimbursement for CAR T-cell therapies, and the pace of innovation in healthcare.

Tisagenlecleucel (Kymriah) has been used successfully to treat children and young adults, up to age 25, with relapsed or refractory acute lymphoblastic leukemia, explained Shannon L. Maude, MD, PhD, assistant professor of pediatrics in the Division of Oncology at the Children's Hospital of Philadelphia, and medical director of the Center for Cellular Immunotherapies at the University of Pennsylvania Perelman School of Medicine.

In the trials that led to FDA approval, patients treated with tisagenlecleucel had a remission rate of 81% after relapsing more than once after the best standard of care.[1] In some of the longer-term data now being seen, patients who went into remission have a relapse-free survival rate of 66%.[2]

The other FDA-approved therapy, axicabtagene ciloleucel (Yescarta), is indicated in adults with diffuse large B-cell lymphoma, which typically affects people in their 60s and 70s, said John W. Sweetenham, MD, FRCP, FACP, FASCO, professor of medicine and associate director of clinical affairs at the Harold C. Simmons Comprehensive Cancer Center at UT Southwestern. For 15 to 20 years, treatment for disease has be relatively the same: chemotherapy is front line followed by a bone marrow transplant. But if those 2 treatments are unsuccessful, the patients had essentially no other options.

Now, there have been extraordinary responses with CAR T-cell therapy, he said. There are patients who, in the past, he would have anticipated have a bad outcome after relapsing, who have now survived more than a year after treatment.

"This treatment is like nothing we've ever seen before in terms of its ability to turn very sick people around," Sweetenham said.

However, because these therapies are so different from conventional treatments, there are still plenty of unknowns. For example, there have not been any randomized trials to compare the CAR T-cell therapy treatment with more standard treatments.

As a result of how successful CAR T-cell therapies have been and how unique they are, they cost upwards of $373,000 per treatment[3]—the good news, said Erika Miller, JD, senior vice president and counsel at CRD Associates, is that patients only need the treatment once. The problem is that regulators and legislators are concerned about safeguarding the Medicare trust fund, and these therapies are a big hit, financially.

There is concern that if Medicare pays the full cost, that it "is sending a signal" to drug makers that the price tag is not a problem, and they might even be able to ask for more for the next treatment.

"[Regulators and legislators] are concerned about how many patients are going to get this," Miller said. "They're afraid of a tsunami. And then, this is all happening at the same time that everyone in Washington [DC] is talking about the price of drugs."

She echoed Sweetenham and Maude's comments that everyone is still waiting to see how effective the treatments will be in the long term. In addition, a greater concern is that there are other CAR T-cell therapies in the pipeline, which will only add to the costs.

"Medicare doesn't change on a dime," she said. "It takes them a long time to change their policy. They have mechanisms for payment that have been in place for a long time that they are reluctant to change."

The pace of innovation has been, perhaps, too fast. It has outpaced changes in payment, but also, "in some ways, we're ahead of the evidence," Sweetenham said.

"We don't want to end up in a situation where patients are potentially missing out on effective treatment because it's taking us too long to get the evidence that we really need," he added.

Putting together clinical trials is complicated and expensive, and researchers need a solid partnership with all the stakeholders in terms of getting needed clinical trials moving, Sweetenham said.

Regulators and legislators "are concerned about how many patients are going to get this. They're afraid of a tsunami. And then, this is all happening that everyone in Washington is talking about the price of drugs."

—Erika Miller, JD,
senior vice president and counsel, CRD Associates

Maude added that when trials are set up, they need to be optimized so researchers can identify which patients will benefit the most from CAR T-cell therapies and, thus, improve the current outcomes. There is additional cost in setting up those types of trials, but they will be more cost effective in the long run, she said.

Moving forward, improving patient access to these treatments is critical, Miller said. The cost of CAR T-cell therapies is so high that academic medical centers are losing out on more than $100,000 for each patient treated.[4] As a result, there are some centers that are deciding not to offer CAR T-cell therapy.

Maude and Sweetenham also highlighted the access challenges. Because so few centers offer CAR T-cell therapy, patients often have geographic barriers and must drive long distances in order to get treatment. Patients with commercial insurance tend to have less trouble getting the treatment approved than patients who receive Medicare.

Although the current administration has been reluctant to pay the full price tag for these therapies, it has shown it is very focused on promoting innovation, Miller said. "There's recognition that there's innovation here that can't be choked off," she added. The administration is listening, and there has been some progress with the increased new technology add-on payment,[5] but with an

election next year, there could be a new administration in the White House with a different perspective.

When asked to peer into the future, Miller predicted there would be a payment model for CAR T-cell or cellular therapies being tested. Next year, there might be a CAR T-cell therapy for multiple myeloma, which has a large patient base, so there will be more pressure on CMS to create a payment model.

Maude and Sweetenham are hoping to see more longer-term follow-up data and better predictions about which patients will benefit the most. Sweetenham is also anticipating that these treatments will move more into the outpatient setting and hopes to see patients getting better access to the treatments.

"Pessimistically, I haven't seen the field really move that far in 5 years," Sweetenham said. ◆

REFERENCES

1. Maude SL, Laetsch TW, Buechner J, et al. Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. *N Engl J Med.* 2018;378(5):439-448. doi:10.1056/NEJMoa1709866.
2. Grupp SA, Maude SL, Rives S, et al. Tisagenlecleucel for the treatment of pediatric and young adult patients with relapsed/refractory acute lymphoblastic leukemia: updated analysis of the ELIANA clinical trial. *Biol Blood Marrow Transplant.* 2019;25(3):S126-S127. doi: doi.org/10.1016/j.bbmt.2018.12.410.
3. Andrews M. Staggering prices slow insurers' coverage of CAR T cancer therapy. Kaiser Health News. http://www.khn.org/news/staggering-prices-slow-insurers-coverage-of-car-t-cancer-therapy/. Published July 17, 2018. Accessed January 2, 2020.
4. Manz CR, Porter DL, Bekelman JE, et al. Innovation and access at the mercy of payment policy: the future of chimeric antigen receptor therapies [published online ahead of print November 1, 2019]. *J Clin Oncol.* doi: 10.1200/JCO.19.01691.
5. Rosenberg J. CMS proposes increased reimbursement for CAR T-cell therapy; price hikes for rural hospitals. *The American Journal of Managed Care.*® http://www.ajmc.com/newsroom/cms-proposes-increased-reimbursement-for-car-tcell-therapy-price-hikes-for-rural-hospitals. Published April 24, 2019. Accessed January 2, 2020.

INNOVATION & NOVEL THERAPIES

Innovation in Care Also Means a Better Patient Experience

Laura Joszt

WHEN ONE HEARS THE TERM *innovation* in oncology care, the first thought can be keeping up with unprecedented advances in therapy. But changes to the delivery system—the use of navigators, the rise of data-driven quality measurement, the advance of decision-support tools—are equally important in bringing therapies to patients.

How do health systems keep up and turn the corner? It's not easy, according to a panel, Innovation in Oncology Care and Treatment, at Patient-Centered Oncology Care® in Philadelphia, Pennsylvania, held November 8, 2019.

"Innovations are coming at a pace that I've never seen before. And I've been doing this for 23-plus years," said event Cochair Joseph Alvarnas, MD, who moderated the panel featuring:

BO GAMBLE, director of Strategic Practice Initiatives for the Community Oncology Alliance;

JENNIFER ATKINS, vice president, Network Solutions for the Blue Cross Blue Shield Association;

SONIA TAJALLI OSKOUEI, vice president, Innovation and Solution Development, Premier Inc, of Charlotte, North Carolina; and

JUDITH BACHMAN, RN, BSN, MSN, CNAA, chief operating officer at Fox Chase Cancer Center, Philadelphia.

"It's an exciting time because there's so much happening so very fast," Gamble said. The infrastructure of oncology practice—especially reimbursement systems—has not caught up to advances in therapies and technology. On one hand, Gamble said, CMS tells oncologists that the old fee-for-service billing model is "archaic," and many doctors agree. But when it comes to finding new ways to measure the value of new technology, agreement has proven elusive, he said.

"We can't even agree on which is better: overall survival or progression-free survival," Gamble said.

Hospitals operating on slim margins must figure out how to advance the delivery system while staying at the forefront of care, said Bachman. "We want to invest in all these new technologists," but a new diagnostic tool must be balanced against deferred maintenance and "all the bread-and-butter stuff," such as replacing software systems.

"You're constantly rolling the dice and trying to measure the risk for the organization," she said. "And very few businesses run on the kinds of margins that we run on. I mean, even a good hospital today, they're lucky if they're making 6% to 8% margin. I don't think any of the companies that we have to interface with would tolerate that."

