SPECIAL ISSUE: **PCOC® MEETING RECAP**

AJMC®
THE AMERICAN JOURNAL OF MANAGED CARE®

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RESEARCH & LEADERSHIP

# Evidence-Based ONCOLOGY™

FEBRUARY 2017
VOL. 23 • NO. 3

**5TH ANNUAL PATIENT-CENTERED ONCOLOGY CARE® 2016** | NOV 17-18, 2016 | RENAISSANCE HOTEL, BALTIMORE, MD

## HIGHLIGHTS FROM THE MEETING

- A provider, a regulator, and a diagnostics expert discuss the contradiction presented by immuno-oncology agents in the world of precision medicine, **SP103**.
- Panelists discuss how meaningful quality-of-care measures that are relevant to patients can be incorporated into alternative payment models, **SP108**.
- A discussion on patient behavior when faced with the burden of cost sharing, **S110**.
- Read how the "wedge" of health IT has revolutionized cancer care, **S112**.
- Specialty pharmacies can support critical components in a value-based care delivery model: 2 presenters explained how this can be achieved, **SP113**.


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## IN HR+ ADVANCED BREAST CANCER


G=gap phase; M=mitosis; S=synthesis phase.

**References: 1.** O'Leary B, Finn RS, Turner NC. Treating cancer with selective CDK4/6 inhibitors. *Nat Rev Clin Oncol.* 2016;13(7):417-430. **2.** Anders L, Ke N, Hydbring P, et al. A systematic screen for CDK4/6 substrates links FOXM1 phosphorylation to senescence suppression in cancer cells. *Cancer Cell.* 2011;20(5):620-634. **3.** Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. *Nature.* 2012;490(7418):61-70. **4.** Sandal T. Molecular aspects of the mammalian cell cycle and cancer. *Oncologist.* 2002;7(1):73-81.

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**Precise targeting of CDK4/6** leads to the induction of growth arrest, blocking the cell cycle before cells are irreversibly committed to replication.[1,4]

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# SPECIAL ISSUE / PCOC® MEETING RECAP

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Attendees at the 5th Annual Patient-Centered Oncology





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PCCC16

## FROM THE CHAIRMAN

# *AJMC®'s* Oncology Meeting a Melting Pot of Healthcare Experts


MIKE HENNESSY, SR

**AS 2016 DREW TO A CLOSE,** *The American Journal of Managed Care®* assembled experts from across the healthcare landscape who share the calling to improve outcomes for patients with cancer. Clinicians, drug and device developers, regulators, payers, and patients participated on panels and presented their thoughts through presentations at the 5th Annual Patient-Centered Oncology Care® Meeting.

The first day of the meeting provided an in-depth look at the challenges of developing immunotherapy products in oncology. Describing modified T cells as "living drugs," David L. Porter, MD, from the University of Pennsylvania Health System, dove deep into the latest clinical developments involving chimeric antigen receptor (CAR)-T cells in patients diagnosed with chronic lymphocytic leukemia and acute lymphoblastic leukemia. Despite some severe side effects that patients experience with CAR-T treatments, Porter is very hopeful and expects the treatment to expand to solid tumors.

During a subsequent panel, however, while answering a question on treatment costs, he acknowledged that CAR-T treatment is very expensive. He said drug manufacturers would have to provide maximal support to sustain the momentum gained by this revolutionary treatment. When asked if the FDA can create a dent in the cost discussion, Sean Khozin, MD, MPH, senior medical officer, FDA, said that the FDA is thinking about value across the entire spectrum of drug development.

Value-based care also tops the payer agenda. Keynote speaker Roy Beveridge, MD, senior vice president and chief medical officer at Humana, commented, "Whether we call it value- or risk-based care, it is coming." For Cigna, the patient is front and center—the health plan's medical home model has a huge emphasis on information sharing, mutual decision making, early palliation, and addressing emotional and physical symptoms.

However, whereas patient-centered care models ensure quality care for the patient, increased cost sharing can create a huge burden that might lead to adherence issues or force a patient to forego treatment. During a discussion on cost sharing, panelists explained that although patient assistance programs are a stopgap, patients may not always access the resources available to them.

The other challenge that Samantha Watson, MBA, founder and CEO of the Samfund, pointed out is that patients may not always be ready to bring up cost discussions when their primary concern is survival. "A lot of the legwork and decisions about value-based care need to be made behind the scenes," Watson said.

With steps taken by the new administration to dismantle the Affordable Care Act, healthcare in the United States might be in for a turbulent time. However, the priority should be to ensure that access is not disrupted.

As always, thank you for your continued support and readership.

Sincerely,
*Mike Hennessy, Sr*
CHAIRMAN AND CEO

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.

# AGENDA

## THURSDAY, NOVEMBER 17, 2016

| | |
|---|---|
| 4:00 PM | **REGISTRATION OPENS** |
| 5:00 PM - 5:10 PM | **Opening Remarks & Introduction to Poster Competition** |
| **Moderator & Chair:** Joseph Alvarnas, MD | |
| 5:10 PM - 5:40 PM | **Session 1: Immunotherapy and CAR-T Updates**<br>David L. Porter, MD |
| 5:40 PM - 6:20 PM | **Panel: Immuno-Oncology vs Precision Medicine: Where Is Cancer Care Headed?**<br>David Fabrizio; Sean Khozin, MD, MPH; David L. Porter, MD |
| 6:20 PM - 6:50 PM | **Session 2: Patient Education on Immuno-Oncology Toxicities**<br>Debra L. Madden, BA |
| 6:50 PM - 7:30 PM | **Keynote Presentation: How Value-Based Care May Affect Oncology**<br>Roy Beveridge, MD |
| 7:30 PM - 9:30 PM | **Networking Reception**<br>*Presentation at 8:00 PM*<br>Allison Morse, BA |

## FRIDAY, NOVEMBER 18, 2016

| | |
|---|---|
| 7:30 AM | **REGISTRATION OPENS & BREAKFAST** |
| **Moderator:** Bruce A. Feinberg, DO | |
| 8:00 AM - 8:30 AM | **Session 3: Value in Healthcare**<br>Nell Wood Buhlman, MBA |
| 8:30 AM - 9:10 AM | **Panel: How Patient-Centered Are Payment Models?**<br>Bhuvana Sagar, MD; Ted Okon, MBA; Stuart L. Goldberg, MD |
| 9:10 AM - 9:50 AM | **Panel: Managing Cancer Care Costs While Ensuring Adequate Outcomes and Quality of Care**<br>Kim D. Eason, MEd ; Karen E. Lewis, MS, MM, CGC; Michael Ruiz de Somocurcio, MBA; Bhuvana Sagar, MD |
| 9:50 AM - 10:05 AM | **BREAK** |
| **Moderator:** Joseph Alvarnas, MD | |
| 10:05 AM - 10:35 AM | **Session 4: Pairing the Latest Therapies With High-Touch and High-Tech Support: How Specialty Pharmacies Are Transforming Cancer Care**<br>J. Ike Nicoll; Joshua A. Rademacher, MBA |
| 10:35 AM - 11:05 AM | **Session 5: A Study of Precision Medicine in Practice to Advance Evidence, Genomic Test Development, and Coverage Policy**<br>Pam Mangat, MS |
| 11:05 AM - 11:45 AM | **Panel: Does Cost Sharing Influence Patient Adherence and Outcomes in Oncology?**<br>Jonas A. de Souza, MD, MBA; Daniel J. Klein, MHS; William H. Shrank, MD, MSHS; Samantha Watson, MBA |
| 11:45 AM - 12:30 PM | **LUNCH** |
| **Moderator:** Bruce A. Feinberg, DO | |
| 12:30 PM - 1:00 PM | **Session 6: Telehealth in Palliative Care**<br>Michael D. Fratkin, MD |
| 1:00 PM - 1:40 PM | **Panel: Surmounting Health IT Challenges in Oncology Care**<br>Suzanne Belinson, PhD, MPH; Jonathan Hirsch, MSc; Carrie Tompkins Stricker, PhD, RN, AOCN |
| 1:40 PM - 2:40 PM | **Panel: Oncology Care 2017**<br>Robert W. Carlson, MD; Scott Gottlieb; MD, Ted Okon, MBA; Kavita Patel, MD, MS |
| 2:40 PM - 3:00 PM | **Announcement of Poster Winner & Concluding Remarks** |

# FACULTY BIOS

## CHAIR & CO-MODERATOR

### Joseph Alvarnas, MD

*Director of Value-Based Analytics*
*Director of Clinical Quality, Alpha Clinic*
*Associate Professor, Department of Hematology and 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 worked at the City of Hope – Banner Transplant Program, where he helped found the program. Dr Alvarnas subsequently worked as director of the Hematopoietic Stem Cell Processing Laboratory and chair of the Quality Committee for the transplant program. He is currently an associate clinical professor in the Department of Hematology/Hematopoietic Cell Transplantation at City of Hope, where he also serves as the director of Value-Based Analytics for the institution. He is the national co-chair for 2 Bone Marrow Transplant Clinical Trials Network clinical trials studying stem cell transplantation in patients infected with HIV. Dr Alvarnas serves on the American Society of Hematology (ASH) Committee on Practice and as an ASH liaison to the Committee on Quality.

## CO-MODERATOR

### Bruce A. Feinberg, DO

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

Bruce A. Feinberg, DO, is a leading oncologist recognized for his expertise in oncology and the business of specialty healthcare. He serves as vice president and chief medical officer for the Clinical Pathways business of Cardinal Health Specialty Solutions. Clinical Pathways aims to control costs, improve the quality of care, and increase predictability—all critical goals for payers and providers who drive the pathways process.

Prior to joining the Cardinal Health team, Dr Feinberg was instrumental in establishing Georgia Cancer Specialists (GCS), the largest and first integrated oncologic specialty practice in the Southeast. As chief executive officer and president of GCS, he expanded community access to oncology care by bringing the latest cancer treatments, technologies, and clinical trials closer to the patient. In 2012, Specialty Solutions launched PathWare Decision Transaction Solutions, software technology to improve the workflow process for payers and physicians that Dr Feinberg was instrumental in designing.

A highly sought-after speaker on cancer-related topics, he is the author of the bestselling *Breast Cancer Answers* and its follow-up book, *Colon Cancer Answers*. Dr Feinberg regularly publishes in peer-reviewed journals, including the *Journal of the American Medical Association*, *Cancer*, *Oncology Issues*, and *Community Oncology*. He is often consulted by the national media, including *The New York Times*, *Wall Street Journal*, *Forbes*, and CNN.

Dr Feinberg was an early adopter of information technology. He incorporated electronic medical records (EMRs) at GCS in 1999 and subsequently developed OASIS, a proprietary EMR software application that incorporates artificial intelligence logic into common EMR functions. Dr Feinberg is the innovator behind ChemoOrders.com, a free, online disease management system for healthcare providers. Launched in June 2007, ChemoOrders.com now has more than 10,000 visitors and thousands of regular users worldwide.

## KEYNOTE SPEAKER

### Roy Beveridge, MD

*Chief Medical Officer*
*Humana*
*Louisville, KY*

Roy Beveridge, MD, is Humana's senior vice president and chief medical officer (CMO), where he is responsible for developing and implementing the company's clinical strategy and advancing its integrated care delivery model. He is known for creating collaborative environments among physician communities and providing thought leadership, publishing extensively in the fields of medical oncology, quality design, ethics, and population health. Previously, Dr Beveridge served as CMO for McKesson Specialty Health and as executive vice president and CMO for US Oncology. He practiced for more than 20 years in medical oncology and stem cell transplant in northern Virginia.

## FACULTY

### Suzanne Belinson, PhD, MPH

*Executive Director*
*Center for Clinical Effectiveness*
*Blue Cross Blue Shield Association*
*Chicago, IL*

Suzanne Belinson, PhD, MPH, is the executive director of the Center for Clinical Effectiveness at the Blue Cross Blue Shield Association (BCBSA), a national federation of 36 independent community-based and locally operated BCBS companies. The Blue system is the nation's largest health insurer, covering over 100 million (1 in 3) Americans. As the executive director for the Center for Clinical Effectiveness, Dr Belinson leads the operational and financial responsibilities of the center. In addition, as part of the leadership team in the Office of Clinical Affairs, she focuses on the development of emerging programs and services that enhance clinical effectiveness for the independent BCBS plans.

Before joining BCBSA, Dr Belinson served as a National Institutes of Health clinical cancer fellow at Northwestern University, where her work focused on community-based interventions. Dr Belinson developed and tested community-based models for cervical cancer screening with both domestic and international applications. Dr Belinson continues to serve as an adjunct faculty member at Northwestern University.

### Nell Wood Buhlman, MBA

*Senior Vice President, Clinical and Analytic Services*
*Press Ganey Associates*
*Baltimore, MD*

Nell Wood Buhlman, MBA, has 25 years of industry experience, which includes quality measures development and reporting, healthcare business strategy, and payment reform. As Press Ganey's senior vice president for Clinical and Analytic Services, Ms Buhlman runs the company's clinical products business unit, which comprises data collection, reporting, and analysis tools that enable clients to measure, assess, and improve quality of care, as well as meet a broad range of reporting mandates. This suite of solutions includes the National Database of Nursing Quality Indicators, Core Measures, Hospital Clinical Quality eMeasures, and Patient-Reported Outcome Measures. Ms Buhlman also runs Press Ganey's research and analytics team, which houses the teams responsible for survey and measurement methodology, as well as designing integrated analytics that enable clients to better understand the relationships between measurement domains and leverage that understanding to address the challenges under value-based delivery and payment.

Prior to Press Ganey, Ms Buhlman spent 16 years at the Quality Indicator (QI) Project, a leading provider of quality measures reporting and consulting services. At the QI Project, she was vice president for Business Development, overseeing marketing, communications, and strategic partnerships. Ms Buhlman started her career at The Advisory Board Company, a Washington, DC–based healthcare management consulting firm. She earned a BA degree from Connecticut College and an MBA degree from Johns Hopkins Carey Business School.