Asked for the payer's perspective, Atkins said, the Blues are focused on improving coordinating of care and improving patient experience. "Everything that we do as a payer is focused on [the] member and that member experience," she said, and fixing "what we continue to see as a fragmented system is our ultimate calling."

"I do think that we have made a lot of progress," Atkins said.

Advances in treatment such as chimeric antigen receptor (CAR) T-cell therapy initially caught payers off guard, but the Blues responded by designating facilities as CAR T-cell specialists. "I felt like the manufacturers had gotten a little bit ahead of us, but we were able to launch our Blue Distinction Centers on January 1, 2019, for CAR T therapy,[1] and we envision that as a chassis to build off of for additional therapies," she said.

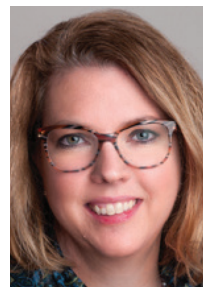
Oskouei, whose firm provides actionable data to improve delivery and pharmacy operations for health systems, said just keeping up with the tidal wave of information is a challenge. "There's a statistic that there's new evidence development every 26 seconds," she said. Converting all that information to "optimize patient care is a big challenge."

Giving providers good point-of-care clinical decision-support tools lets them offer patients the best outcomes, she said.

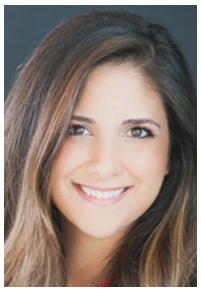
With all these challenges, Alvarnas asked, "How do you make sure that innovation stays patient centric?" And, how can health systems make the pace of change sustainable from a physician point of view?

Atkins said keeping innovation patient centric starts with asking, "What are your goals in treatment? Do you want to go to your daughter's wedding? Is this about getting to a graduation?" This shifts the definition of patient-reported outcomes to one "that I think we can certainly drive in a meaningful way." »

GAMBLE
Bo Gamble, director of Strategic Practice Initiatives, Community Oncology Alliance



ATKINS
Jennifer Atkins, vice president, Network Solutions, Blue Cross Blue Shield Association



OSKOUEI

Sonia Tajalli Oskouei, vice president, Innovation and Solution Development, Premier Inc.

BACHMAN

Judith Bachman, RN, MSN, CNAA, chief operating officer, Fox Chase Cancer Center

So, Alvarnas asked, what are the barriers to more of this happening now?

"You know, I'm going to be really transparent with you," Atkins said. Incorporating patient-recorded outcomes is not easy, because the data are less traditional and not as rigorous as registry data. As a payer, "I've had to challenge my own thinking on it."

Bachman said listening to the patient is "a huge part" of what happens at Fox Chase—via patient surveys and service gap analyses. Through this process, the staff learned that what matters most to patients is reliability.

"Imagine being in the hospital and having a schedule and actually knowing when something is going to happen to you," she said. Fox Chase built systems with navigators and better scheduling to make commitments to its patients and deliver on them "and measure our ability to do that."

Gamble said in other areas, technology makes it possible for consumers to expect greater value for what they pay, but oncology and healthcare generally haven't followed this approach. Alvarnas pointed out that the system is increasingly unsustainable—more and more responsibility is being pushed onto the physician as science rapidly evolves. Oskouei said that's where technology can play a role in clinical decision support—by updating staging criteria, new treatment guidelines, and rapidly changing product indications.

"Having that information at the fingertips is critical," she said.

But, Alvarnas said, patient education must be part of the equation, too. "At a deep level, you're talking about investment, when someone is at home using wearables or other technology to monitor them."

"We need to have specific education strategies for all the stakeholders, patient first and foremost, but also for the payers themselves, [and for] the employers are having to pay for the insurance," Gamble said." Federal rules can create barriers to innovation that make change unaffordable.

"It's going to take a lot of teamwork and bringing up bright minds to say, 'Lead the charge.' Let's not be afraid of it. Let's tackle it," he said.

But how? Bachman said information technology investments will be essential. Physicians must be surrounded by teams. Navigators work. Alvarnas said much of this change must be captured in coding, so that payers will reimburse. Atkins highlighted a Blue Cross Blue Shield of Minnesota program that is trying to do this.

And then, Alvarnas asked, how will we know change is working?

"So, we focus on measurement, measurement, measurement measurement, and we are not measured developers, you know, we rely on our colleagues across the industry," Atkins said, referring to groups such as the National Comprehensive Cancer Network. Transparency is paramount, which includes using data sources everyone can see. Gamble raised the issue of measuring survival, and there was a discussion of using "workarounds" to get past the limits of claims data.

As the discussion concluded, Lalan Wilfong, MD, of Texas Oncology said, "One of the issues that I struggle with a lot is, just because something's new doesn't make it novel or innovative. There's a lot of things coming out that really don't move the bar in patient care," he said. Immunotherapy works well in certain disease types, but makes no difference in others.

"As leaders in this space, how do you distinguish between innovation that's real and impactful for patient care versus something that's just new?" he asked.

Gamble offered his thoughts. "Insert guidelines for any new pharmaceutical drug, so that you've got some sort of requirement says, this is how I'm meeting a universal mission for quality and value," he said. "Then, I have standard metrics for all innovations. So that we could look at in a way that says yes, this is really improving the life of the patient." ◆

Technology Remains a Small Part of Innovating Cancer Care Delivery

Laura Joszt

CONTRARY TO POPULAR BELIEF, innovation in healthcare does not necessarily refer to technology, although technology can assist. Innovation is about improving experiences, explained Rebecca Kaul, MBA, vice president and chief innovation officer at The University of Texas MD Anderson Cancer Center.

The greatest new technology is not actually about the technical specs, she said. When Apple released the first iPod, the interest it generated, and its ultimate success, was not necessarily about the technical details, but instead that the iPod was something small and convenient that delivered an experience people wanted.

"For me, success is not completion of a project plan," Kaul said. "Success is delivery of value, delivery of experience." If new inventions cannot be converted into something people can use to change their lives, "have you really driven change? Have you really innovated?" she asked.

When comparing the healthcare sector to the consumer environment, the industry falls short, she said.

"I would say that our experience in healthcare is, at most, functional, not necessarily desirable," Kaul said, and as a result, the industry is seeing big companies, like Apple and Amazon, trying to enter the industry to disrupt it. However, these companies are not necessarily bringing novel technology, they are trying to innovate how healthcare is delivered to bring an experience people need and want.

Delivering better care and a better experience means going beyond metrics and truly understanding the person you are delivering care to. There is a lot of buzz about data in healthcare and how to aggregate it, create interoperability, and utilize artificial intelligence to make meaning of the data. "We have to be careful with data," Kaul said, "because correlation doesn't necessarily mean causality."

For instance, she provided the example that the divorce rate in Alabama correlates with per capita consumption of high fructose corn syrup. However, that doesn't mean divorce rates in Alabama are caused by consumption of high fructose corn syrup.

So, data are important, but it's also important to know what to do with the data and how to dig deeper and understand what the data are saying.

"You look for those themes and patterns in data," Kaul said. "You make creative leaps and inferences you can test. But then, the most important part is using qualitative design research to verify [or] debunk. And that's really the point here: You can't just take what you're seeing in the data at face value."

As someone who has worked in the field of innovation for a decade, Kaul has learned that 99% of efforts should be spent finding solutions to human problems and only 1% on solutions to technology problems. She ran a technology development center, where the employees built the technology they thought would be most valuable, but it's crucial to first understand the problem being solved and the experience that should be delivered.

Kaul provided the example of an employee at MD Anderson who showed her a 30-day predictive algorithm that had been developed, but the person who created it had never thought about how the doctor would use it in practice. What should the doctor do after receiving the prediction? What intervention should there be?

"So, the question becomes: How useful is a prediction if we don't know how we're going to action it—if we're not actually going to translate that prediction into something that actually impacts our patients impacts our experience?" she asked.

In another example, Kaul explained the challenge of ill-defined problems. At MD Anderson, she was told early on that there needed to be more chairs in the infusion center. This didn't seem like a problem in her area, but she decided to take a look and found that during the course of a day, there was never a time when a chair was not available, but there was still a waiting room full of people.

She then dug deeper to understand why people weren't getting past the waiting room faster and found a myriad of issues including orders weren't signed, labs weren't ready, drugs weren't mixed, and even nurses weren't available.

The underlying problem was how to make an appointment meaningful and optimize patient flow. This was an instance when technology was useful, because the cancer center was able to utilize machine learning to understand the best time to make an appointment because everything that had to happen to meet that commitment could actually be done in time.

However, there were times when technology was not the answer. MD Anderson has been expanding its footprint with new buildings in the community, so people have a convenient place to receive care closer to home. The people in operations and technology wanted to make these new buildings more efficient so that patients could check in at a kiosk, get a wristband, and do everything else they need to do, such as pay the bill, at the computer.

Next, they took the time to understand the experience this setup would deliver. Patients would be greeted with a computer screen and as a medical record number. So, then the employees in operations and technology went to talk to the patients.

"What patients wanted was a human experience," Kaul said. "They're scared. They just got diagnosed with cancer."

Usually, patients are coming in for multiple procedures, such as examinations, imaging, labs, and potentially chemotherapy.

"They're usually coming in for appointment after appointment, having to address something that is really scary, and what they want is someone to greet them, someone to give them the feeling that it's going to be okay, and that they are being taken care of now," she explained.

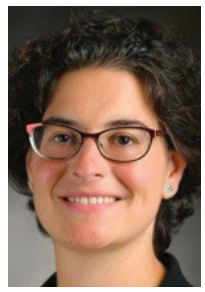
Yes, patients want efficiency, but they want a human experience, too. This finding resulted in designing a better experience even before the patient arrives at the center by reviewing schedules, providing directions to get around the facility, and filling out paperwork before they arrive.

MD Anderson also created a new role for someone to greet patients as they arrived. Instead of sitting behind the desk, this staff member would be out on the floor, wearing an identifiable shirt, available to help answer questions and make patients feel comfortable when they arrived.

And in the end, they did incorporate technology in the form of biometrics to gather patient information and maintain patient records. However, "technology ends up being that last mile," Kaul said.

Technology alone isn't the solution, she said. Everything that goes around technology makes up the solution to a problem.

"We can't just follow shiny objects," Kaul added. "We can't implement technology for technology's sake; we have to understand the problem space." ◆



KAUL

Rebecca Kaul, MBA, vice president, chief innovation officer, The University of Texas MD Anderson Cancer Center

Personalized Medicine Brings Diagnostics to the Value Equation

Mary Caffrey

LOY

Bryan Loy, MD, MBA, physician lead for Oncology, Laboratory, and Personalized Medicine, Humana

ABRAHAMS

Edward Abrahams, PhD, president, Personalized Medicine Coalition

ALMAS

James Almas, MD, vice president and national medical director, Clinical Effectiveness Labcorp

CAN ONCOLOGY CARE follow pathways—ensuring patients receive evidence-based care—and at the same time meet individual needs? That was the question for the panel, "Personalized Medicine and Value-Based Care," at Patient-Centered Oncology Care®. Moderator and co-chairman Joseph Alvarnas, MD, led the discussion with:

BRYAN LOY, MD, MBA, physician lead for Oncology, Laboratory, and Personalized Medicine at Humana;

EDWARD ABRAHAMS, PHD, president of the Personalized Medicine Coalition, which represents more than 200 innovators, scientists, providers, and payers; and

JAMES ALMAS, MD, vice president and national medical director of Clinical Effectiveness, LabCorp.

Loy said that as a pathologist, one view of the term "personalized medicine" is targeting therapies to the right patient based on abnormalities. But it is more than that, he continued. "At least at my payer, it's what can we learn about our members—or your patients if you're a doctor—and how can we create a better experience?"

But Loy said using diagnostics to select the best therapy will not help if patients go home to an empty refrigerator or have no transportation for follow-up care. Thus, the broader meaning of personalized medicine is to identify the "highest-quality, least toxic, most effective, and convenient care for our members."

Abrahams agreed, adding that personalized medicine means "marrying diagnostics and learning everything we can about the patient in order to prescribe the right therapies," while accounting for patient values and experiences. This makes the term different from precision medicine, which he said is preferred by scientists.

Almas said his view of the term is informed by his experience working on the joint CMS and FDA parallel review[1] for Foundation Medicine's CDx product, which was later reopened for a National Coverage Determination.[2] From there, Almas served as a medical director for the Molecular Diagnostics Services (MolDX) Program at Palmetto GBA, the Medicare administrative contractor that developed early expertise in approving diagnostics. Based on these experiences, he still sees some barriers. In clinical trials, Almas said, "we still run into resistance with some commercial barriers—not so much with Medicare."

Reimbursement has often been the rub, Alvarnas said. Value-based care is supposed to be about arriving at care that is high quality and sustainable, not a race to low-cost care. How can that be achieved, he asked.

At times, Loy said, "value-based care overemphasizes the dollars when, in fact, this should be about the patient's values, which in my mind leads into shared decision making and real-world evidence."

Abrahams agreed, saying, "Value-based care, in my estimation, is not the least expensive, it's the most effective."

Both Alvarnas and Almas commented that it is not always that simple, and Almas noted that is why the development of real-world evidence is important. Testing companies are often asked if they have a randomized clinical trial to prove the clinical utility of their products, but designing such trials is difficult. Partnering with payers to develop evidence is more sensible, he said.

Designing the right data models is also challenging, Alvarnas pointed out. The numbers must be large enough to ensure that researchers "get it right," but turnaround is important, too. Still, the field has moved a long way from registry studies that did not provide answers for 5 to 10 years. "The rate of innovation is outpacing our old models of gathering data," Alvarnas said.

Key considerations, according to the panelists, include:

- the quality of the test or diagnostic being used;
- addressing knowledge gaps that lead to physicians not ordering the right tests;
- dealing with situations when the test is ordered, but the results are ignored, so the patient gets no benefit; and
- ensuring that reimbursement discussions address not only tests for genomic alterations but also screening, such as increasing the population tested.

Alvarnas said all these problems call for changes in physician behavior. "This is a real challenge, and it doesn't happen infrequently," he said. "How do you keep this from happening?"

Loy noted that current reimbursement models also do not reward physicians for the most important test of all: does the patient want a $300,000 treatment, or a drug that costs $10,000 a month? "I don't think we can afford to run the test without first asking the question, 'Do you want to be treated?'"

Payment models must be flexible, he said, because not all practices are at the same point in transitioning from fee-for-service to value-based care.

Alvarnas asked whether commercial payers or Medicare are more likely to drive change, and Loy credited the Center for Medicare and Medicaid Innovation for "cracking the ice" with the Oncology Care Model. There are "refinements" that commercial payers can offer, especially making sure the voice of the employer is heard.

"Employers are in a unique position to experiment creatively around the next steps," said Alvarnas, whose portfolio includes employer strategy at City of Hope, where he is a hematologist/oncologist.

Rewarding physicians for taking time to understand what patients want is essential, Almas said. "You're going to want to talk to patients to truly have shared decision making about whether they want to pursue targeted treatment," he said. If patients don't want to do the test, "we don't want to do a test," because it is wasteful when the results are not used.

"That doesn't help anybody," Almas said. ◆

REFERENCES

1. Ramamurthy L, Maxwell K, Sawchyn B, Anhorn R. Perspective: FDA/CMS parallel review advances coverage for cancer comprehensive genomic profiling. *Am J Manag Care* 2018; 24(SP6):SP193-SP196.
2. Inserro A, Caffrey M. CMS agrees to cover NGS for Medicare patients with breast, ovarian, other cancers. *The American Journal of Managed Care®* website. ajmc.com/newsroom/cms-agrees-to-cover-ngs-for-medicare-patients-with-breast-ovarian-other-cancers. Published January 27, 2020. Accessed February 4, 2020.

Money, Mandate Are Keys to FDA's Drive for Use of Real-World Evidence, Gottlieb Says

Mary Caffrey

USE OF REAL-WORLD EVIDENCE in the drug approval process will accelerate rapidly, former FDA Commissioner Scott Gottlieb, MD, told attendees at Patient-Centered Oncology Care®, because Congress has given the agency both the money and a mandate to make this happen.

Real-world evidence, which can include data from electronic health records or claims, allows regulators to "fill in the blanks," which Gottlieb said can eliminate the need for strict randomization when evaluating treatments for rare conditions or other unmet medical needs.

Gottlieb stepped down from the FDA in April 2019, capped after 2 whirlwind years that brought a record pace of approvals and policy actions covering everything from high drug prices to teen vaping. The policy agenda was still on his radar in November as he took the podium in Philadelphia, Pennsylvania, where he addressed the annual gathering of oncology reimbursement stakeholders held by *The American Journal of Managed Care®*.

He began his talk by sharing that he was in the midst of a Twitter spat with a Trump administration official who thought he'd wasted his time on tobacco regulation. "I just got a text from someone pretty senior asking me to calm down," he said, causing the room to erupt in laughter. Then it was down to business.