### Robert W. Carlson, MD

*Chief Executive Officer*
*National Comprehensive Cancer Network*
*Fort Washington, PA*

Robert W. Carlson, MD, is the chief executive officer (CEO) at the National Comprehensive Cancer Network (NCCN). Dr Carlson joined NCCN as CEO in January 2013, following an esteemed history of leadership positions within the organization—most notably, including acting as representative to the NCCN Board of Directors, chair of the Breast Cancer Guidelines Panel, member and founding chair of the Breast Cancer Risk Reduction Guidelines Panel, and chair of the Survivorship Guidelines Panel.

Prior to his appointment as CEO at NCCN, Dr Carlson served as professor of Medicine in the Division of Oncology and Stanford Medical Informatics at Stanford University Medical Center, as well as medical director of Inpatient Oncology and Hematology at Stanford Cancer Institute in California.

Dr Carlson is a graduate of Stanford University Medical School. He completed his internship and junior residency in Internal Medicine at Barnes Hospital Group in St. Louis before returning to Stanford University to complete his senior residency. He earned his BS degree with distinction from Stanford University, specializing in Biological Sciences. Dr Carlson is board certified in Medical Oncology and Internal Medicine.

### Jonas A. de Souza, MD, MBA

*Assistant Professor of Medicine*
*The University of Chicago*
*Chicago, IL*

Jonas A. de Souza, MD, MBA, is a medical oncologist at the University of Chicago. He is originally from Brazil and attended the University of Texas Houston for his residency in Internal Medicine. He then pursued a fellowship in Medical Oncology at The University of Chicago, where he currently is an assistant professor of Medicine. He also holds an MBA degree from the University of Chicago Booth School of Business. His research is focused on patient-centered outcomes and value-based healthcare, including the financial toxicity due to cancer and its treatments, value-based reimbursement models, and personalized value.

### Kim D. Eason, MEd

*Manager, Episodes of Care Program*
*Horizon Blue Cross Blue Shield of New Jersey*
*Newark, NJ*

Kim D. Eason, MEd, manager of Episodes of Care at Horizon Blue Cross Blue Shield of New Jersey, is building bundled care models in orthopedics, oncology, pregnancy, colonoscopy, and other innovative Episode programs. Ms Eason and Horizon are working collaboratively with physician practices to change how healthcare is delivered in New Jersey.

Ms Eason brings over 30 years of healthcare experience to this role. Her expertise in physician contracting and relations, customer service, call center »

operations, claims processing, and consumer appeals allows her to seek end-to-end solutions for the new patient-centered programs.

Ms Eason is a graduate of Rutgers College, where she received her BA degree in English, and Rutgers Graduate School of Education, where she earned her MEd degree in English Education.

### David Fabrizio

*Leader, Cancer Immunotherapy*
*Foundation Medicine, Inc*
*Cambridge, MA*

David Fabrizio has over 12 years of experience in the drug discovery industry and, more recently, in the application of next-generation sequencing (NGS) technologies to discover methods for cancer immunotherapy response. Mr Fabrizio's early work helped lead to the discovery of a novel BMP signaling molecule, RGMb (DRAGON), which was later discovered to be a receptor for the immune checkpoint PD-L2, and was published in the Journal of Biochemistry in 2005. Mr Fabrizio joined Adnexus Therapeutics in 2004 and went on to develop checkpoint inhibitor–based immunotherapies, helping to lead the PD-1/PD-L1 preclinical drug discovery effort, which was eventually acquired by Bristol-Myers Squibb (BMS) in 2007. Additionally, his work led to several issued patents, including for those describing novel EGFR- and IGFR-targeting therapeutics, as well as a method for improved drug pharmacokinetics through human serum albumin binding motifs. While at BMS, Mr Fabrizio also invented a novel drug selection technology, ASCENT, to rapidly identify protein-based therapeutic binders using a reconstituted mRNA/protein fusion system. In 2013, he joined the startup, AbVitro, and focused on developing an NGS immune cell–sequencing/antigen target identification technology, which was recently acquired by Juno Therapeutics. Mr Fabrizio joined Foundation Medicine in 2015 and currently leads the Cancer Immunotherapy group, which is utilizing NGS techniques to identify methods for the identification of responders to immunotherapies, including checkpoint inhibitors.

### Michael D. Fratkin, MD

*Founder*
*Resolution Care*
*Eureka, CA*

Michael D. Fratkin, MD, is an educator and palliative care physician. With a passion for innovation, he is a leader in driving the critically needed transformation in how we care for people completing their lives. ResolutionCare is a pioneering technology-enabled palliative care program, and Dr Fratkin and his team are breaking the mold on what it means to care for people by simply doing what makes sense. He is inspired to enhance our understanding of death and dying, along with life and living, for all that choose to serve people at the end of their lives.

### Stuart L. Goldberg, MD

*Attending, Leukemia, Chief Medical Officer*
*Cancer Outcomes Tracking and Analysis*
*John Theurer Cancer Center*
*Hackensack, NJ*

Stuart L. Goldberg, MD, is a hematologist/oncologist and specializes in the treatment of leukemia, myelodysplastic syndromes (MDS), and bone marrow failure syndromes. He has extensive experience with traditional and experimental chemotherapy approaches to these diseases, as well as stem cell transplantation options. Over the past decade, Dr Goldberg has developed a research interest in chronic myeloid leukemia (CML), including leading the John Theurer Cancer Center (JTCC) team in the registration trials for all 5 targeted therapies approved for this disease. He has lectured about CML worldwide and serves as a medical advisor to the National CML Society and a medical educational website (managingcml.com). He currently is a member of the Executive Steering Committee of the Simplicity Trial, the largest observational database in CML involving over 1400 patients at more than 220 centers in 7 countries.

Dr Goldberg also founded JTCC's MDS program, which was designated a Center of Excellence by the MDS Foundation. He has redefined the incidence of MDS using the Medicare database and has worked closely with industry to develop iron-chelation strategies in this disease, including serving as the principal researcher on several trials. His research efforts, which include over 200 publications, were recognized by the Association of Community Cancer Centers—the nation's largest association of cancer providers—with the 2015 David King Clinical Scientist Award.

Dr Goldberg also serves as the chief medical officer of COTA (Cancer Outcomes Tracking and Analysis). COTA is a cloud-based data and analytics platform, developed at the JTCC, that provides physicians with data and provides 3 unique real-time functions: disease sorting at the highest level of clinical and molecular fidelity, outcome tracking, and reporting. COTA seeks to find value in cancer care and provide new strategies in medical reimbursement, thereby shaping the future of national medical care reform.

### Scott Gottlieb, MD

*Resident Fellow*
*American Enterprise Institute*
*Washington, DC*

Scott Gottlieb, MD, is a practicing physician and resident fellow at the American Enterprise Institute, where his work focuses on providing insights into the economic and technological forces driving the transformation of healthcare. Dr Gottlieb previously served as the FDA deputy commissioner for Medical and Scientific Affairs, and before that, as a senior advisor to the FDA commissioner and as the FDA's director of Medical Policy Development. He also worked on implementation of the new Medicare Part D Drug Benefit as a senior advisor to the administrator of CMS, where he supported policy work on quality improvement and the agency's coverage process, particularly related to new medical technologies. In 2013, Dr Gottlieb was appointed by the Senate majority leader to serve on the Federal Health Information Technology Policy Committee, which advises HHS on healthcare information technology.

Dr Gottlieb is a regular contributor to the editorial page of the *Wall Street Journal* and Forbes.com, and he has held editorial positions on the *British Medical Journal* and the *Journal of the American Medical Association*. Additionally, his work appears in *USA Today*, *The New York Times*, and the *Los Angeles Times*. He is also a guest commentator on CNBC cable channel and on Fox News Channel. Dr Gottlieb is an editorial board member of the journal, *Value-Based Cancer Care*, and the Food and Drug Law Institute's Food and Drug Policy Forum, and is a member of the board of advisors of Cancer Commons.

Dr Gottlieb serves as an advisor to the National Comprehensive Cancer Network and the National Coalition for Cancer Survivorship, and as a member of the policy boards to the Leukemia and Lymphoma Society and the Society of Hospitalist Medicine. He previously served as a healthcare advisor to the 2012 presidential campaign of Mitt Romney and as a senior advisor to the 2016 presidential campaign of Governor Scott Walker.

Dr Gottlieb advises healthcare investors and is a board member of life science and healthcare services companies, including the US subsidiary of Daiichi Sankyo Pharmaceuticals. He is also a member of GlaxoSmithKline's Product Investment Board.

Dr Gottlieb is a clinical assistant professor at the New York University School of Medicine in Manhattan. He completed a residency in Internal Medicine at the Mount Sinai Hospital in New York and is a graduate of the Mount Sinai School of Medicine in New York and of Wesleyan University, in Middletown, Connecticut, where he studied Economics.

*(continued on SP94)*

DARZALEX® + Rd or Vd after first relapse in multiple myeloma

# DISCOVER MORE

with the first and only CD38-directed monoclonal antibody (mAb)[1]

## Indication

DARZALEX® (daratumumab) is indicated in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.

Rd=lenalidomide and dexamethasone; Vd=bortezomib and dexamethasone.

## Important Safety Information

**Warnings and precautions include:** infusion reactions, interference with serological testing, neutropenia, thrombocytopenia, and interference with determination of complete response.

**In patients who received DARZALEX® in combination with lenalidomide and dexamethasone, the most frequently reported adverse reactions (incidence ≥20%) were:** neutropenia (92%), thrombocytopenia (73%), upper respiratory tract infection (65%), infusion reactions (48%), diarrhea (43%), fatigue (35%), cough (30%), muscle spasms (26%), nausea (24%), dyspnea (21%) and pyrexia (20%). The overall incidence of serious adverse reactions was 49%. **Serious adverse reactions were:** pneumonia (12%), upper respiratory tract infection (7%), influenza (3%) and pyrexia (3%).

**In patients who received DARZALEX® in combination with bortezomib and dexamethasone, the most frequently reported adverse reactions (incidence ≥20%) were:** thrombocytopenia (90%), neutropenia (58%), peripheral sensory neuropathy (47%), infusion reactions (45%), upper respiratory tract infection (44%), diarrhea (32%), cough (27%), peripheral edema (22%), and dyspnea (21%). The overall incidence of serious adverse reactions was 42%. **Serious adverse reactions were:** upper respiratory tract infection (5%), diarrhea (2%) and atrial fibrillation (2%).

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

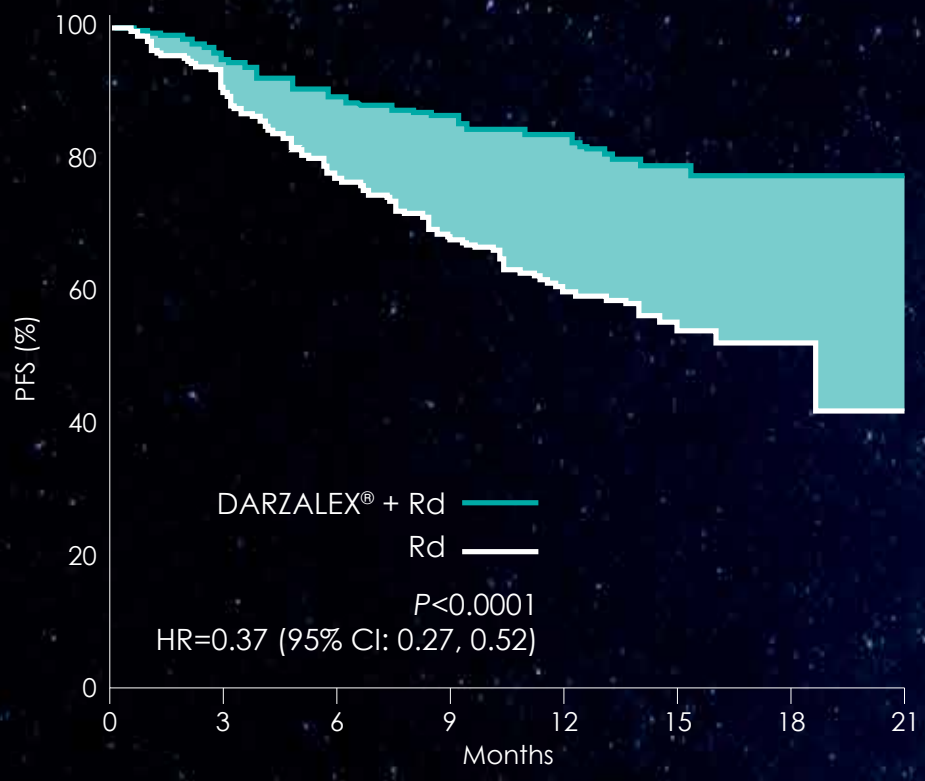
DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

DARE TO DREAM

# Superior efficacy in combination

POLLUX

## DARZALEX® (daratumumab) + Rd significantly improved PFS vs Rd alone[1]




**63%**
reduction in the risk of disease progression or death with DARZALEX® + Rd

POLLUX was an open-label, randomized, active-controlled phase 3 trial comparing treatment with DARZALEX® 16 mg/kg + Rd (n=286) to Rd alone (n=283) in multiple myeloma patients who received a minimum of 1 prior therapy. Patients were treated until unacceptable toxicity or disease progression. Efficacy was evaluated by PFS based on International Myeloma Working Group (IMWG) criteria.[1]

**91.3%** **ORR** with DARZALEX® + Rd vs **74.6%** with Rd alone (*P*<0.0001). CR or better was 42.3% with DARZALEX® + Rd vs 18.8% with Rd alone. VGPR was 32.2% vs 24.4%, and PR was 16.8% vs 31.4% with DARZALEX® + Rd vs Rd alone, respectively.[1]

Rd=lenalidomide and dexamethasone; PFS=progression-free survival; HR=hazard ratio; ORR=overall response rate; CR=complete response; VGPR=very good partial response; PR=partial response.

## Indication

DARZALEX® (daratumumab) is indicated in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.