As FDA commissioner, Gottlieb advanced the use of real-world evidence with the December 2018 framework document that spelled out how the agency would comply with Congress' directive under the 21st Century Cures Act.[1] The $50 million that Congress authorized the FDA to spend on a database of at least 10 million lives means that regulators will have to demonstrate how they are making use of that investment.[2]

"Why this is really an inflection point," Gottlieb said, "is now the agency has an obligation to figure out how to use practical data to answer regulatory questions."

The FDA now has money and direction from Congress, he said, "So it has to do it."

Real-world evidence is not a complete unknown at the FDA. Gottlieb said that some later indications for imatinib (Gleevec) were based on what today would be called *real-world evidence*. The difference now, he said, is that when a sponsor comes in with an application that makes use of electronic health records or claims data, regulators will be tasked with coming up with ways to incorporate that evidence in their decision-making process.

"You're going to be pushing on an open door," Gottlieb said. "That really, in my view, changes the equation."

Science Leads the Way

Gottlieb, who has returned to the American Enterprise Institute, is credited with creating a productive atmosphere at the FDA that led to 59 approvals of novel drugs and biologics through the Center for Drug Evaluation and Research during 2018.[3] The previous all-time high was 53 in 1996; the division's 10-year average had been 33 approvals.

"Leadership can have an impact at the margins," the former commissioner said, but in an indirect way. The jump in approvals, he said, "was not just because we were making policy changes or because the culture had changed," but because Gottlieb said he took steps to "insulate" the regulatory staff from politics so they could focus on their work. "I testified 19 times on Capitol Hill," he said, more than anyone "not facing indictment or under investigation."

"By and large, what was influencing the review cycle was the nature of the science," he said. Sponsors were coming in more prepared, with a better grasp of the populations that would benefit from new therapies. The agency was willing to embrace new trial methods like basket trials and the first tissue-agnostic approval (pembrolizumab for patients with unresectable or metastatic, microsatellite instability–high or mismatch repair–deficient solid tumors).[4]

Most of all, Gottlieb said, early in clinical trial development, in small sets of patients, "We're seeing outsize responses." For regulators, that meant there were compelling reasons to give patients access to these therapies quickly.

More Advances to Come

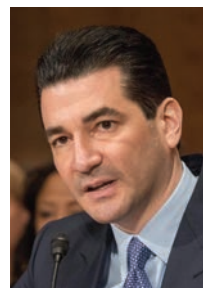
Gottlieb pointed to a pair of changes that he believes will yield important dividends in the years ahead. The first is a decision to include rules for digital health tools that can aid adherence in promotional labeling instead of product labeling, so they do not slow down innovation.[5] Sponsors have not exploited this so far, but it's still early, he said.

Second, Gottlieb sees much to gain from the movement toward "structured review," which he said would bring more predictability in the approval process through a 52-member Office of Drug Evaluation Science, which will (1) create a platform for filing applications so time is not wasted reformatting submissions and (2) bring more uniformity to the process across divisions and reviewers.

"Right now, if you go from division to division, the nature of how they review is very different; it's very different from person to person in a lot of ways," he said.

Gottlieb said when it comes to incorporating real-world evidence, he knows that some might ask, "What's taking so long?"

"Actually," he said, "It's moving pretty quickly relative to historical precedent." ◆



GOTTLIEB

Scott Gottlieb, MD, is a resident fellow at the American Enterprise Institute. He served as FDA commissioner from 2017 to 2019.

REFERENCES

1. US Food and Drug Administration. Framework for FDA's real-world evidence-program. http://www.fda.gov/media/120060/download. FDA website. Published December 2018. Accessed January 1, 2020.
2. Gottlieb S. FDA budget matters: a cross-cutting data enterprise for real-world evidence. FDA website. http://www.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/fda-budget-matters-cross-cutting-data-enterprise-real-world-evidence. Published June 10, 2018. Accessed January 1, 2020.
3. Mezher M. FDA's record year: a look at 2018 new drug approvals. Regulatory Focus. https://www.raps.org/news-and-articles/news-articles/2019/1/fdas-record-year-a-look-at-2018-new-drug-approva. Published January 7, 2019. Accessed January 1, 2020.
4. FDA approves first cancer treatment for any solid tumor with a specific genetic feature [press release]. Silver Spring, MD: FDA Newsroom; May 23, 2017. http://www.fda.gov/news-events/press-announcements/fda-approves-first-cancer-treatment-any-solid-tumor-specific-genetic-feature. Accessed January 2, 2020.
5. FDA takes steps to advance new framework to promote development of digital tools than can inform the safe and effective use of prescription drugs [press release]. Silver Spring, MD: FDA Newsroom; November 19, 2018. http://www.fda.gov/news-events/fda-brief/fda-brief-fda-takes-steps-advance-new-framework-promote-development-digital-tools-can-inform-safe Accessed January 2, 2020.

Community Oncology Can Still Innovate for Less, Patton Says

Mary Caffrey

PATTON

Jeffrey Patton, MD, chief executive officer, Tennessee Oncology; co-founder, OneOncology

MOST PATIENTS WHO WANT the most advanced cancer care, such as the chance to take part in a clinical trial, can find it close to home in a community oncology practice. But experts say this type of care, which flourished throughout the 1990s, is under siege.

If nothing changes, the cost of care will rise for everyone, according to Jeffrey Patton, MD, chief executive officer of Tennessee Oncology. Payers have a crucial role in the future of community oncology, he said, because it's in their interest to help this lower-cost option thrive.

"I say this at least 5 times a week. I'm a business guy now. And in most businesses, the low-cost, high-quality provider gets rewarded. And I think the payers are starting to recognize it," Patton said. "That's us!"

Payers, he said, should reward community oncology practices by sending patients where care costs less. Academic medical centers should handle the small percentage of cases that can be handled only there. "But let's work together and recognize what you already know," Patton said. "Push patients our way."

Patton's presentation, "Innovation Is Disruptive," offered attendees at Patient-Centered Oncology Care® a history of community oncology's contributions to better care and improved survival, which picked up steam with the 1991 approval of ondansetron (Zofran) to treat nausea caused by chemotherapy. Suddenly, patients could drive to infusion appointments and go straight home. "This really revolutionized how we give chemotherapy," Patton said. "It's probably the most patient-centric thing that's happened in my career."

Innovation at the community level didn't stop there, Patton said. With each evolution of the delivery system, community practices kept pace:

- When the early 2000s brought a rise in the use of oral medication, community practices opened their own on-site pharmacies.
- To save money, in 2011 Raintree created the first national oral oncology group purchasing organization with community oncology practices.
- In 2012, Barbara McAneny, MD, a future president the American Medical Association, developed the Community Oncology Medical Home (COME HOME) pilot, which tested principles that CMS later used to create the Oncology Care Model (OCM).
- Community practices account for 85% of OCM participants.

Today, Patton is living through another wave of disruption, one brought on by the transition to value-based payment models that promote same-day appointments, aim to keep patients out of the emergency department, and seek greater patient and caregiver involvement through advanced care planning. As a founder of OneOncology, he has formed a partnership that aims to help community practices stay independent by leveraging technology and shared insights, creating the scale that practices need to gain attention from payers and pharmaceutical companies for value-based programs.

The trend toward care given closer to home led to 85% of chemotherapy being given in community practices by the late 1990s, he said. Since then, the pendulum has swung the other way, brought on by economic forces favoring larger enterprises. Government policies often gave hospitals an advantage, such as Medicaid's 340B program that allowed hospitals to buy chemotherapy drugs at discount and policies that work against community practices when they treat dual-eligible patients. Many practices could no longer compete and were bought out by hospital systems, and the result is higher costs, Patton said.

He presented data showing that physician offices now account for 54% of chemotherapy administration; meanwhile, since 2004, the percent of chemotherapy administered in 340B hospitals increased from 3% to 23.1%.

"Patient choice is not talked about enough in being patient-centric," he said. If patients were choosing the community setting, then limiting access to this delivery system fails to give them what they want, he said.

Community oncology clinics in Tennessee have delivered on changes such as offering more access to clinical trials and improving practice management. Entities such as The US Oncology Network showed that business techniques could be delivered at scale while keeping high-quality care close to patients, Patton said.

Academic centers have a different role in innovation, Patton said. He pointed in particular to the development of the National Comprehensive Cancer Network guidelines. "They really were at the forefront of standardizing care," he said. As the idea for clinical pathways took shape, the University of Pittsburgh Medical Center partnered with community oncology groups to develop pathways, which became Via Oncology.

In the area of advocacy, community oncology has taken the lead, he said, with the Community Oncology Alliance (COA) was formed in a community oncology office in Memphis, Tennessee. "Today, COA is the voice of advocacy and policy for oncology," he added.