## Important Safety Information

**CONTRAINDICATIONS:** None

### WARNINGS AND PRECAUTIONS

#### Infusion Reactions

DARZALEX® can cause severe infusion reactions. Approximately half of all patients experienced a reaction, most during the first infusion. Infusion reactions can also occur with subsequent infusions. Nearly all reactions occurred during infusion or within 4 hours of completing an infusion. Prior to the introduction of post-infusion medication in clinical trials, infusion reactions occurred up to 48 hours after infusion. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, laryngeal edema and pulmonary edema. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting and nausea. Less common symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, and hypotension.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt infusion for reactions of any severity and institute medical management as needed. Permanently discontinue therapy for life-threatening (Grade 4) reactions. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

#### Interference with Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

#### Neutropenia

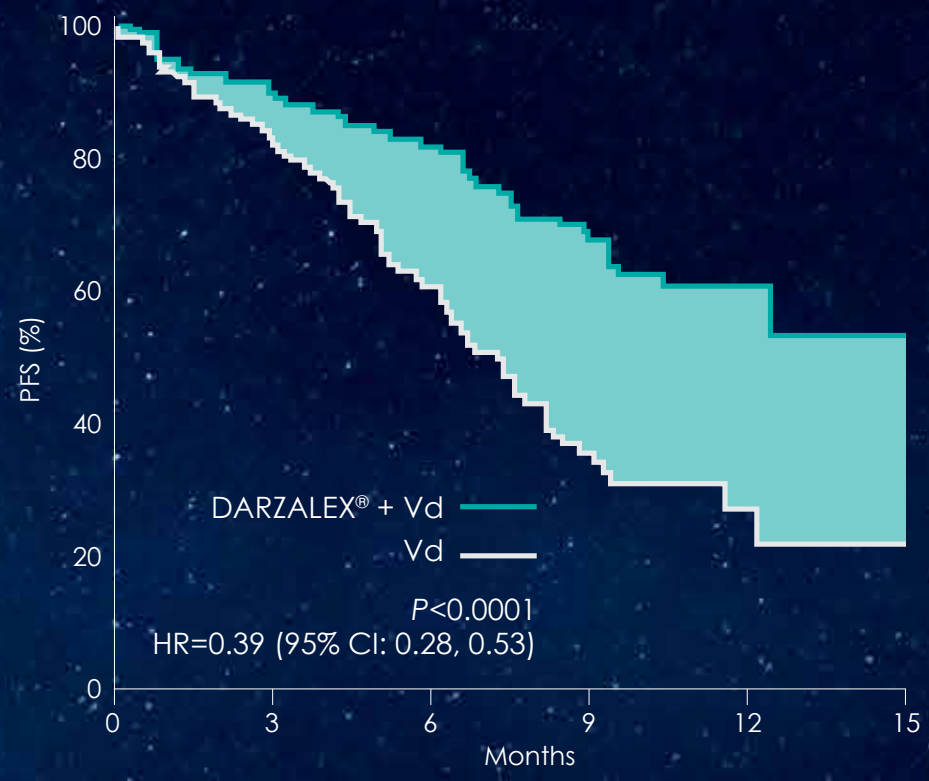
DARZALEX® may increase neutropenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. DARZALEX® dose delay may be required to allow recovery of neutrophils. No dose reduction of DARZALEX® is recommended. Consider supportive care with growth factors.

#### Thrombocytopenia

DARZALEX® may increase thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. DARZALEX® dose delay may be required to allow recovery of platelets. No dose reduction of DARZALEX® is recommended. Consider supportive care with transfusions.

CASTOR

## DARZALEX® + Vd significantly improved PFS vs Vd alone[1]




**61%**
reduction in the risk of disease progression or death with DARZALEX® + Vd

CASTOR was an open-label, randomized, active-controlled phase 3 trial comparing treatment with DARZALEX® 16 mg/kg + Vd (n=251) to Vd alone (n=247) in multiple myeloma patients who received a minimum of 1 prior therapy. DARZALEX® was given until disease progression. Efficacy was evaluated by PFS based on International Myeloma Working Group (IMWG) criteria.[1,2]

**79.3%** **ORR** with DARZALEX® + Vd vs **59.9%** with Vd alone (*P*<0.0001). CR or better was 18.3% with DARZALEX® + Vd vs 8.5% with Vd alone. VGPR was 38.2% vs 19.0%, and PR was 22.7% vs 32.4% with DARZALEX® + Vd vs Vd alone, respectively.[1]

*Vd=bortezomib and dexamethasone.

## Important Safety Information (cont'd)

### Interference with Determination of Complete Response

Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

### Adverse Reactions

In patients who received DARZALEX® in combination with lenalidomide and dexamethasone, the most frequently reported adverse reactions (incidence ≥20%) were: neutropenia (92%), thrombocytopenia (73%), upper respiratory tract infection (65%), infusion reactions (48%), diarrhea (43%), fatigue (35%), cough (30%), muscle spasms (26%), nausea (24%), dyspnea (21%) and pyrexia (20%). The overall incidence of serious adverse reactions was 49%. Serious adverse reactions were pneumonia (12%), upper respiratory tract infection (7%), influenza (3%) and pyrexia (3%).

In patients who received DARZALEX® in combination with bortezomib and dexamethasone, the most frequently reported adverse reactions (incidence ≥20%) were: thrombocytopenia (90%), neutropenia (58%), peripheral sensory neuropathy (47%), infusion reactions (45%), upper respiratory tract infection (44%), diarrhea (32%), cough (27%), peripheral edema (22%), and dyspnea (21%). The overall incidence of serious adverse reactions was 42%. Serious adverse reactions were upper respiratory tract infection (5%), diarrhea (2%) and atrial fibrillation (2%).

### DRUG INTERACTIONS

Effect of Other Drugs on Daratumumab: The coadministration of lenalidomide or bortezomib with DARZALEX® did not affect the pharmacokinetics of daratumumab.

Effect of Daratumumab on Other Drugs: The coadministration of DARZALEX® with bortezomib did not affect the pharmacokinetics of bortezomib.

063483-161117

**Please see brief summary of full Prescribing Information on adjacent pages.**

For more information, visit **www.darzalexhcp.com**

**References: 1.** DARZALEX® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Palumbo A, Chanan-Khan A, Weisel K, et al; the CASTOR Investigators. *N Engl J Med.* 2016;375(8):754-766.

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 01/17 064370-161209

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

DARE TO DREAM

**DARZALEX® (daratumumab) injection, for intravenous use**
**Brief Summary of Full Prescribing Information**

## INDICATIONS AND USAGE

DARZALEX is indicated:

- in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.
- as monotherapy, for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

## CONTRAINDICATIONS

None.

## WARNINGS AND PRECAUTIONS

### Infusion Reactions

DARZALEX can cause severe infusion reactions. Approximately half of all patients experienced a reaction, most during the first infusion.

Infusion reactions can also occur with subsequent infusions. Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX. Prior to the introduction of post-infusion medication in clinical trials, infusion reactions occurred up to 48 hours after infusion.

Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, laryngeal edema and pulmonary edema. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting and nausea. Less common symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, and hypotension *[see Adverse Reactions]*.

Pre-medicate patients with antihistamines, antipyretics and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX therapy for life-threatening (Grade 4) reactions. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion *[see Dosage and Administration (2.1) in Full Prescribing Information]*.

To reduce the risk of delayed infusion reactions, administer oral corticosteroids to all patients following DARZALEX infusions *[see Dosage and Administration (2.2) in Full Prescribing Information]*. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

### Interference with Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum[1] *[see References]*. The determination of a patient's ABO and Rh blood type are not impacted *[see Drug Interactions]*.

Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX. Type and screen patients prior to starting DARZALEX.

### Neutropenia

DARZALEX may increase neutropenia induced by background therapy *[see Adverse Reactions]*.

Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. DARZALEX dose delay may be required to allow recovery of neutrophils. No dose reduction of DARZALEX is recommended. Consider supportive care with growth factors.

### Thrombocytopenia

DARZALEX may increase thrombocytopenia induced by background therapy *[see Adverse Reactions]*.

Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. DARZALEX dose delay may be required to allow recovery of platelets. No dose reduction of DARZALEX is recommended. Consider supportive care with transfusions.

### Interference with Determination of Complete Response

Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both, the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein *[see Drug Interactions]*. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

## ADVERSE REACTIONS

The following serious adverse reactions are also described elsewhere in the labeling:

- Infusion reactions *[see Warning and Precautions]*.
- Neutropenia *[see Warning and Precautions]*.
- Thrombocytopenia *[see Warning and Precautions]*.

### Adverse Reactions in Clinical Trials

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



The safety data described below reflects exposure to DARZALEX (16 mg/kg) in 717 patients with multiple myeloma including 526 patients from two Phase 3 active-controlled trials who received DARZALEX in combination with either lenalidomide (DRd, n=283; Study 3) or bortezomib (DVd, n=243; Study 4) and four open-label, clinical trials in which patients received DARZALEX either in combination with lenalidomide (n=35), or as monotherapy (n=156).

Combination Treatment with Lenalidomide

Adverse reactions described in Table 1 reflect exposure to DARZALEX (DRd arm) for a median treatment duration of 13.1 months (range: 0 to 20.7 months) and median treatment duration of 12.3 months (range: 0.2 to 20.1 months) for the lenalidomide group (Rd) in Study 3. The most frequent adverse reactions (≥20%) were infusion reactions, diarrhea, nausea, fatigue, pyrexia, upper respiratory tract infection, muscle spasms, cough and dyspnea. The overall incidence of serious adverse reactions was 49% for the DRd group compared with 42% for the Rd group. Serious adverse reactions with at least a 2% greater incidence in the DRd arm compared to the Rd arm were pneumonia (12% vs Rd 10%), upper respiratory tract infection (7% vs Rd 4%), influenza and pyrexia (DRd 3% vs Rd 1% for each).

Adverse reactions resulted in discontinuations for 7% (n=19) of patients in the DRd arm versus 8% (n=22) in the Rd arm.

**Table 1: Adverse reactions reported in ≥ 10% of patients and with at least a 5% frequency greater in the DRd arm in Study 3**

| Adverse Reaction | DRd (N=283) % | | | Rd (N=281) % | | |
|---|---|---|---|---|---|---|
| | Any Grade | Grade 3 | Grade 4 | Any Grade | Grade 3 | Grade 4 |
| Infusion reactions[a] | 48 | 5 | 0 | 0 | 0 | 0 |
| **Gastrointestinal disorders** | | | | | | |
| Diarrhea | 43 | 5 | 0 | 25 | 3 | 0 |
| Nausea | 24 | 1 | 0 | 14 | 0 | 0 |
| Vomiting | 17 | 1 | 0 | 5 | 1 | 0 |
| **General disorders and administration site conditions** | | | | | | |
| Fatigue | 35 | 6 | < 1 | 28 | 2 | 0 |
| Pyrexia | 20 | 2 | 0 | 11 | 1 | 0 |
| **Infections and infestations** | | | | | | |
| Upper respiratory tract infection[b] | 65 | 6 | < 1 | 51 | 4 | 0 |
| **Musculoskeletal and connective tissue disorders** | | | | | | |
| Muscle spasms | 26 | 1 | 0 | 19 | 2 | 0 |
| **Nervous system disorders** | | | | | | |
| Headache | 13 | 0 | 0 | 7 | 0 | 0 |
| **Respiratory, thoracic and mediastinal disorders** | | | | | | |
| Cough[c] | 30 | 0 | 0 | 15 | 0 | 0 |
| Dyspnea[d] | 21 | 3 | < 1 | 12 | 1 | 0 |

Key: D=daratumumab, Rd=lenalidomide-dexamethasone.

[a] Infusion reaction includes terms determined by investigators to be related to infusion, see description of Infusion Reactions below.
[b] upper respiratory tract infection, bronchitis, sinusitis, respiratory tract infection viral, rhinitis, pharyngitis, respiratory tract infection, metapneumovirus infection, tracheobronchitis, viral upper respiratory tract infection, laryngitis, respiratory syncytial virus infection, staphylococcal pharyngitis, tonsillitis, viral pharyngitis, acute sinusitis, nasopharyngitis, bronchiolitis, bronchitis viral, pharyngitis streptococcal, tracheitis, upper respiratory tract infection bacterial, bronchitis bacterial, epiglottitis, laryngitis viral, oropharyngeal candidiasis, respiratory moniliasis, viral rhinitis, acute tonsillitis, rhinovirus infection
[c] cough, productive cough, allergic cough
[d] dyspnea, dyspnea exertional

Laboratory abnormalities worsening during treatment from baseline listed in Table 2.

**Table 2: Treatment-emergent hematology laboratory abnormalities in Study 3**

| | DRd (N=283) % | | | Rd (N=281) % | | |
|---|---|---|---|---|---|---|
| | Any Grade | Grade 3 | Grade 4 | All Grades | Grade 3 | Grade 4 |
| Anemia | 52 | 13 | 0 | 57 | 19 | 0 |
| Thrombocytopenia | 73 | 7 | 6 | 67 | 10 | 5 |
| Neutropenia | 92 | 36 | 17 | 87 | 32 | 8 |
| Lymphopenia | 95 | 42 | 10 | 87 | 32 | 6 |

Key: D=Daratumumab, Rd=lenalidomide-dexamethasone.

Combination Treatment with Bortezomib

Adverse reactions described in Table 3 reflect exposure to DARZALEX (DVd arm) for a median treatment duration of 6.5 months (range: 0 to 14.8 months) and median treatment duration of 5.2 months (range: 0.2 to 8.0 months) for the bortezomib group (Vd) in Study 4. The most frequent adverse reactions (>20%) were infusion reactions, diarrhea, peripheral edema, upper respiratory tract infection, peripheral sensory neuropathy, cough and dyspnea. The overall incidence of serious adverse reactions was 42% for the DVd group compared with 34% for the Vd group. Serious adverse reactions with at least a 2% greater incidence in the DVd arm compared to the Vd arm were upper respiratory tract infection (DVd 5% vs Vd 2%), diarrhea and atrial fibrillation (DVd 2% vs Vd 0% for each).