Payers and pharmacy leaders can support the lower-cost option of community oncology by entering into value-based contracts and doing more to ease the administrative burdens on practices. He pointed to data that show the number of healthcare administrators is rising far faster than the number of physicians.

"All of the increase in administration—it's just to get paid," Patton said. These are dollars that are not being spent to hire a dietitian or a social worker, he said, which would add value for patients.

OneOncology and other network affiliations in the community oncology realm are the most recent innovation to keep practices from being forced into hospital systems. Each one is different, Patton said. "Economies of scale works for everything—insurance, anything you purchase. It also frees you up to have capital to invest in other ancillary services," he said.

The network also allowed the group of practices to collectively announce plans to use biosimilars, which Patton said was important to dispel the myth that physicians profit by prescribing high-cost drugs. "It's just not true. It's been published," he said. "We have chosen publicly to choose the less expensive drug. And I think this is a narrative that we should be jumping on together."

As payers get wise to the savings in community practice, they stand to save between $16,000 and $37,000 per patient per year, based on data from UnitedHealth Group, he said. That translates to $4 billion year.

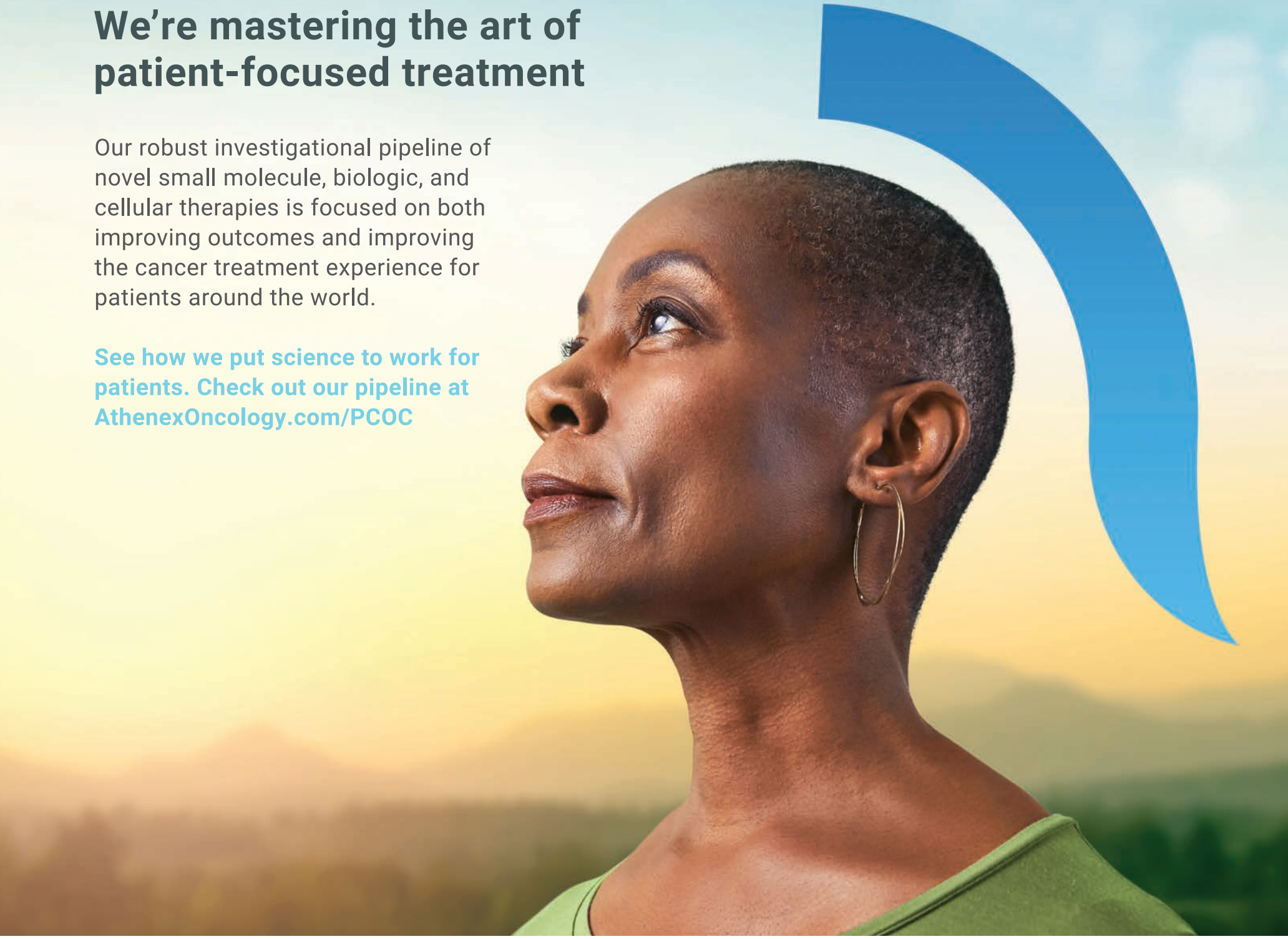
Finally, community practices are an essential resource for patients to support research, whether a clinical trial or the expanded use of real-world evidence. "The good news is, there's more opportunity coming," he said. ◆

Empowered to be bold.

We’re mastering the art of patient-focused treatment

Our robust investigational pipeline of novel small molecule, biologic, and cellular therapies is focused on both improving outcomes and improving the cancer treatment experience for patients around the world.

See how we put science to work for patients. Check out our pipeline at AthenexOncology.com/PCOC



AthenexOncology.com/PCOC **Follow us @AthenexOncology**

Athēnex oncology

The Patient's Voice Matters, but What's the Best Way to Measure It?

Mary Caffrey

EDGE
Stephen B. Edge, MD, FACS, FASCO, vice president and professor, Roswell Park Cancer Institute

PITZEN
Collette Pitzen, RN, BSN, CPHQ, clinical measure developer, Minnesota Community Measurement

PATEL
Amila Patel, PharmD, BCOP, director, Clinical Product & Content, Oncology, Flatiron Health

GOSSE
Nate Gosse, PhD, vice president, Product Management, McKesson

HOW WELL PATIENTS SAY they are faring, both during and after cancer treatment, is more important than ever to payers. But measuring that feedback isn't easy, and ensuring that measurement is fair to both patients and providers is harder still.

Kashyap Patel, MD, cochair of Patient-Centered Oncology Care®, led the discussion, "Patient-Reported Outcomes and Quality Metrics" just days after the Center for Medicare and Medicaid Innovation (CMMI) presented its outline for the successor to the Oncology Care Model (OCM), called Oncology Care First (OCF). A distinguishing feature of OCF is its call for the use of electronic patient-reported outcomes (ePROs),[1] something that Kashyap Patel says makes sense in theory but could be hard to implement with patients who are poor or live in rural areas.

"Half of my patients still don't have a smartphone—they use a flip phone," he said. Giving patients a preloaded iPad to answer questions about symptoms may not solve the problem, because internet service may be spotty where patients live, or patients may not be able to afford service.

"So, how do we circumvent those issues?" he asked.

The following panel members joined Kashyap Patel for the discussion:

STEPHEN B. EDGE, MD, FACS, FASCO, the vice president for Healthcare Outcomes Policy and professor of oncology at the Roswell Park Cancer Institute;

COLLETTE PITZEN, RN, BSN, CPHQ, a clinical measure developer at Minnesota Community Measurement;

AMILA PATEL, PHARMD, BCOP, the director of Clinical Product & Content, Clinical Oncology at Flatiron Health; and

NATE GOSSE, PHD, vice president of Product Management at McKesson.

Edge said the point of data collection and quality measures should not be to yield results that compare physicians for comparison's sake. "Unfortunately, I still see too many people saying we need to find quality measures that differentiate one doctor from another doctor to say that, "They're a good doctor. They're a bad doctor.' "

Measurement, Edge said, should be used to highlight problems and swiftly turn around data to implement change quickly. A system that spots the fact that a doctor hasn't started a patient on chemotherapy, for example, helps both the doctor and the patient.

He and Amila Patel agreed that ePROs are valuable to this process. Amila Patel said for data collection to yield meaningful results, the process must be integrated into the workflow. "You really need to build tools that work for patients and providers and reduce the burden."

Edge said when he was developing early quality measures for the Commission on Cancer, he learned the importance of asking patients what *they* find valuable.

Gosse said when it comes to incorporating ePROs into McKesson's system, which supports 20,000 oncology providers, these measures are "1 slice of how we're bringing the broader patient voice to the care discussions and into care operations." He agreed with the need to integrate the process into the physician's workflow.