**DARZALEX®** (daratumumab) injection

Adverse reactions resulted in discontinuations for 7% (n=18) of patients in the DVd arm versus 9% (n=22) in the Vd arm.

**Table 3: Adverse reactions reported in ≥ 10% of patients and with at least a 5% frequency greater in the DVd arm Study 4**

| Adverse Reaction | DVd (N=243) % | | | Vd (N=237) % | | |
|---|---|---|---|---|---|---|
| | Any Grade | Grade 3 | Grade 4 | Any Grade | Grade 3 | Grade 4 |
| Infusion reactions[a] | 45 | 9 | 0 | 0 | 0 | 0 |
| **Gastrointestinal disorders** | | | | | | |
| Diarrhea | 32 | 3 | < 1 | 22 | 1 | 0 |
| Vomiting | 11 | 0 | 0 | 4 | 0 | 0 |
| **General disorders and administration site conditions** | | | | | | |
| Edema peripheral[b] | 22 | 1 | 0 | 13 | 0 | 0 |
| Pyrexia | 16 | 1 | 0 | 11 | 1 | 0 |
| **Infections and infestations** | | | | | | |
| Upper respiratory tract infection[c] | 44 | 6 | 0 | 30 | 3 | < 1 |
| **Nervous system disorders** | | | | | | |
| Peripheral sensory neuropathy | 47 | 5 | 0 | 38 | 6 | < 1 |
| **Respiratory, thoracic and mediastinal disorders** | | | | | | |
| Cough[d] | 27 | 0 | 0 | 14 | 0 | 0 |
| Dyspnea[e] | 21 | 4 | 0 | 11 | 1 | 0 |

Key: D=daratumumab, Vd=bortezomib-dexamethasone.

[a] Infusion reaction includes terms determined by investigators to be related to infusion, see description of Infusion Reactions below.
[b] edema peripheral, edema, generalized edema, peripheral swelling
[c] upper respiratory tract infection, bronchitis, sinusitis, respiratory tract infection viral, rhinitis, pharyngitis, respiratory tract infection, metapneumovirus infection, tracheobronchitis, viral upper respiratory tract infection, laryngitis, respiratory syncytial virus infection, staphylococcal pharyngitis, tonsillitis, viral pharyngitis, acute sinusitis, nasopharyngitis, bronchiolitis, bronchitis viral, pharyngitis streptococcal, tracheitis, upper respiratory tract infection bacterial, bronchitis bacterial, epiglottitis, laryngitis viral, oropharyngeal candidiasis, respiratory moniliasis, viral rhinitis, acute tonsillitis, rhinovirus infection
[d] cough, productive cough, allergic cough
[e] dyspnea, dyspnea exertional

Laboratory abnormalities worsening during treatment are listed in Table 4.

**Table 4: Treatment-emergent hematology laboratory abnormalities in Study 4**

| | DVd (N=243) % | | | Vd (N=237) % | | |
|---|---|---|---|---|---|---|
| | Any Grade | Grade 3 | Grade 4 | Any Grade | Grade 3 | Grade 4 |
| Anemia | 48 | 13 | 0 | 56 | 14 | 0 |
| Thrombocytopenia | 90 | 28 | 19 | 85 | 22 | 13 |
| Neutropenia | 58 | 12 | 3 | 40 | 5 | <1 |
| Lymphopenia | 89 | 41 | 7 | 81 | 24 | 3 |

Key: D=Daratumumab, Vd=bortezomib-dexamethasone.

Monotherapy

The safety data reflect exposure to DARZALEX in 156 adult patients with relapsed and refractory multiple myeloma treated with DARZALEX at 16 mg/kg in three open-label, clinical trials. The median duration of exposure was 3.3 months (range: 0.03 to 20.04 months). Serious adverse reactions were reported in 51 (33%) patients. The most frequent serious adverse reactions were pneumonia (6%), general physical health deterioration (3%), and pyrexia (3%).

Adverse reactions resulted in treatment delay for 24 (15%) patients, most frequently for infections. Adverse reactions resulted in discontinuations for 6 (4%) patients.

Adverse reactions occurring in at least 10% of patients are presented in Table 5. Table 6 describes Grade 3–4 laboratory abnormalities reported at a rate of ≥10%.

**Table 5: Adverse reactions with incidence ≥10% in patients with multiple myeloma treated with DARZALEX 16 mg/kg**

| | DARZALEX 16 mg/kg N=156 | | |
|---|---|---|---|
| | Incidence (%) | | |
| **Adverse Reaction** | **Any Grade** | **Grade 3** | **Grade 4** |
| Infusion reaction[a] | 48 | 3 | 0 |
| **General disorders and administration site conditions** | | | |
| Fatigue | 39 | 2 | 0 |
| Pyrexia | 21 | 1 | 0 |
| Chills | 10 | 0 | 0 |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Cough | 21 | 0 | 0 |
| Nasal congestion | 17 | 0 | 0 |
| Dyspnea | 15 | 1 | 0 |
| **Musculoskeletal and connective tissue disorders** | | | |
| Back pain | 23 | 2 | 0 |
| Arthralgia | 17 | 0 | 0 |
| Pain in extremity | 15 | 1 | 0 |
| Musculoskeletal chest pain | 12 | 1 | 0 |

**Table 5: Adverse reactions with incidence ≥10% in patients with multiple myeloma treated with DARZALEX 16 mg/kg (continued)**

| | DARZALEX 16 mg/kg N=156 | | |
|---|---|---|---|
| | Incidence (%) | | |
| **Adverse Reaction** | **Any Grade** | **Grade 3** | **Grade 4** |
| **Infections and infestations** | | | |
| Upper respiratory tract infection | 20 | 1 | 0 |
| Nasopharyngitis | 15 | 0 | 0 |
| Pneumonia[b] | 11 | 6 | 0 |
| **Gastrointestinal disorders** | | | |
| Nausea | 27 | 0 | 0 |
| Diarrhea | 16 | 1 | 0 |
| Constipation | 15 | 0 | 0 |
| Vomiting | 14 | 0 | 0 |
| **Metabolism and nutrition disorders** | | | |
| Decreased appetite | 15 | 1 | 0 |
| **Nervous system disorders** | | | |
| Headache | 12 | 1 | 0 |
| **Vascular disorders** | | | |
| Hypertension | 10 | 5 | 0 |

[a] Infusion reaction includes terms determined by investigators to be related to infusion, see below.
[b] Pneumonia also includes the terms streptococcal pneumonia and lobar pneumonia.

**Table 6: Treatment emergent Grade 3-4 laboratory abnormalities (≥10%)**

| | Daratumumab 16 mg/kg (N=156) | | |
|---|---|---|---|
| | **All Grade (%)** | **Grade 3 (%)** | **Grade 4 (%)** |
| Anemia | 45 | 19 | 0 |
| Thrombocytopenia | 48 | 10 | 8 |
| Neutropenia | 60 | 17 | 3 |
| Lymphopenia | 72 | 30 | 10 |

Infusion Reactions

In clinical trials (monotherapy and combination treatments; N=717) the incidence of any grade infusion reactions was 46% with the first infusion of DARZALEX, 2% with the second infusion, and 4% with subsequent infusions. Less than 1% of patients had a Grade 3 infusion reaction with second or subsequent infusions.

The median time to onset of a reaction was 1.5 hours (range: 0.02 to 72.8 hours). The incidence of infusion modification due to reactions was 41%. Median durations of infusion for the 1st, 2nd and subsequent infusions were 7.0, 4.3, and 3.5 hours respectively.

Severe (Grade 3) infusion reactions included bronchospasm, dyspnea, laryngeal edema, pulmonary edema, hypoxia, and hypertension. Other adverse infusion reactions (any Grade, ≥5%) were nasal congestion, cough, chills, throat irritation and vomiting.

Herpes Zoster Virus Reactivation

Prophylaxis for Herpes Zoster Virus reactivation was recommended for patients in some clinical trials of DARZALEX. In monotherapy studies, herpes zoster was reported in 3% of patients. In the randomized controlled combination therapy studies, herpes zoster was reported in 2% each in the DRd and Rd groups respectively (Study 3) and in 5% versus 3% in the DVd and Vd groups respectively (Study 4).

Infections

In patients receiving DARZALEX combination therapy, Grade 3 or 4 infections were reported with DARZALEX combinations and background therapies (DVd: 21%, Vd: 19%; DRd: 28%, Rd: 23%). Pneumonia was the most commonly reported severe (Grade 3 or 4) infection across studies. Discontinuations from treatment were reported in 3% versus 2% of patients in the DRd and Rd groups respectively and 4% versus 3% of patients in the DVd and Vd groups respectively. Fatal infections were reported in 0.8% to 2% of patients across studies, primarily due to pneumonia and sepsis.

**Immunogenicity**

As with all therapeutic proteins, there is the potential for immunogenicity. In clinical trials of patients with multiple myeloma treated with DARZALEX as monotherapy or as combination therapies, none of the 111 evaluable monotherapy patients, and 1 (0.4%) of the 234 combination therapy patients, tested positive for anti-daratumumab antibodies. This patient administered DARZALEX as combination therapy, developed transient neutralizing antibodies against daratumumab. However, this assay has limitations in detecting anti-daratumumab antibodies in the presence of high concentrations of daratumumab; therefore, the incidence of antibody development might not have been reliably determined.

Immunogenicity data are highly dependent on the sensitivity and specificity of the test methods used. Additionally, the observed incidence of a positive result in a test method may be influenced by several factors, including sample handling, timing of sample collection, drug interference, concomitant medication and the underlying disease. Therefore, comparison of the incidence of antibodies to daratumumab with the incidence of antibodies to other products may be misleading.

**DARZALEX®** (daratumumab) injection

## DRUG INTERACTIONS

**Effects of Daratumumab on Laboratory Tests**

Interference with Indirect Antiglobulin Tests (Indirect Coombs Test)

Daratumumab binds to CD38 on RBCs and interferes with compatibility testing, including antibody screening and cross matching. Daratumumab interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt daratumumab binding[1] *[see References]* or genotyping. Since the Kell blood group system is also sensitive to DTT treatment, K-negative units should be supplied after ruling out or identifying alloantibodies using DTT-treated RBCs.

If an emergency transfusion is required, non-cross-matched ABO/RhD-compatible RBCs can be given per local blood bank practices.

Interference with Serum Protein Electrophoresis and Immunofixation Tests

Daratumumab may be detected on serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for monitoring disease monoclonal immunoglobulins (M protein). This can lead to false positive SPE and IFE assay results for patients with IgG kappa myeloma protein impacting initial assessment of complete responses by International Myeloma Working Group (IMWG) criteria. In patients with persistent very good partial response, consider other methods to evaluate the depth of response.

## USE IN SPECIFIC POPULATIONS

**Pregnancy**

Risk Summary

There are no human data to inform a risk with use of DARZALEX during pregnancy. Animal studies have not been conducted. However, there are clinical considerations *[see Clinical Considerations].* The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

*Fetal/Neonatal Adverse Reactions*

Immunoglobulin G1 (IgG1) monoclonal antibodies are transferred across the placenta. Based on its mechanism of action, DARZALEX may cause fetal myeloid or lymphoid-cell depletion and decreased bone density. Defer administering live vaccines to neonates and infants exposed to DARZALEX in utero until a hematology evaluation is completed.

Data

*Animal Data*

Mice that were genetically modified to eliminate all CD38 expression (CD38 knockout mice) had reduced bone density at birth that recovered by 5 months of age. In cynomolgus monkeys exposed during pregnancy to other monoclonal antibodies that affect leukocyte populations, infant monkeys had a reversible reduction in leukocytes.

**Lactation**

Risk Summary

There is no information regarding the presence of daratumumab in human milk, the effects on the breastfed infant, or the effects on milk production. Human IgG is known to be present in human milk. Published data suggest that antibodies in breast milk do not enter the neonatal and infant circulations in substantial amounts.

The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for DARZALEX and any potential adverse effects on the breast-fed child from DARZALEX or from the underlying maternal condition.

**Females and Males of Reproductive Potential**

Contraception

To avoid exposure to the fetus, women of reproductive potential should use effective contraception during treatment and for 3 months after cessation of DARZALEX treatment.

**Pediatric Use**

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

**Geriatric Use**

Of the 156 patients that received DARZALEX monotherapy at the recommended dose, 45% were 65 years of age or older, and 10% were 75 years of age or older. Of 561 patients that received DARZALEX with various combination therapies, 40% were 65 to 75 years of age, and 9% were 75 years of age or older. No overall differences in safety or effectiveness were observed between these patients and younger patients *[see Clinical Studies (14) in Full Prescribing Information].*

## OVERDOSAGE

The dose of DARZALEX at which severe toxicity occurs is not known.

In the event of an overdose, monitor patients for any signs or symptoms of adverse effects and provide appropriate supportive treatment.

## REFERENCES

1. Chapuy, CI, RT Nicholson, MD Aguad, et al., 2015, Resolving the daratumumab interference with blood compatibility testing, Transfusion, 55:1545-1554 (accessible at http://onlinelibrary.wiley.com/doi/10.1111/trf.13069/epdf).