So, how are measures developed that represent meaningful results for people with cancer? Pitzen outlined a process that led to a measure in the National Cancer Information System (NCIS) for the severity of nausea on particular days of a chemotherapy cycle. It began with convening a stakeholder group, and it followed what Pitzen called "guiding principles," which include:

- ensuring that measures are appropriate for PROs—measures in cancer will be different than those in other conditions, such as diabetes;
- using strong "psychometric properties," so that measures are valid; and
- ensuring that outcomes can be quantified.

Ideally, measures are in the public domain, Pitzen said. "We don't want to tamper with the validity and reliability of the tool," she said. Many national measures now in use started this way.

Kashyap Patel asked the panelists to discuss how to strike the right balance between gathering enough information without overwhelming patients with questions—and how to find methods that make sense and will not overwhelm clinical staff. He brought the group back to his flip phone example.

"We want to make sure that we're building technology to account for all of those situations," said Amila Patel. "We can't just build tools for people that are literate and have access. . . . We need to build tools for patients from different socioeconomic backgrounds that take literacy into account, different language barriers."

Mobile phones and apps are not for everyone, she said. Having more than 1 method, whether it's using tablets in the clinic, or giving caregivers different options to log into a computer—and training them on how to do this—are all ways to boost adoption.

"First, I think we need to keep the tools simple," Edge said. Tools that *help* patients and doctors, as much as assessing them, will be used and will make a difference, he said. Reducing barriers, including financial ones, is essential.

"There is evidence that we would save money by providing people with the smartphone, by providing them with the iPad," he said, citing studies in chronic disease management.

Kashyap Patel said that as CMMI develops the OCF, these costs could be factored into an alternative payment model. He then asked Gosse what kinds of challenges these ideas would present to McKesson if ePROs had to be incorporated quickly.

Gosse said ePRO implementation creates 2 distinct customers: the patients and the providers. Even if patients have a smartphone, will they want to fill out a survey every time they get a text message? Patients may ask, "Is it worth my time? What am I going to get from it?"

From the provider standpoint, it's only worthwhile to set up the patient to send in ePROs if its feeding into a dashboard that someone sees and can act upon quickly. "We've got to get those 2 teams really empowered, as seeing value on both sides, before we can really start to bring value to our payers or to our pharma partners," he said.

"We're very interested in getting beyond the patient-reported outcomes, and [we're] rapidly looking at where the market is going, into patient-originated data," Gosse said.

Workflow issues are critical, because apps can create enrollment issues, and it's difficult to add another process to the clinic setting—there can't be a new enrollment for every new drug. "There's lots of opportunity," he said, "We're working to get things past the real active, manual effort it takes to be successful today."

Kashyap Patel said usefulness of these data still comes down to what's being measured, and he asked Pitzen if measures will account for the socioeconomic differences such as those he sees in his practice, which is located in South Carolina.

Pitzen said the NCIS tool measures 3 symptoms—nausea, pain, and constipation—which are symptoms "that regardless of where you are on your cancer journey, those symptoms need to be addressed in pretty rapid fashion so that chemotherapy can continue."

The NCIS tool is free and practices can add additional symptoms to track, but she would not recommend tracking every symptom for every patient. An academic medical center using the tool is experimenting with using different collection methods, including paper. One concept is installing patient portals in the clinic, so that patients can log in their symptoms when they arrive at an appointment.

Edge said this method would save time for providers. Methods that provide information before the appointment starts save time, but this can also include better nursing assessments.

Kashyap Patel said making changes to add ePROs will require up-front investment, but that this could lead to long-term savings. When his practice adjusted its scheduling and operations to free up 2 slots for same-day appointments—to meet requirements of the OCM—it seemed like a money-loser. But the reduction in emergency department visits and hospital stays has made the change a winner. He said the question is, what kind of electronic collection device will make ePROs worth the investment in 5 years?

Wearable devices are 1 solution, Amila Patel said. They don't require surveys—and the information comes straight to the provider. Many parameters must be worked out, she noted.

"I think we're going to have to make them part of our daily life," Edge said of PROs. To some extent, PROs are already here, but clinics have not always put them to use.

Investments can be worth it, Gosse said. Oncology networks already working with McKesson to incorporate new tools have seen the efficiencies that result, as well as patient satisfaction. "The effort of getting the new mindset in place, the new staffing in place—you're changing the phone trees and how the people are answering the phones; you're empowering nurses or care teams in new ways. And that's a significant transformation—that's more than technology. . . . It's really rewiring the practice in some ways."

Ultimately, Pitzen said, "You can't improve something if you're not measuring it."

She agreed with Edge that the best approach to metrics is not punitive but rather a method that measures symptoms so patients can continue chemotherapy and have a better experience. "It's what is actually best for patients," she said. ◆

REFERENCE

1. Caffrey M. CMS, CMMI seek feedback on Oncology Care First, successor to OCM. *The American Journal of Managed Care*® website. ajmc.com/newsroom/cms-cmmi-seek-feedback-on-oncology-care-first-successor-to-ocm. Published November 3, 2019. Accessed February 9, 2020.

Learning From the Oncology Care Model to Move APMs Forward

Mary Caffrey

When **LALAN WILFONG, MD**, was approached with the offer, "Hey, want to do some quality work?" His reply was, "Oh, that sounds like fun."

A few chuckles filtered through the room as Wilfong shared this story during "Future of Oncology Advanced Alternative Payment Models," in the afternoon session of Patient-Centered Oncology Care®. But Wilfong, who now serves as executive vice president for Value-based Care and Quality Programs at Texas Oncology, said his motivation for taking on "quality work," or helping a 490-physician practice transition to alternate payment models (APMs), was a long time coming.

"One of the things I struggled with from the time I started medicine in private practice was the fee-for-service [FFS] model. I always felt it was wrong," said Wilfong, who believed the premise of "turning patients through to get paid" was counter to his objective of giving all patients the level of care they needed.

The idea that doctors should be rewarded based on how patients respond to treatment and the quality of their experience, all at a reasonable cost, is behind the goal of moving to an APM. But progressing from FFS to APMs in a way that's fair for doctors and patients has been easier said than done, panelists shared during the session, led by meeting cochair **KASHYAP PATEL, MD**. In addition to Wilfong and Patel, the panelists were:

STEVEN D'AMATO, RPH, BS PHARM, BCOP, executive director and clinical pharmacy specialist at New England Cancer Specialists, based in Maine;

JEFFREY ODELL, director of Provider Collaboration Programs at Anthem; and

RANI KHETARPAL, MBA, vice president, Oncology Value-Based Partnerships at New Century Health.

The bottom line from all the panelists? Implementing APMs in oncology is a complicated process. The models are not perfect, especially the Centers for Medicare and Medicaid Services' Oncology Care Model (OCM), although several panelists saw improvements in the proposed successor model, Oncology Care First (OCF).

"There's a lot to learn and a lot to implement along the way," D'Amato said. OCM has been a "great first step" in redefining how practices think about care delivery. "There have been massive »

WILFONG

Lalan Wilfong, MD, executive vice president, Value-Based Care and Quality Programs, Texas Oncology

D'AMATO

Steven D'Amato, RPh, BSPharm, BCOP, executive director, clinical pharmacy specialist, New England Cancer Specialists

PATEL

Moderator and Co-Chair Kashyap Patel, MD, CEO, Carolina Blood and Cancer Care Associates

KHETARPAL

Rani Khetarpal, MBA, vice president, Oncology Value-Based Partnerships, New Century Health

ODELL

Jeffrey Odell, director, Provider Collaboration Programs, Anthem

changes that have occurred due to the OCM. But I do believe that OCM is a flawed model."

Others agreed with D'Amato that the "elephant in the room is the drugs." For all the positive changes made in promoting care coordination, care planning, palliative care, and quality measurement, the model suffers greatly from the "data lag," both for tracking drug prices so practices can be paid correctly, and for letting practices know how they are doing so they can make changes.

"We have to figure out a way to keep oncology providers whole and in order, to support the services that we provide and enhance the services," Wilfong said.

Odell pointed out that the OCM is not the only APM in cancer care; he directs Anthem's oncology medical home model, and the payer is looking at the OCF. He's also considering bundled payments and the successes in primary care with the patient-centered medical home for improvements.

Khetarpal said her company, New Century Health, is known for aligning with payers, and her role is to lead the alignment with providers as well.

"There is a tremendous opportunity for providers to be in the driver's seat as current APM models are being developed," she said. Over the next 1 to 3 years, it will be critical for these groups to work together on payment model reform instead of allowing models to develop in "silos."

Patel asked D'Amato what he would recommend to the Center for Medicare and Medicaid Innovation (CMMI) to avoid the phenomenon of practices being "punished" for having too many patients with certain high-cost cancers. D'Amato agreed that this must addressed, and that having all the data the OCM has produced shows "there's no getting around the drug costs."

"When you look at the total cost of care today [in] our particular geographic area, [the drug cost] approaches 70% of the total cost of care. That's a huge amount of money," D'Amato said. Practices that were already efficient were getting measured against themselves.

"I knew we were dead coming out the gate," he said. CMMI must create a model that works to "level the playing field."

Besides dealing with compensation for drug costs, panelists said oncology APMs, and the successor to OCM in particular, must do more to address patient attribution and transparency. Wilfong said it appears that CMMI has "listened to us" in revising the OCF to address low-risk patients—patients who are seen infrequently, for whom practices should not assume the risk. Instead, he believes the risk should stay with the primary care practice.

But the future of APMs will come down to having an appropriate system for how practices are evaluated for spending on drugs. D'Amato and Wilfong agreed that biosimilars have a role to play; however, practices should not be forced to carry 4 or 5 options of a reference product to accommodate various payers. If practices assume the risk, then let them decide, they said. If immunotherapy is needed for a patient with lung cancer, physicians should prescribe it without worrying that the pricing doesn't fit the model.

"That's the thing we have to figure out: How do we hold physicians accountable for drug [costs] when [we] need to be held accountable, but not hold us accountable when it truly is time for us to do novel therapies?" Wilfong asked.

"When, at the end of the day, the physician's responsibility is to their patients, to provide them with the best care that they can based on the patient's goals and values in a setting of shared decision-making, that's my job," he said. "My job isn't to withhold care from a patient who may benefit from care." ◆

COLLABORATION IN NETWORKS

Through Networks, Collaboration Keeps Oncology Care in the Community

Mary Caffrey

HOW CAN COMMUNITY ONCOLOGY practices keep up with changing federal regulations and the constant flow of new scientific evidence, while delivering quality care in the era of payment reform?

The answer, said panelists during the final session of Patient-Centered Oncology Care®, is to stay independent by working together. "Oncology Networks: Collaboration for Value-Based Care," moderated by cochairman Kashyap B. Patel, MD, examined the growing role of practice networks in community oncology. The panel featured the following participants:

SIBEL BLAU, MD, medical oncologist at Northwest Medical Specialties PLLC, and president and chief executive officer, Quality Cancer Care Alliance (QCCA)

TERRILL JORDAN, JD, LLM, president and chief executive officer, Regional Cancer Care Associates

BRAD PRECHTL, MBA, chief executive officer, Florida Cancer Specialists (FCS) and American Oncology Network (AON)

ERICH MOUNCE, MSHA, chief operating officer at OneOncology.

Blau noted that practice networks can take different forms; QCCA, in fact, began as an alliance before members voted in February 2018 to become a clinically integrated network. Some collaboration models use a single tax identification number; others have turned to private equity for investment in technology and infrastructure to fuel their transformation.

The bottom line, Blau said, is that collaboration helps practices stay independent while bringing certain infrastructure needs to scale. "The health-care system is changing. Value-based care is coming to our door, and we need to figure this all out," she said.

Jordan, of RCCA, which operates in New Jersey, Connecticut, and Maryland, said he takes a broader view of collaboration. "For value-based care, it means you actually include all the partners you work with," he said. That would include payers, hospitals, and primary-care providers. Conversations with payers are much less hostile than they were 7 to 8 years ago.

"I think those deep community relationships, and the care we bring to those communities, is what will distinguish us," he continued. "We think that's how we're going to grow."

"Creating scale allows the culture to stay at the physician-practice level, which is a fundamental principle with OneOncology. The issue is driving scale of economy and scale of intelligence across that platform."

—Eric Mounce, MSHA,
Chief Operating Office, OneOncology

A distinguishing feature of community oncology networks is their ability to operate across state lines while allowing practices to retain their local flavor. Community oncology networks operate with the practices front and center, which creates a different dynamic from a hospital buying out a practice. Prechtl, who is bringing the FCS model to 8 other states through AON, said there is often "pushback" when trying to collaborate with health systems, who are looking out for their own interests.

Mounce, who has been with the OneOncology network for a little over a year, said the arrival of new payment models, such as the Oncology Care Model (OCM), the Merit-based Incentive Payment System (MIPS), and models offered by commercial payers, makes collaborative networks essential for community oncology to survive and thrive. "Creating scale allows the culture to stay at the physician-practice level, which is a fundamental principle with OneOncology," he said. "The issue is driving scale of economy and scale of intelligence across that platform," while allowing for the nuances of individual practices and states.

Depending on the model, networks can work with practices at different stages of the transition to two-sided risk. "There are some states that don't even know what value-based care means," said Mounce. "And then there are states that are very sophisticated … That's why you let cultures survive across state lines."

Patel asked Prechtl to discuss the challenges of moving into a new market that is unaccustomed to value-based care.

"It's going to take time to build size and scale within that state," Prechtl said. Health systems may even refuse to sign leases with practices in their medical office buildings. "They immediately assume that there's going to be some radical pulling out of services from the health system, instead of looking for the opportunity to keep those physicians community-based, keeping patients local, and growing the market share. But that's what we're experiencing when we go out of state."

Patel also asked what lessons had been gained from the OCM experience. Small practices, Prechtl responded, have a difficult time with shared savings contracts in the OCM, which is why they look to organizations like AON to help manage the transition. Florida Cancer Specialists will move to two-sided risk in 2020.

"We've done very well under the OCM," Prechtl said. "But, you know, there [were] a lot of good arguments where the OCM isn't perfect. A lot of these practices definitely can use the sophistication of a large organization to help them."

Jordan explained that the OCM is still a MIPS program, along with financing to make the transition. Regional Cancer Care Associates joined OCM with the idea that it would get some funds for making the shift to taking on risk and learning how to manage it. "Perhaps, a little naively, we thought we'd learn a lot more than we've learned. It's been a little harder than we thought," he said.

Groups outside the OCM that think they are avoiding the two-sided risk are not; it may just take a different form, Jordan said. "All the learning that we've gained from OCM we apply across all our programs," including the commercial value-based models. "So, overall, it's been a great experience."

Blau discussed the challenges of gaining financing for the transition to value-based care, and Mounce said the new way of delivery care brings costs such as data scientists, whom no one had hired in the past. These are costs that can be shared across a network.

Jordan sees signs that the vendors who work with oncology practices aren't interested only in large groups, they want to work with medium- and small-size practices, too. "What's happening right now is we're at the beginning of a journey, and it's a journey that can be expensive when you start. And we don't know where we're going, and there's a lot of change, so a small practice will have a hard time at the outset."

In the long run, Jordan expects that both large and small practices will take part in care transformation; although that may make things complex, it will also help share the burden. "We're going to find out that's an advantage," he said.

Technology "is the great equalizer."

Prechtl said he's amazed that payers continue to pay higher reimbursement rates for hospital care than they do for community oncology, as hospitals "gobble up" community clinics only to drive up prices. "I just don't understand how there's not more of a focus on driving patients to community-based practices," he said.

"Scale means everything," Mounce said—and Blau agreed—and that happens when companies are managing the relationship between the payer and the oncologist. "Trust me, every payer in the country is trying to lower costs."

Blau had her own thoughts on how to get there.

"My practice is one of the top-performing practices of the OCM," she said, and her group will be pursuing two-sided risk. "We're very proud of it."

But if the funding associated with the OCM goes away, things will change, and practices must find "like-minded" partners with whom they can be clinically integrated, so that they can demonstrate how they are delivering value to a large group of payers. Otherwise, Blau warned, OCM-type models are not sustainable.

"We're different in many ways," she said. "but we're all trying to do the same thing." ◆

Pharmacy Times

Payment Models for Pricey Pharmaceuticals
Read more at: **pharmacytimes.com/link/293**

BLAU
Sibel Blau, MD, Northwest Medical Specialties, PLLC; president and chief executive officer, Quality Cancer Care Alliance

JORDAN
Terrill Jordan, JD, LLM, president and chief executive officer, Regional Cancer Care Associates

PRECHTL
Brad Prechtl, MBA, chief executive officer, Florida Cancer Specialists and American Oncology Network

MOUNCE
Eric Mounce, MSHA, chief operating officer, OneOncology

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 Matthew Gavidia

NOTE: this section has been edited for clarity

John Sweetenham, MD, on Payment for CAR T-cell Therapy

Sweetenam is a professor in the Department of Internal Medicine, UT Southwestern Medical Center and Associate Director, Clinical Affairs, UTSW's Harold C. Simmons Comprehensive Cancer Center

How has reimbursement for chimeric antigen receptor (CAR) T-cell therapy been altered? Are providers more inclined to offer the therapy when compared to the past?