**DARZALEX®** (daratumumab) injection

## PATIENT COUNSELING INFORMATION

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

Infusion Reactions

Advise patients to seek immediate medical attention for any of the following signs and symptoms of infusion reactions:

- itchy, runny or blocked nose; chills, nausea, throat irritation, cough, headache, shortness of breath or difficulty breathing *[see Warnings and Precautions and Adverse Reactions].*

Neutropenia

- Advise patients that if they have a fever, they should contact their healthcare professional *[see Warnings and Precautions and Adverse Reactions].*

Thrombocytopenia

- Advise patients to inform their healthcare professional if they notice signs of bruising or bleeding *[see Warnings and Precautions and Adverse Reactions].*

Interference with Laboratory Tests

Advise patients to inform healthcare providers including blood transfusion centers/personnel that they are taking DARZALEX, in the event of a planned transfusion *[see Warnings and Precautions and Drug Interactions].*

Advise patients that DARZALEX can affect the results of some tests used to determine complete response in some patients and additional tests may be needed to evaluate response *[see Warnings and Precautions and Drug Interactions].*

Manufactured by:
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Horsham, PA 19044
U.S. License Number 1864



063323-161115

# FACULTY BIOS

*(continued from SP88)*

## Jonathan Hirsch, MSc

*President and Founder*
*Syapse*
*Palo Alto, CA*

Jonathan Hirsch, MSc, is the founder and president of Syapse, which enables the transformation of healthcare through precision medicine. At Syapse, Mr Hirsch works closely with healthcare providers, creating software that integrates complex genomic and clinical data to provide physicians with actionable insights at point of care. Mr Hirsch is the chair of the Data Committee for GBM AGILE (a global brain tumor clinical trial), a member of the Global Alliance for Genomics and Health Clinical Working Group, and a member of the University of California, San Francisco, Technology Advisory Group. Earlier in his career, he worked in neuroscience commercial development at Abbott Laboratories, where he developed strategies to fund drug development through partnerships and private equity financing. His research at the Center for Molecular Neurobiology at the University of Chicago helped to establish the effect of exercise on promoting hippocampal neurogenesis and combating Alzheimer's disease. Mr Hirsch received an MSc degree in Neuroscience from Stanford University and an AB degree in Biology and Political Philosophy from the University of Chicago.

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*US Food and Drug Administration*
*Silver Spring, MD*

Sean Khozin, MD, MPH, is a thoracic oncologist and senior medical officer at the FDA's Office of Hematology and Oncology Products. He is the founder of Information Exchange and Data Transformation (INFORMED), an FDA oncology initiative designed to advance regulatory science by building organizational and technical infrastructure for the analysis of aggregated clinical trial datasets and emerging pipelines of data from sources, such as electronic health records and mobile sensor technologies. Previously, Dr Khozin was in private practice in New York City, an attending physician at New York Medical College St. Vincent's Hospital in Manhattan, and an entrepreneur specializing in building health information technology systems with virtual patient management (eg, video, structured e-mail, short message service [SMS]), remote biometric monitoring, and point-of-care data visualization/analytics capabilities. Dr Khozin received his MD degree from the University of Maryland School of Medicine and MPH degree from George Washington University. He completed his internship and residency in Internal Medicine at New York Medical College and fellowship in Medical Oncology at the National Cancer Institute (NCI). Dr Khozin continues to serve as an attending physician at NCI.

## Daniel J. Klein, MHS

*President and Chief Executive Officer*
*Patient Access Network Foundation*
*Washington, DC*

Daniel J. Klein, MHS, brings over 30 years of executive experience to the Patient Access Network (PAN) Foundation. Mr Klein came to the PAN Foundation from the Cystic Fibrosis (CF) Foundation, where he was senior vice president for Patient Access Programs and, prior to that, senior vice president for the CF Services specialty pharmacy.

His leadership at the CF Foundation was exemplified by the CF Services pharmacy that he helped organize and implement to provide financial assistance and case management services for underinsured individuals with CF. While running the CF Services pharmacy, he also developed a pharmaceutical call center business unit to support the launch of new specialty medications for those with CF.

Mr Klein has had numerous leadership roles in the health and information technology (IT) sectors, including, as chairman and chief executive officer of Panurgy Corporation, a leading mid-market IT services company, as well as a consultant on health planning and health promotion for the World Health Organization and HHS, respectively.

## Karen E. Lewis, MS, MM, CGC

*Solution Management Director – Genetic Testing*
*Board-Certified Genetic Counselor*
*AIM Specialty Health*
*Chicago, IL*

Karen E. Lewis, MS, MM, CGC, has been a board-certified genetic counselor for 25 years, with clinical experience in prenatal, adult, and cancer genetics. Additionally, Ms Lewis has provided clinical genetic counseling and developed serum screening and cancer genetics programs at Spectrum Health in Grand Rapids, Michigan. For the past 11 years, she has worked in health insurance, primarily at Priority Health, writing medical policies and working closely with the medical directors for genetic testing management. As of August 2016, Ms Lewis is now the Solution Management director for Genetic Testing for AIM Specialty Health in Chicago. In this current role, she is responsible for overseeing a utilization management program for genetic testing for payers.

In addition to her professional positions, Ms Lewis is involved with the National Society of Genetic Counselors Payer Task Force as the representative for the AMA CPT Coding Advisory Committee. The utilization of genetic counseling, testing, and associated cost control has been a special interest of hers, and she has been part of several CDC collaborative agreements looking at these issues over the past 10 years.

## Debra L. Madden, BA

*Cancer Research Advocate/Patient Representative*
*ECOG/ACRIN Cancer Research Group*
*National Breast Cancer Coalition*
*Newtown, CT*

Debra L. Madden, BA, is a 2-time cancer survivor who was diagnosed with Hodgkin's lymphoma as a young adult and breast cancer nearly 20 years later—thought to be secondary to the radiation she had received for her original cancer treatment. She is an active cancer research advocate who is a member of numerous cancer support and research organizations, including the Eastern Cooperative Oncology Group (ECOG)/American College of Radiology Imaging Network (ACRIN) Cancer Research Group's Cancer Research Advocate Committee, Breast Core, Cancer Care Delivery Research Committee, and the E/A Cardiotoxicity Working Group. In addition, she serves on several national grant review committees and advisory panels as a patient representative, including for the FDA, the Department of Defense's Breast Cancer Research Program, the Dr Susan Love Research Foundation's Army of Women Scientific Advisory Committee, and the Patient-Centered Outcomes Research Institute's inaugural Advisory Panel on the Assessment of Prevention, Diagnosis, and Treatment Options. Ms Madden blogs at "Musings of a Cancer Research Advocate" (https://draemadden.wordpress.com/) and is also a regular contributor for *The American Journal of Managed Care®* (*AJMC®*)'s contributor page and *AJMC*'s *Evidence-Based Oncology™* journal. She is also on Twitter at @AdvocateDebM.

## Pam Mangat, MS

*Associate Director, TAPUR*
*American Society of Clinical Oncology*
*Alexandria, VA*

Pam Mangat, MS, is an epidemiologist at the American Society of Clinical Oncology (ASCO), the world's largest professional organization representing physicians who care for people with cancer, where she manages ASCO's first clinical trial, the Targeted Agent and Profiling Utilization Registry (TAPUR) Study. Prior to joining ASCO, she held roles in increasing responsibility as a research professional on large multi-site National Institutes of Health–funded studies. She earned a »

BSc degree in Cell and Molecular Biology from Simon Fraser University in Canada and received her MS in Epidemiology from The George Washington University.

### Allison Morse, BA

*Young Adult Cancer Survivor*
*Patient Advocate*
*Medford, MA*

Allison Morse, BA, always wanted to save the world, but she thought it would be by joining the Foreign Service or Peace Corps. When she was diagnosed with stage IV Hodgkin's lymphoma a month after her 23rd birthday, her international development dreams were deferred, but a new life purpose was revealed: amplifying the voices of young adult survivors of cancer and other serious illness.

Reflecting on her unique position on the oncology floor—too old to be in the children's wing, but too young to have a robust support system, secure career, or abundant savings—she became a frequent speaker, writer, and commentator on young adult survivorship topics, such as financial insecurity, sexuality and dating, and rebuilding your sense of self after treatment ends. After outliving 5 years of misdiagnosis, Ms Morse has also embarked on a mission to educate high school and college students about how to effectively advocate for themselves in the medical world.

Ms Morse was a 2016 recipient of Massachusetts General Hospital Cancer Center's "the one hundred," which honors "100 everyday amazing individuals and groups whose commitment to the fight against cancer inspires us all to take action," for her social media advocacy connecting young adults to each other and eliminating isolation among this population. She is an active "Sambassador" for The Samfund and is also involved with Colleges Against Cancer, First Descents, and Next Step.

Ms Morse currently works as the social media and digital content specialist at Brandeis University. She earned a BA degree from Brandeis in International & Global Studies and Politics, and minors in Latin American Studies and Environmental Science. She is currently pursuing a Master's degree in Digital Marketing and Design from the same institution.

### J. Ike Nicoll

*President*
*The Morrison Group*
*Denver, CO*

J. Ike Nicoll is an entrepreneurial healthcare executive with over 25 years of proven experience in strategic organizational growth and innovation, and a unique skillset in strategy and business development. He has a long track record of effectively working at the physician, payer, and pharmaceutical executive level, bridging business and clinical domains, and developing and implementing new oncology business frameworks and best practices.

Mr Nicoll's recent career history includes a position as the president and CEO of Cancer Clinics of Excellence (CCE). Under his leadership, CCE became a national oncology services company representing over 250 medical oncologists in 16 states, focused on materially improving the quality and cost-effectiveness of cancer care through the development and implementation of clinical pathways, molecular diagnostic–guided clinical research, population health–based financial models, and distribution/supply chain services.

Before launching CCE, Mr Nicoll served as general manager of Provider Innovation for Oncology Therapeutic Network (OTN)/McKesson Corporation, where he led the company's efforts to identify and develop novel specialty solutions, focused on creating meaningful and sustainable value. Prior to joining OTN/McKesson, he held numerous management and leadership positions with the Global Healthcare Division of IBM.

Mr Nicoll is a member of the Center for American Progress/Brookings Institute Oncology Bundled Payment working group, which focused on developing a clinical/operational framework for adoption by government and commercial payers. He also serves as an advisor to Oregon Health Sciences University regarding the development and commercialization of a cloud-based genomic analytic solution that enhances the speed, accuracy, and effectiveness of cancer research.

### Ted Okon, MBA

*Executive Director*
*Community Oncology Alliance*
*Washington, DC*

Ted Okon, MBA, is a nationally recognized expert on the policy and politics of cancer care. He is quoted extensively in the press, including guest appearances on TV and radio news shows. Mr Okon has testified before Congress on cancer issues and is frequently on Capitol Hill discussing the nation's cancer care delivery system. His target areas of expertise include the cost of cancer treatment, healthcare reform, Medicare reimbursement, drug shortages, and the changing landscape of cancer care delivery in the United States.

Mr Okon has dedicated his career to healthcare business and policy. He has worked for several pharmaceutical companies, including Merck, Warner Lambert (now part of Pfizer), and IMS Health. He co-founded and took public the healthcare information business, Medical Marketing Group. He also founded 2 oncology companies. As executive director of the Community Oncology Alliance, Mr Okon oversees the strategic direction of this nonprofit organization dedicated to patients and providers in the community cancer care setting, under the direction of a dedicated board of oncologists and practice administrators.

Mr Okon has traveled extensively to China, India, Singapore, the United Kingdom, and the Middle East, analyzing and discussing cancer care delivery. He also travels the country speaking to state oncology societies, professional organizations, and companies about the challenges facing the nation's cancer care delivery system. He has authored numerous articles and studies relating to cancer care policy and politics, reimbursement, and clinical issues.

He holds a BS degree from Fairfield University and an MBA degree from the Carnegie-Mellon University Tepper School of Business.

### Kavita Patel, MD, MS

*Nonresident Fellow*
*The Brookings Institution*
*Washington, DC*

Kavita Patel, MD, MS, is a nonresident fellow at the Brookings Institution and a cofounder of Tuple Health—a physician-led company focused on practical clinical solutions to bring care back to health—as well as a practicing primary care physician at Johns Hopkins Medicine. In her role at the Brookings Institution, Dr Patel was instrumental in the development of several specialty payment models, including the Oncology Care Model Initiative and the Next Generation Accountable Care Organization model. Dr Patel was previously a director of Policy for The White House under President Obama and a senior advisor to the late Senator Edward Kennedy. Her prior research in healthcare quality and community approaches to mental illness have earned national recognition, and she has published numerous papers and book chapters on healthcare reform and health policy. She has testified before Congress several times and is a frequent guest expert on NPR, CBS, NBC, and MSNBC, in addition to serving on the editorial board of the *Health Affairs* journal.

### David L. Porter, MD

*Director, Bone Marrow Transplantation*
*Jodi Fisher Horowitz Professor in Leukemia Care Excellence*
*University of Pennsylvania Health System*
*Philadelphia, PA*

David L. Porter, MD, is the Jodi Fisher Horowitz Professor of Leukemia Care Excellence at the Perelman School of Medicine and Abramson Cancer Center, and director of the Blood and Marrow Transplantation and Cellular Therapeutics Program at the Hospital of the University of Pennsylvania. Dr Porter is a graduate of the University of Rochester and earned an MD degree at Brown University. He completed his internship and residency at Boston University Hos-

pital and his fellowship training at Brigham and Women's Hospital and Harvard Medical School in Boston.

Dr Porter chairs and serves on numerous local, national, and international committees focused on hematologic malignancies and hematopoietic stem cell transplantation. He is a member of the Board of Directors of the National Marrow Donor Program and the American Board of Internal Medicine Hematology Exam Committee. He is also a member of the American Society of Hematology, the American Society of Clinical Oncology, and the American Society of Blood and Marrow Transplantation. Dr Porter has authored more than 140 research articles and book chapters, is an associate editor for the *American Journal of Hematology*, and has served as a manuscript reviewer for numerous high-impact medical journals. He is annually recognized as a "Top Doc" in Philadelphia Magazine and by Castle Connolly. Additionally, in 2007, he was the recipient of the Leukemia and Lymphoma Society Service to Mankind Award.

Dr Porter has expertise in the care of patients with hematologic malignancies, including acute and chronic leukemia, and in all aspects of autologous and allogeneic stem cell transplant (SCT). He also leads numerous local and national research activities and is an accomplished clinical investigator with principal research interests in the development of novel methods of cellular therapy, stem cell transplantation, and allogeneic adoptive immunotherapy. Recent research highlights include the successful use of genetically modified T cells to treat B-cell cancers like acute lymphoblastic leukemia and chronic lymphocytic leukemia, novel trials designed to prevent graft versus host disease after allogeneic SCT by blocking lymphocyte trafficking, and studies to enhance graft versus tumor activity at the time of transplant, after nonmyeloablative therapy, and for relapse after SCT.

### Joshua A. Rademacher, MBA

*Executive Vice President*
*Enterprise Solutions and Business Development*
*Avella Specialty Pharmacy*
*Phoenix, AZ*

Joshua A. Rademacher, MBA, serves as the executive vice president of Enterprise Solutions and Business Development of Avella Specialty Pharmacy. In his role, Mr Rademacher is responsible for the development of the company's strategic priorities, new growth initiatives, investments, and strategic planning.

Prior to joining Avella, Mr Rademacher accumulated 10 years of corporate development and executive management experience in the specialty pharmacy, compounding, revenue cycle management, and primary care industries. Before entering the healthcare industry full time, he was an associate at Madison Capital Funding and an analyst at Lazard executing middle-market mergers and acquisitions.

Mr Rademacher graduated from Marquette University with a bachelor's degree in Economics in 2004 and holds an MBA degree from the University of Chicago's Booth School of Business.

### Michael Ruiz de Somocurcio, MBA

*Vice President of Payer and Provider Collaboration*
*Regional Cancer Care Associates*
*Hackensack, NJ*

Michael Ruiz de Somocurcio, MBA, is vice president of Payer and Provider Collaboration for Regional Cancer Care Associates (RCCA), a 100+ oncology provider group located in New Jersey and Maryland. His responsibilities include contracting, developing value-based arrangements with health plans and other providers, and supporting growth strategies for expansion. Prior to RCCA, Mr Ruiz de Somocurcio spent over 15 years on the health plan side working for national, regional, and start-up health plans. Most recently, he held officer roles at Amerigroup NJ, Oscar Insurance, and AmeriHealth NJ, where he was the plan lead for contracting, operations, and medical cost containment. Throughout his career, Mr Ruiz de Somocurcio has developed innovative partnerships to transform the delivery of care through network design and outcomes. He holds an MBA degree from Rutgers University, teaches healthcare courses at Berkeley College, and speaks both locally and nationally on healthcare trends.

### Bhuvana Sagar, MD

*Board-Certified Medical Oncologist*
*National Medical Director*
*Cigna Health Care*
*Houston, TX*

Bhuvana Sagar, MD, joined Cigna in May of 2013 as a medical director. At Cigna, Dr Sagar provides oncology clinical consultation for the Oncology Specialty case management program and the Coverage Policy Unit. Dr Sagar is the physician lead for Cigna's Collaborative Oncology pay-for-performance program, Specialty Care Collaborative in Oncology. She also has Medicare Advantage management experience.

Dr Sagar completed her MD degree at Kilpauk Medical College in Chennai, India, and her residency in Internal Medicine at St. Luke's Roosevelt Hospital in New York City. After finishing her fellowship in Medical Oncology at the University of Texas Medical Branch at Galveston, Dr Sagar practiced for 11 years in single specialty and large multi-specialty groups in the Houston area. Dr Sagar is board certified in Internal Medicine and Medical Oncology and holds an active license in the state of Texas. She has been a member of American Society of Clinical Oncology since 2002.

### William H. Shrank, MD, MSHS

*Chief Medical Officer*
*UPMC Health Plan*
*Pittsburgh, PA*

William H. Shrank, MD, MSHS, joined University of Pittsburgh Medical Center (UPMC)'s Health Plan Division in June 2016 as the company's new chief medical officer. In this role, Dr Shrank will focus on the design and implementation of new payment and delivery models to promote improved population health and further advance UPMC's integrated clinical business strategies.

Prior to joining UPMC, Dr Shrank served as senior vice president, chief scientific officer, and chief medical officer of Provider Innovation for CVS Health, where he led the development of solutions to support providers, manage risk, and deliver better care for the populations they serve. Prior to joining CVS, Dr Shrank served as the inaugural director of Research and Rapid-Cycle Evaluation for the Center for Medicare & Medicaid Innovation at CMS, where he helped design and lead the evaluation of new payment reform models tested by the Center, such as Pioneer ACOs, bundled payments, and progressive primary care models. Dr Shrank began his career as a practicing physician with Brigham Internal Medicine Associates at Brigham and Women's Hospital in Boston, as well as an assistant professor at Harvard Medical School. His research at Harvard focused on improving the quality of prescribing and the use of chronic medications, and he published nearly 200 papers on these topics.

Dr Shrank received his MD degree from Cornell University Medical College, served his residency in Internal Medicine at Georgetown University, and was a fellow in Health Policy Research at University of California, Los Angeles (UCLA), RAND. He earned his MS degree in Health Services from the UCLA and his bachelor's degree from Brown University.

Dr Shrank has served on various national committees and advisory boards, such as the National Advisory Committee for the FDA, CMS, White House (Networking Information, Technology Research, and Development Program), HHS, and Agency for Healthcare Research and Quality. Among the many achievement awards Dr Shrank has received is the 2015 Healthcare Executive Transformation Award from the Los Angeles County Medical Association. He also was the recipient of the Robert Wood Johnson Pioneer Award to evaluate the effect of innovative prescription label design on adherence to chronic medication and health outcomes. »

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# FACULTY BIOS


**Carrie Tompkins Stricker, PhD, RN, AOCN**
*Oncology Nurse Practitioner, Abramson Cancer Center, University of Pennsylvania*
*Chief Clinical Officer & Co-Founder, Carevive Health Systems, Inc*
*Philadelphia, PA*


Carrie Tompkins Stricker, PhD, RN, AOCN, is co-founder and chief clinical officer of the oncology-focused health information technology company, Carevive Health Systems, Inc, and also maintains an active practice as an oncology nurse practitioner at the University of Pennsylvania (Penn)'s Abramson Cancer Center in Philadelphia, Pennsylvania. Additionally, she serves as a lecturer and has held an adjunct faculty post in the School of Nursing at Penn for more than 15 years, focusing primarily on the education of advanced practice nurses in oncology. Dr Stricker is recognized for her clinical and research expertise in cancer survivorship care, as well as in evidence-based symptom assessment and management, particularly in women with breast cancer.

In her 20 years of experience as an oncology nurse, Dr Stricker has fulfilled many roles—hospital-based nurse caring for patients with hematologic malignancies, ambulatory chemotherapy/infusion nurse, and nurse practitioner (NP) caring for a caseload of individuals undergoing active treatment and follow-up care for various malignancies—including spending the past 10 years with a specialization in breast cancer care. In her most recent post at Penn as director of Clinical Programs for the Cancer Survivorship Center of Excellence from 2007 to 2013, she oversaw the development, implementation, and evaluation of the center's clinical survivorship programs, and developed and staffed an independent NP-led clinic that provided consultative and ongoing care to breast cancer survivors. In this position, she also led and collaborated on a variety of federally and foundation-funded research projects, including a multi-center pilot study investigating the feasibility and impact of a survivorship care-planning intervention in breast cancer survivors at 9 US centers. Notably, study findings suggested the positive impact of a nurse-led consultative intervention for improving care coordination and symptom management in breast cancer survivors; yet, her associated research revealed that less than 10% of such patients were receiving such interventions due to time, resource, and other system barriers.

In 2013, driven by a desire to overcome gaps in care by leveraging information technology solutions, Dr Stricker co-founded Carevive Systems, Inc, with a company mission to build and deliver innovative technologies for cancer clinicians and patients that improve clinical outcomes, decrease symptom burden, and lower healthcare costs.

Carevive's supportive care planning and symptom management platform helps cancer centers drive evidence-based supportive and survivorship care and meet evolving quality mandates while supporting patients and families in self-management of symptoms and supportive care. At Carevive, Dr Stricker is responsible for overseeing the clinical development, implementation, and evaluation of the company's software and content solutions.


**Samantha Watson, MBA**
*Chief Executive Officer and Founder*
*The Samfund*
*Boston, MA*


Samantha Watson, MBA, a 2-time cancer survivor, began her career as a health advocate when she founded The Samfund in 2003. The Samfund is a Boston-based nonprofit organization uniquely designed to support young adults across the country in their financial recovery from cancer treatment.

Diagnosed in 1999 with Ewing's sarcoma, and in 2001 with secondary myelodysplastic syndrome (with a bone marrow transplant in August of 2001), she received her treatment in New York City. Upon returning to Boston and integrating back into the "real world," she saw how little support there was for young adults who were struggling once treatment ended. As she quickly came to learn, cancer isn't free, and since then, Ms Watson has evolved into a passionate thought leader and expert in the financial after-effects of treatment in young adult cancer survivors.

During her career, Ms Watson has simultaneously held the position of adjunct lecturer at Brandeis University and has been a featured speaker at cancer-related symposiums, conferences, and hospitals, including Dana-Farber Cancer Institute and Memorial Sloan-Kettering Cancer Center. She is a regular contributor of articles in the oncology space, and her story of survival is highlighted in the Jim Rendon book, *Upside: The New Science of Post-Traumatic Growth* (2015).

Ms Watson received her BA degree from Brandeis University and an MBA degree in Mission-Driven Management from the Heller School for Social Policy and Management at Brandeis. ◆


Attendees at the 5th Annual Patient-Centered Oncology Care® meeting. © Dave McIntosh/Patient-Centered Oncology Care® 2016

# Responding to Patient Needs Central to Providing Value in Cancer Care

*Christina Mattina*

**NELL WOOD BUHLMAN, SENIOR VICE PRESIDENT** of clinical and analytic services at Press Ganey, discussed how oncologists can use patient surveys to anticipate and respond to their patients' needs during her presentation at the Patient-Centered Oncology Care® meeting, held November 17-18, 2016, in Baltimore.

Buhlman's presentation, "Understanding & Responding to Patient Needs: The Cancer Patient Experience," was built upon her work to harness information from patient experiences and use that data to create a strategy toward personalized care. At Press Ganey, Buhlman said, there is a focus on identifying "opportunities that are going to deliver the greatest benefit" to organizations and patients.

According to Buhlman, one of these opportunities is to reduce patient suffering by providing compassionate care. Press Ganey was one of the first to introduce the concept of patient suffering, which is just now starting to be acknowledged after it had initially been rejected by some as sounding too "sensational." The organization classified patient suffering into "inherent suffering" and "avoidable suffering."

Inherent suffering, or the suffering associated with cancer diagnosis and treatment, may not be possible for providers to mitigate or eliminate entirely. It includes psychosocial pain, such as the loss of autonomy and privacy that often accompanies oncology treatment. Oncologists may view these anxieties as outside their domain of responsibility, but these worries can have a dramatic impact on a patient's overall wellness and response to treatment, Buhlman said.

Providers can help alleviate this type of suffering by ensuring that patients receive information they understand, by safeguarding patient privacy, and by empowering patients to make choices regarding their treatment. Overall, the best way to respond to inherent suffering is to meet patient needs by providing care in an empathic way, she explained.

The other type of suffering, avoidable suffering, arises from anything done by the healthcare industry "that causes additional suffering to be layered upon the patient." Avoidable suffering should be eliminated entirely, in part by avoiding unnecessary delays and improving the coordination of care among providers. While offering adequate amenities can help prevent avoidable suffering, Buhlman cautioned that a disproportionate focus on the extras can distract providers from what is most important to the patient. A focus on "delighting" or "wowing" these patients "assumes you have everything else taken care of. If you are baking chocolate chip cookies and offering massages and manicures and pedicures, you better have all of the tough stuff under lock."

Healthcare providers, she said, must work toward improving the patient experience at every opportunity because "we don't, as an industry, have the right to make care worse for patients." To become more patient centered, practices must strategically leverage the information gathered from patient surveys. These surveys can provide insight into "defects in the process" that are important to the patient, like long wait times, poor teamwork, or lack of patient input in decision making.

Press Ganey recommends that its clients use a framework that organizes the domains within the surveys around patients and their needs, not around providers. They have developed a realigned survey that reflects a pyramid of patient-centered domains: culture is the foundation and above that are operational efficiency, clinical excellence, and finally caring behaviors at the tip.

By highlighting the results of a study, Buhlman demonstrated that the patient experience differs based on "micro" factors like condition and setting of care, such that oncology providers looking at surveys from an entire body of patients could miss important nuances. The study, which compared inpatient surveys of cancer patients in 2 settings to a baseline of non cancer patients, indicated that cancer patients in a medical setting have different needs and experiences than those of cancer patients in a surgical setting. Patients receiving surgical care reported that all of their needs in the 4 domains were being met at higher rates than the baseline, while the satisfaction rates of cancer patients in the medical setting lagged behind. For instance, just 61% of medical cancer patients reported that their pain was under control, as opposed to 70% of surgical cancer patients and 64% of non cancer patients.

Another survey revealed perceptions of unmet needs among oncology patients at medical practices. The gaps between optimal performance and actual patient experience were widest in areas that included wait time and preparation for transition. These gaps, Buhlman said, indicate the need to "drill down to understand opportunities for improvement."

Patients can also be segmented by disease to highlight areas of dissatisfaction. To illustrate this point, Buhlman summarized another study that compared the unmet need among lung cancer and breast cancer patients with assessments by cancer patients overall. Breast cancer patients gave more positive assessments of their care than the average of all cancer patients, while lung cancer patients reported some opportunities for improvement. Compared with the baseline of all cancer patients, fewer lung cancer patients said they received instructions on how to care for themselves at home or felt that the staff was concerned about their privacy, among other examples.

In response to an audience question about the capabilities of information technology (IT) to integrate data across providers, Buhlman indicated there is still work left to be done. "It's going to be like Monet's Water Lilies. When you think about the picture we're going to paint, you know what you're looking at," Buhlman said. "It's not going to be the most precise thing, but as the IT and the information services side gets better, we'll be able to grab it and do a photograph-like version of it as well." ◆

BUHLMAN

Attendees at the 5th Annual Patient-Centered Oncology Care® meeting. © Dave McIntosh/Patient-Centered Oncology Care® 2016

# Making Sense of Value for the Payer in Oncology Care

*Surabhi Dangi-Garimella, PhD*

**AS THE HEALTHCARE WORLD TRANSITIONS TO** value-based care and providers and health plans face major challenges, payers have faith in the move, said Roy Beveridge, MD, senior vice president and chief medical officer at Humana.