It depends on the insurer. I think in general, for commercial insurance [based on] what I'm hearing, our experience and the experience of many of the people I speak to, is that we're pretty well getting the treatment covered for patients who are insured commercially. With Medicare, I would say that we still confront the same problems we had before. So, the recent coverage determination has improved the situation, and we can typically recover about 80% of the cost, and that's helpful, no question. But in terms of how we move forward, it is very challenging. We know that every patient that we treat at the moment, we're at significant financial risk, especially if it is a Medicare patient. I think what we're likely to see in the coming months and years is a gradual shift of CAR-T cell therapy to the outpatient setting. Part of the reason for that is the way that it's reimbursed, because outpatient therapy is slightly more favorable–so, financially it is better. The problem is that these are very toxic treatments, and many of the patients are not going to be manageable in the outpatient setting; but I do see that a factors which is influencing a slow transition to outpatient CAR-Ts. ◆

Rani Khetarpal, MBA, on Clearing Up Doubts About Clinical Pathways

Khertarpal is vice president, Oncology Value-Based Partnerships, New Century Health

What is the biggest misconception that clinicians and practices have about clinical pathways?

That they're super restrictive and trying to control what doctors do. I think that the biggest push-back we get is that it's going to take away the ability for the physician to give the patient the treatment they want. I think that is a misconception that as we have one-to-one conversations, are able to make sure and clear up; but I think that, and rightfully so, there's always been this perspective because pathways from a New Century Health standpoint have been pushed down because of a payer contract. But now that we're moving into the provider segment and aligning ourselves with providers, the discussion is a little bit different.

So, the discussion is, you can still do for the patients what you need to, you can still prescribe the therapy that you need to, but for a good number of your patients, you should be able to stay on pathway because it's what you're doing anyway. So, once they're able to look at the pathways and they actually see what is considered, our Level I pathways, or any pathways that are kind of the primary pathway for that particular tumor type or that patient, then they're like "OK, this is actually not that bad. We can actually work with this." The devil is in the details, and the devil is in actually looking at the pathways and really understanding what the pathways are trying to do. It's not trying to restrict and take control of treating the patient from the physician; it's actually trying to enhance that for the physician and take the guesswork of how to do that out of it. ◆

Jennifer Atkins, MBA, on Defining Innovation in Cancer Care

Atkins is vice president, Network Solutions, Blue Cross Blue Shield Association

How do we define what is working and what isn't when implementing innovations in cancer care?

Cancer care, in and of itself, is not unique when we evaluate the efficacy of a program. Data is where we can drive our insights into what works and what doesn't work. One thing that we do across all Blue Cross Blue Shield companies is use third-party data sets to help us evaluate measurement in the area. This also helps us transparently communicate back with providers about what is working and what isn't working. Then, the providers can evolve their practices and innovate in a way that makes sense among the payer, the provider, and of course keeping the member at the center. ◆

Joshua Ofman, MD, MSHS, on Grail and Value-Based Care

Ofman is the chief of Corporate Strategy and External Affairs, Grail Inc.

Where does Grail fit into various payment models that have been deployed, either by CMS or commercial payers?

Right now, this is a very transformational approach to early cancer detection. More work needs to be done, and it's very early, but we know the opportunity to improve public health is enormous. So, if you're a payer or a healthcare system or a large self-insured employer, the opportunity to improve the proportion of the population that gets screened, and then to use a single blood test to detect over 20 cancers is unprecedented. For most of the systems, payers, and employers, it's an enormous opportunity to diagnose cancer earlier in their population, where cancers are more treatable, and cancers are even curable. That is one of the biggest opportunities to improve the population's health. ◆

Brief Summary of Prescribing Information for YONSA® (abiraterone acetate) tablets
This Brief Summary does not include all the information needed to use YONSA safely and effectively.
See full prescribing information for YONSA.

See package insert for full Prescribing Information
Initial U.S. approval: 2011

INDICATIONS AND USAGE:

YONSA (abiraterone acetate) is indicated in combination with methylprednisolone for the treatment of patients with metastatic castration-resistant prostate cancer.

CONTRAINDICATIONS:

YONSA is contraindicated for use in pregnant women. YONSA can cause fetal harm and potential loss of pregnancy.

DOSAGE AND ADMINISTRATION:

Recommended dose: YONSA 500 mg (four 125 mg tablets) administered orally once daily in combination with methylprednisolone 4 mg administered orally twice daily. Patients receiving YONSA should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

To avoid medication errors and overdose, be aware that YONSA tablets may have different dosing and food effects than other abiraterone acetate products.

WARNINGS AND PRECAUTIONS:

YONSA may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Monitor patients for hypertension, hypokalemia, and fluid retention at least once a month. Control hypertension and correct hypokalemia before and during treatment with YONSA.

Monitor for symptoms and signs of adrenocortical insufficiency. Increased dosage of corticosteroids may be indicated before, during and after stressful situations.

Hepatotoxicity can be severe and fatal. Measure serum transaminases (ALT and AST) and bilirubin levels prior to starting treatment with YONSA, every two weeks for the first three months of treatment and monthly thereafter.

ADVERSE REACTIONS:

The most common adverse reactions (≥10%) are fatigue, joint swelling or discomfort, edema, hot flush, diarrhea, vomiting, cough, hypertension, dyspnea, urinary tract infection and contusion.

The most common laboratory abnormalities (>20%) are anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia, elevated AST, hypophosphatemia, elevated ALT and hypokalemia.

DRUG INTERACTIONS:

CYP3A4 Inducers: Avoid concomitant strong CYP3A4 inducers during YONSA treatment. If a strong CYP3A4 inducer must be co-administered, increase the YONSA dosing frequency.

CYP2D6 Substrates: Avoid co-administration of YONSA with CYP2D6 substrates that have a narrow therapeutic index. If an alternative treatment cannot be used, exercise caution and consider a dose reduction of the concomitant CYP2D6 substrate.

USE IN SPECIFIC POPULATIONS:

Females: Women who are pregnant or women who may be pregnant should not handle YONSA tablets without protection, e.g., gloves.

Males of Reproductive Potential: Males with female partners of reproductive potential should use effective contraception.

Hepatic Impairment: Do not use YONSA in patients with baseline severe hepatic impairment (Child-Pugh Class C).

Pediatric Use: Safety and effectiveness of abiraterone acetate in pediatric patients have not been established.

To report SUSPECTED ADVERSE REACTIONS, contact Sun Pharmaceutical Industries, Inc. at 1-800-818-4555, FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Manufactured for:
Sun Pharma Global FZE

Distributed by:
Sun Pharmaceutical Industries, Inc.
Cranbury, NJ 08512

YONSA is a registered trademark of Sun Pharma Global FZE

PM-US-YON-0296

Rx ONLY

SUN PHARMA

Yonsa®
(abiraterone acetate)
125 mg tablets

MICRONIZATION MATTERS

THE ONLY ABIRATERONE ACETATE FORMULATION WITH NO FOOD RESTRICTIONS[1,2]

YONSA® DOSING AND ADMINISTRATION

Patients have the flexibility to take YONSA® with or without food, in combination with methylprednisolone.[1]

ONCE-DAILY DOSING

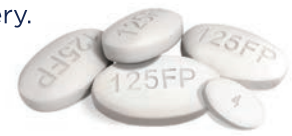
YONSA® 500 mg (four 125 mg tablets) is administered orally once daily in combination with oral methylprednisolone (4 mg twice daily).

SIMILAR BIOAVAILABILITY TO 1000 MG DOSE

One 500 mg dose of YONSA® offers similar bioavailability to the 1000 mg dose of abiraterone acetate plus corticosteroid.[3]

DOSE MODIFICATION

- For patients with baseline moderate hepatic impairment (Child-PughClass B), reduce the YONSA® starting dose to 125 mg once daily
- For patients who develop hepatotoxicity during treatment,hold YONSA® until recovery. Retreatment may be initiated at a reduced dose. YONSA® should be discontinued if patients develop evere hepatotoxicity



Tablets not to scale. The tablets should be swallowed whole with water. Do not crush or chew tablets.

INDICATION

YONSA® (abiraterone acetate) in combination with methylprednisolone is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

Important Administration Instructions

YONSA® may not be interchangeable with other abiraterone acetate products. To avoid substitution errors and overdose, be aware that YONSA® tablets may have different dosing and food effects than other abiraterone acetate products.

Patients receiving YONSA® should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

YONSA is contraindicated for use in pregnant women. YONSA® can cause fetal harm and potential loss of pregnancy.

Please see additional Important Safety Information throughout and the Brief Summary of the Prescribing Information on the following page.

SUN PHARMA

Yonsa®
(abiraterone acetate)
125 mg tablets