**"A LOT OF DECISIONS IN THE FFS [FEE-FOR-SERVICE] WORLD THAT ARE BEING MADE BY THE PAYER WILL NOW BE MADE BY CLINICIANS."**

—Roy Beveridge, MD

Beveridge was the keynote speaker at the 5th annual Patient-Centered Oncology Care® (PCOC®) meeting, hosted by *The American Journal of Managed Care®*, November 17-18, 2016, in Baltimore, and walked the audience through the transition toward value-based care.

Beveridge provided context to the move toward value-based care: 5 to 10 years ago, the insurance industry underwrote its plans, which gave actuaries the power to decide which populations would receive insurance. "Underwriting has now disappeared, which means any person who comes to an insurance plan, they can be underwritten," which is definitely a patient-centered move. This means, however, that the responsibility to ensure that the enrolled population is healthy rests on the health plan's shoulders, along with the providers.

Thus, health plans have a tremendous challenge on their hands, Beveridge said, with burgeoning obesity rates and an increasing percentage of Americans living with unmanaged chronic conditions, including:

- 50% with hypertension
- More than 80% with hyperlipidemia
- 43% who are hyperglycemic

With healthcare costs rising steeply over the years, and currently tallying at 18.3% of the nation's GDP, chronic conditions account for 80% of healthcare spending, Beveridge said. These statistics are staggering and need to be reduced. Therefore, the top priority for health plans is to change the health of the population. To add to this, changes within the reimbursement system—which eliminated the Sustainable Growth Rate "patch" and replaced it with the Medicare Access and CHIP Reauthorization Act—are steadily moving toward value-based payments. CMS has set its goals to tie nearly 50% of Medicare payments to quality, through alternate payment models, by 2018.

"Whether we call it value or risk-based care, it is coming," said Beveridge. He then provided a perspective of what this transition means for the payers in terms of benchmarking the costs. "In the old world of fee-for-service (FFS), the payer was only managing the ceiling, or the upper limit of the costs." So, the payers developed systems to deal with this ceiling and to identify the cause of variations in resource use. However, the current transition toward risk-based payment models, Beveridge said, is forcing payers—CMS as well as private health plans—to think about the floor of the variance, to ensure that providers are paying attention to the quality of care that they render.

Beveridge explained that bundled payments can bridge the transition of provider groups from no-risk FFS to full-risk payment models. And value-based care has achieved its objectives for Humana. Beveridge showed that Humana's Medicare Advantage members had much better outcomes in a value-based healthcare setting compared with an FFS setting. This paralleled a 20% reduction in overall medical costs, "Which is why CMS is trying to move enrollees from FFS to risk-based models," he said.

Beveridge then went on to explain the distinct role of the various providers in a value-based healthcare world. In primary care, unlike in oncology, moving from FFS to value-based care results in a 20% reduction in global costs. This, Beveridge said, will force primary care physicians (PCPs) to take on an increasing amount of responsibility for their patient's health, since a PCP's payments will be based on the patient's health. "So, a lot of decisions in the FFS world that are being made by the payer will now be made by clinicians who are looking at the quality and structure. The patient–PCP relationship will be much stronger, because they will be the focal point for which people now obtain specialist care."

Care will be more integrated and team-based, and there will be greater communication between the PCP and specialists, which will also involve a tremendous amount of data exchange. The emphasis, when choosing the specialist, Beveridge believes, will be their track record of quality care and outcomes, which will indirectly impact the PCP's share of risk.

"Diagnostics will help guide choice of value treatments," said Beveridge, adding that the pharmaceutical industry, overall, will undergo greater scrutiny with a push for innovative products.

He also believes that in-home care will be increasingly popular, as it has been proven to be significantly less expensive than hospital-based care, but hospitals will simultaneously have to evolve and address high costs. "Palliative care will continue to expand significantly," Beveridge added, stating that the existing lack of communication between the patient and the provider is what is responsible for the patient being administered chemotherapy 3 to 4 weeks before death. ◆


Roy Beveridge, MD, delivers the keynote speech at Patient-Centered Oncology Care®.
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# Developments in Immunotherapy at PCOC®: The "Living Drugs"

*Surabhi Dangi-Garimella, PhD*

PORTER

**IMMUNOTHERAPY AGENTS THAT TARGET** specific proteins in the immune response pathways have enraptured providers of cancer care. Monoclonal antibodies, including PD-1 inhibitors nivolumab and pembrolizumab, and the PD-L1 inhibitor atezolizumab, have improved outcomes in a variety of cancer types (both solid and liquid), alone and as combination therapies.

Another exciting field in immunotherapy is chimeric antigen receptor (CAR)-T cells. To provide an overview of this evolving field, *The American Journal of Managed Care*® invited David L. Porter, MD, director, Bone Marrow Transplantation; Jodi Fisher Horowitz, professor in leukemia care excellence, University of Pennsylvania (U-Penn) Health System, Philadelphia, to kick off the 5th annual Patient-Centered Oncology Care® (PCOC®) meeting in Baltimore on November 17, 2016.

The CAR-T cells have a dual purpose, Porter explained. They are modified to recognize and bind a specific protein on the surface of cancer cells and to improve the binding of the T cell to the cancer cell surface. Additionally, there are signals that promote T-cell activation, growth, and survival, which are achieved via transfecting a lentiviral vector into the T cells.

"At U-Penn, we have treated about 340 patients with CAR-T cells," Porter said. This includes:

- 62 adults with chronic lymphocytic leukemia (CLL)
- 153 children and adults with acute lymphoblastic leukemia (ALL)
- 39 adults with non-Hodgkin leukemia
- 12 adults with multiple myeloma
- 74 adults with other cancer types

Porter explained that, CLL, which is thought of as a slow-growing cancer, "can be aggressive and life threatening and result in the accumulation of malignant B cells." With a median survival time between 2 and 20 years, patients with relapsed/refractory CLL have a poor prognosis and are in need of more potent therapies, he said. Although allogenic bone marrow transplant or allogenic stem cell transplant (ASCT) is an option, it is a very risky procedure and many patients are ineligible due to their age, advanced disease stage, or comorbidities. Porter stated that these challenges make it vital to develop newer options for patients with CLL.

Porter then explained the specific steps involved in the treatment process:

- **Cell collection.** T cells are collected from the patient by a process called "apheresis," where blood is drawn from the patient, one or more blood components are removed, and the remaining blood is then returned to the body.
- **In vitro manipulation.** T cells are reengineered, by transfection with a lentiviral vector, to produce CARs on their surface. The T cells are now called CAR-T cells.
- **Expansion.** The reengineered cells are then "expanded" by allowing them to multiply in the laboratory. "T cells can expand between 1000- and 10,000-fold…they are living drugs," Porter said.
- **Infusion.** A majority of patients are treated with a chemotherapy agent before they are infused with the reengineered CAR-T cells.

Porter shared results from a trial evaluating CTL109 treatment, which is a CAR-T treatment being developed by Novartis, in CLL (**Table 1**).

**TABLE 1.** Overall Response to CTL019 in Relapsed/Refractory CLL

| RESPONSE | N | PERCENT RESPONSE |
|---|---|---|
| Complete response | 11/43 | 26% |
| Partial response | 10/43 | 23% |
| Overall response | 21/43 | 49% |

CLL indicates chronic lymphocytic leukemia.

"One of the 43 patients who participated in the trial achieved complete remission and had no measurable evidence of leukemia by day 31," Porter said. By summer of 2016, the patient remained in remission, 6 years following infusion with CTL109.

Another category of patients with poor outcomes is those with relapsed/refractory ALL. With a median survival rate less than 1 year and a 3-year survival less than 25%, these patients do not respond well to ASCT, making them ideal recipients for CAR treatment.

Porter went on to show results from multiple ALL trials that are ongoing at different sites within the United States (**Table 2**).

**TABLE 2.** Response to CAR-T Cells in Relapsed/Refractory ALL: Presented at the 2016 ASCO Annual Meeting

| STUDY | CONSTRUCT | N | COMPLETE RESPONSE (%) |
|---|---|---|---|
| Seattle | CD3z 4-1BB | 27/205 | 94% |
| U-Penn | CD3z 4-1BB | 34/205 | 72% |
| MSKCC | CD3z CD28 | 46/205 | 78% |
| Seattle Children's | CD3z 4-1BB | 36/205 | 91% |
| U-Penn | CD3z 4-1BB | 59/205 | 93% |

ALL indicates acute lymphoblastic leukemia; ASCO, American Society of Oncology; CAR, chimeric antigen receptor; U-Penn, University of Pennsylvania; MSKCC, Memorial Sloan Kettering Cancer Center.

## Toxicity

The treatment does not result in much infusional toxicity, "but the treatment results in hepatotoxicity and renal toxicity, which are reversible and associated with hypotension," Porter said. While tumor lysis syndrome is common, it can be managed; however, cytokine release syndrome, or CRS, is the most serious toxicity associated with CAR-T treatment. Almost all patients who respond to treatment develop CRS 1 to 14 days after infusion with the modified T cells.

CRS, Porter said, is characterized by high fever, myalgias, nausea, fatigue, anorexia, hypoxia, and hypotension. Patients who respond to CAR-T treatment present with a significant spike in IL-6, modest spike in IFN-gamma and TNF-alpha, and a mild increase in IL-2. Currently, tocilizumab, an IL-6 receptor antagonist, is administered between days 2 to 18 to rapidly reverse CRS. "However, the question is, when do we start treatment without affecting the efficacy of CAR-T treatment?" Porter said.

Porter ended his talk saying, "CAR-T–cell therapy is here to stay with trials expanding to other B cell malignancies and solid tumors." ◆

# Immuno-Oncology Versus Precision Medicine: Where Is Cancer Care Headed?

*Surabhi Dangi-Garimella, PhD*

**FOR DECADES, ADVANCES IN CANCER CARE** have struggled with improving patient prognosis and extending survival by weeks or a few months, at most, particularly in patients who may have developed an advanced form of the cancer. The advent of immunotherapy, however, has transformed this picture and has even raised the hope of being able to permanently cure these patients.

At the 5th annual Patient-Centered Oncology Care® meeting, hosted by *The American Journal of Managed Care®* (*AJMC®*), November 17-18, 2016, in Baltimore, Joseph Alvarnas, MD, associate professor, Department of Hematology and Hematopoietic Cell Transplantation, City of Hope, Duarte, California, engaged experts with diverse experiences and expertise to discuss the contradiction presented by immuno-oncology agents in the world of precision medicine. Alvarnas is also the editor-in-chief of *Evidence-Based Oncology*™, published by *AJMC®*.

Joining Alvarnas were David Fabrizio, leader of Cancer Immunotherapy, Foundation Medicine, Inc; Sean Khozin, MD, MPH, senior medical officer, FDA; and David L. Porter, MD, director, Bone Marrow Transplantation, Jodi Fisher Horowitz professor in leukemia care excellence, University of Pennsylvania Health System, Philadelphia.

Alvarnas first asked Fabrizio to share his opinion on how a patient's genomic information could best be exploited in treatments that utilize the immune system and the strategy that Foundation Medicine was working on to improve the efficiency of immunotherapy to develop a standard practice.

According to Fabrizio, using an assay score comes down to the human interpretation of a qualitative score, which makes it hard to adopt to standard best practices…and leads to genomic solutions. "One such assay is the tumor mutation burden. We do this with CGP [comprehensive genomic profiling] to understand the number of somatic mutations in a person's cancer genome," Fabrizio said. CGP, he added, gives an estimate of how the immune system will respond, and the company has been making strides with looking for more unified methods of analysis.

How can we bring standardization to the diagnostic industry? "I think standardization is a huge part of the equation," Khozin said. CGP, he believes, requires a substantially different approach, one that has not been typically available at large organizations, including the FDA. "Academic institutions have more data mining skills…what we need is a new approach to data science to develop predictive algorithms." Khozin emphasized the important role of the "omics" approach—proteomics, genomics, the entire microbiome—in patient response to therapy.

Porter added that there have been efforts to integrate omics data in the clinic. "We are looking at biomarkers on T cells. A part of this is committing to and being able to have the right samples and tests," Porter explained. "We are probably missing huge opportunities right now with our clinical trials; we are banking a lot of samples…DNA, RNA, etc…but we don't know how to manage them right now, although we will in the future." He also added that trial design would change in the future and that we may have to settle with smaller and more unique subsets of patients.

Khozin corroborated with Porter that the FDA is looking into such trial designs, as well. "We don't have to run a large study, rather [we have to] leverage [electronic health record] data that is at the point of care." The FDA has focused its attention on how care can be advanced, especially with immunotherapy increasingly being a part of the equation. The recently commissioned Oncology Center of Excellence (OCE)[1] is working to consolidate oncology functions across the FDA to address the continuum of care in a coherent fashion, Khozin told the audience.

## Paying for CGP and Immunotherapy

When asked about payer response to these new genomic technologies, Fabrizio said that payers have been slow to adopt these advancements, but that they are being more proactive and more engaging in discussions with their company. "I see this as an encouraging sign for the most efficient healthcare possible," he added.

Porter also emphasized that because of the scale at which the chimeric antigen receptor (CAR) treatment is being developed, it ends up being very expensive. The treatment is being personalized for each individual patient, with strong biotechnology input. "Third-party payers have not at all been involved in paying for this, »

ALVARNAS

FABRIZIO

PORTER


Panelists discuss the contradiction presented by precision medicine and immunotherapies. © Dave McIntosh/Patient-Centered Oncology Care® 2016

although they have been asked to pay for the standard-of-care treatment," he added. "Supportive care is not really being denied by payers, but academic institutions cannot fund this type of care…the biggest grants can maybe cover a couple patients a year." Porter strongly believes that the pharmaceutical and biotechnology industry would have to provide maximal support for more clinical use of this technology. "We are breaking new ground here and we'd like to see more collaboration," he added. »

As of now, CAR treatment remains in the trial stage.

Can the FDA lend any support with helping payers navigate these novel technologies to develop payment policies?

"The FDA does not traditionally involve itself in cost mandates, but we are thinking about value across the entire spectrum of drug development," Khozin said, adding that Richard Pazdur, MD, who heads the OCE, is thinking of collaborating with the National Cancer Institute and CMS on value creation, »

not the cost of drugs. When asked to provide a view of the direction toward which the field was moving, Fabrizio said that a more personalized approach for immunotherapy was necessary, such as using CGP to uncover neoantigenic epitopes. He added, however, that deciding on trial endpoints is a challenge, especially with a smaller batch of trial participants, the direction toward which the field seems to be moving. "From a diagnostic test point of view, we want to understand actionable genomic targets, such as tumor mutation burden or identifying neoantigens."

According to Porter, CAR-T is "a once-and-done therapy." »

This raises the potential for alternate trial endpoints, such as response rate and achieving minimal residual disease status.

Khozin clarified that the FDA does not always push for overall survival. "We sometimes hear that sponsors say they have to do randomized studies for payers or other agencies…but we ask them not to conduct randomized clinical trials." Referencing the cobas liquid biopsy companion diagnostic that was approved last year,[2] Khozin said that the FDA has » received several other proposals for such liquid biopsy tests, which point to using the levels of circulating tumor cells as a surrogate endpoint.

Porter summed the discussion by saying, "This era of immuno-oncology is revolutionary. It is one of the most exciting times in oncology, and the rate of change is staggering—from a clinical trial, regulatory, and data standpoint. Information is being generated at a very fast pace and needs rapid dissemination, and we need continuous conversation among the various entities to keep the progress going." ◆


REFERENCES

1. Dangi-Garimella, S. 5 Ongoing Initiatives at the FDA. *The American Journal of Managed Care®* website. http://www.ajmc.com/newsroom/5-initiatives-catching-speed-at-the-fda. Published August 26, 2016. Accessed November 18, 2016.

2. Dangi-Garimella, S. First Liquid Biopsy Companion Diagnostic, for Erlotinib, Approved by FDA. *The American Journal of Managed Care®* website. http://www.ajmc.com/newsroom/first-liquid-biopsy-companion-diagnostic-for-erlotinib-approved-by-fda. Published June 2, 2016. Accessed November 18, 2016.


# TAPUR Trial Expands Who Can Join Clinical Trials, If Payers Fund Genomic Tests

*Mary Caffrey*

**WITH TAPUR, THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO)** is pushing the boundaries of who can take part in a clinical trial. Things like being a teenager and a past cancer patient are coming down as barriers—in some cases, even patients with HIV can take part.

But one hurdle—payer coverage—could keep some participants out of the study, whose formal name, Targeted Agent and Profiling Utilization Registry, describes its mission of finding new groups of patients who could benefit from existing cancer drugs, based on their genetic profile.

Pam Mangat, MS, associate director for TAPUR in the research and analysis division of ASCO, offered an update on the study at Patient-Centered Oncology Care® (PCOC®), which took place November 17-18, 2016, in Baltimore, Maryland.

TAPUR seeks to push the envelope of precision medicine in several ways: first, it gives community oncologists and their patients free access to new therapies that have been approved by FDA for 1 or more uses, but show potential for off-label use based on common genetic variants. Second, the trial seeks patients who look more like a real-world population. Finally, TAPUR will educate oncologists from more remote locations and community settings about the process of precision medicine.

The study targets patients with advanced solid tumors, B-cell non-Hodgkins lymphoma, or multiple myeloma who have exhausted current approved treatment options. As Mangat explained, once the oncologist has the patient's genomic test results, if a variant is identified that could suggest a match to one of the 17 drugs being studied in TAPUR, the physician can consult with a volunteer tumor board convened by ASCO to see if the patient's participation is appropriate.

TAPUR's protocol calls for cancer patients to have a genomic test in hand to be screened for the trial. But if a patient's insurer won't fund the test, the chance to gain access to the study drugs could be lost. "This is a challenge in our study," Mangat said. Yet, payers are among the stakeholders who stand to benefit from TAPUR, she said, because they will gain data on test and drug use to inform future coverage decisions.

There are some examples of test coverage: Priority Health in Michigan will pay for genomic tests for participants in that state, and Carolinas HealthCare System has reached an agreement with the test maker Caris Life Sciences to limit out-of-pocket costs for those taking part in North Carolina. As TAPUR expands to 63 participating sites by the end of 2016, Mangat emphasized that the study is "test agnostic," meaning it doesn't prefer a single manufacturer, and that it will use earlier tests instead of requiring a fresh biopsy when a patient is screened for the study.

TAPUR will study 17 different cancer drugs in 15 separate therapeutic regimens. So far, 170 patients have registered and 102 were taking study drugs at the time of PCOC®. Initial cohorts of up to 10 patients are being created, with the patients each taking the same drug for the same cancer based on the same genetic variant. Right now, of course, many cohorts only have 1 patient; Mangat said that as the study evolves, some cohorts may be combined, while others will add 18 patients if at least 2 patients respond to the drug. If 7 patients in that larger group respond, this would indicate a signal, she said.

The study benefits community oncologists and their patients by moving precision medicine beyond major academic centers, Mangat explained. "Not all oncologists have access to an in-house lab," she said. The ability to work with the trial's tumor board to decide whether a patient's genomic test reveals an actionable mutation will be a valuable experience for many oncologists, Mangat added.

But TAPUR's most intriguing feature may be a protocol that allows oncologists to cast a much larger net for potential participants. The study, Mangat said, "has wider criteria for acceptable organ function," and some of the drugs involved can be studied on patients with HIV or brain metastases, if they meet certain criteria.

Mangat was especially excited about upcoming plans to include teenagers in the study. "We've been working with our pharmaceutical companies," she said. ASCO asked, "Can we lower the age if there is some dosing established for your drug? And the response was very positive."

"We are planning to lower the age to 12 years old," by early 2017, she said. ◆

MANGAT

# Bundled Payments and Other Cost-Management Approaches to Oncology Care

*Christina Mattina*

EASON

LEWIS

RUIZ DE SOMOCURCIO

SAGAR

**THE TRANSITION TO VALUE-BASED CARE** has inspired the creation of modified and novel care delivery and payment models. But how easy or difficult would it be to adopt these models when caring for patients with cancer? At the 5th annual Patient-Centered Oncology Care® meeting, experts from the healthcare world—both providers and payers—shared their views on how bundled payments, clinical pathways, and other value-based approaches can fit into the concept of patient-centered oncology care. The discussion, "Managing Cancer Care Costs While Ensuring Adequate Outcomes and Quality of Care," was moderated by Bruce A. Feinberg, DO, vice president and chief medical officer of Cardinal Health Specialty Solutions.

Feinberg began the discussion by asking Kim D. Eason, MEd, manager, at Horizon Blue Cross Blue Shield of New Jersey, about the assumption that bundled care models are a poor fit for cancer care. Eason believes that the bundled payment model is in fact ideal for a chronic disease like cancer. Horizon initiated bundled payments for orthopedics and then progressed to oncology, Eason said, adding that Horizon consults with physicians prior to finalizing coverage decisions for drugs and services.

Another panelist familiar with this process was Michael Ruiz de Somocurcio, MBA, vice president of payer and provider collaboration at Regional Cancer Care Associates (RCCA). He said that when the practice works with its payer partners, like Horizon and Cigna, to develop reimbursement methodologies, the resulting bundles take into account the patient experience and quality metrics based on the Oncology Care Model (OCM). The bundled payment program only entails upside risk for the medical group, he explained, because the model is still a learning experience for RCCA and the other participating providers. "Our practices are still getting their fee-for-service reimbursement, because we believe it's important to understand how things are working," without having an impact on the revenue going out to those practices, Eason told the audience.

According to Bhuvana Sagar, MD, national medical director, Cigna Healthcare, guidelines are key to defining value and ensuring that providers do not take advantage of the "quality floor," which is the baseline minimum quality of care. She emphasized that these patient-centered, evidence-based guidelines and value propositions should come from groups like the National Comprehensive Cancer Network (NCCN) or the American Society of Clinical Oncology, not payers or providers.

Ruiz de Somocurcio added that Sagar and the Horizon medical team had worked with RCCA to discuss the goals of quality metric reporting to align their practices with the OCM. Eason agreed that payers like Horizon want to gather facts from clinicians instead of blindly mandating specific clinical pathways. To help reduce underutilization, she said, Horizon has added a clinical advisory committee that examines the reported data and reaches out to practices if there are patterns that could indicate "cherry picking" of data.

Sagar said that Cigna is also reluctant to dictate specific treatment pathways to practitioners. Instead, the insurer relies on the NCCN guidelines, whenever possible, to avoid the pressure of payer-dictated guidelines and the perception that payers only care about cost, not quality. "We do emphasize that we want the best outcome possible," she said, especially if these outcomes can be achieved at a lower cost.

"Payers want to gather facts from clinicians instead of blindly mandating clinical pathwyas," said Kim D. Eason, MEd.
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Shifting gears, Feinberg discussed the current state of genetic testing reimbursement with Karen E. Lewis, MS, MM, CGC, solution management director of genetic testing at AIM Specialty Health. Lewis suggested that pharmaceutical companies should consider paying for genetic testing, because it can help determine which patients will respond the best to a certain medication, so that "we can utilize our dollars a whole lot better." However, she also cautioned that genetic testing should only be performed if the clinician can envision how the test may benefit the patient and how the results may fit into the structure of the patient's care plan, as opposed to performing tests simply because they are available.

Feinberg stressed that patients in America generally have a "more is better" mentality—whether they seek more information from genetic testing or request alternative treatments or drugs. Sagar and Ruiz de Somocurcio challenged that assumption, saying that value-based programs should encourage more nuanced dialogue on what each patient actually wants and how to address those desires. Patients may not want more drugs and tests, Sagar said, if these services are actually making them sicker and keeping them in the hospital longer.

Panelists emphasized that payers and providers must understand their unique roles in order to provide patient-centered care. Citing the example of end-of-life conversations, Ruiz de Somocurcio said that they may be less appropriate coming from an oncologist than from a primary care physician. Similarly, payers have noted that patients respond better to hearing about payment changes from their trusted physician, as insurers are "just who pays the claims," Eason said.

Responding to the earlier discussion on "more is better," an audience member said that many patients actually choose less aggressive care when they discuss their goals and imperatives with their physicians. Therefore, standard cancer care should include conversations with patients and their families on their desired balance of treatment options and quality of life or financial ramifications, for instance. The panelists agreed when the audience member stated that "if we're really going to be person-centered, we have to focus on all of those things early on." ◆

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# Panel Presents Unique Cost-Sharing Viewpoints in Oncology Care

*Christina Mattina*

DE SOUZA

KLEIN

SHRANK

WATSON

**DURING THE 5TH ANNUAL PATIENT-CENTERED ONCOLOGY CARE® MEETING,** stakeholders with diverse experiences in the cancer care landscape discussed the effects of cost sharing during the panel, "Does Cost Sharing Influence Patient Adherence and Outcomes in Oncology?"

Moderator Joseph Alvarnas, MD, associate professor, Department of Hematology and Hematopoietic Cell Transplantation, City of Hope, Duarte, California, kicked off the discussion by referencing a "poignant and powerful" speech made the night before in which Allison Morse, a cancer survivor, discussed her experiences negotiating drug prices at the pharmacy and having to choose between paying rent or for her cancer medications. To begin the panel discussion, he turned to another patient advocate, Samantha Watson, MBA, founder and CEO of the Samfund, who explained the impacts of cost sharing from the perspective of the patient.

Watson explained that "when the burden of cost sharing falls too heavily on the patient," it forces them to make "impossible decisions" between their financial health and their physical health. In her experience, most patients confronted with this choice will "incur the cost no matter what" by using a credit card, but some will decide to skip treatment altogether.

From a payer perspective, William H. Shrank, MD, MSHS, chief medical officer of the University of Pittsburgh Medical Center Health Plan, said that the harm and suffering experienced by patients in these instances result from "a blunt formulary without really thoughtful consideration about the clinical nuance."

Jonas A. de Souza, MD, MBA, assistant professor of medicine at the University of Chicago, concurred that benefits must be redesigned to alleviate the out-of-pocket cost burden on patients. He compared cancer care to an iceberg, with financial issues like cost sharing being at the tip. "This tip is what will sink the ship," he warned, by bankrupting patients and actually worsening their chances of survival.

As president of the Patient Access Network (PAN) Foundation, Daniel J. Klein, MHS, has seen the consequences of this "broken system" first hand. His organization helps patients navigate their high out-of-pocket (OOP) costs and provides financial assistance that allows 90% of recipients to initiate or stay on their cancer treatments. Without this safety net, however, there are many cracks that patients can fall through, even in programs like Medicare, Klein said.

Shrank added that although patient assistance programs sponsored by pharmaceutical companies are far from ideal, "there are a lot of stopgaps to help patients meet their needs if they know how to access them." Watson agreed, but expressed concern that patients often do not access the significant amount of resources that are available to them. She argued that the disconnect between patients and resources indicates a much larger problem—that the OOP costs affecting patients' treatment decisions are not acknowledged by the current system.

Acknowledging that charitable assistance can be difficult for patients to navigate, Klein said that a bigger issue is actually the ineffectiveness of cost sharing. Patients with cancer are not more likely to become better healthcare consumers when they are asked to pay a copay or deductible, he said. Alvarnas suggested that cost sharing could be used to improve the system by directing patients toward preferred pathways and prioritizing efficient drugs. Shrank agreed that cost sharing at its core is meant to work as a barrier, but that an alternative approach to value could instead reward patients for adhering to their treatment regimens, so "all of those pieces can fit into a rich, value-based contracting design."

The idea that cost sharing could be used as both a tool and a barrier was reinforced by de Souza, who suggested providing incentives to patients for preventive services or palliative care while also discouraging low-value care. He also discussed the possibility of implementing dynamic benefit design, such as different OOP costs for the same drug based on its benefit for the patient's specific condition.

Watson routed the discussion back to the patient's point of view, saying that patients newly diagnosed with cancer may not be ready to discuss cost and value—rather, they may be more concerned with their chances of survival. "In that case, a lot of the legwork and decisions about value-based care need to be made behind the scenes," she said, so that when patients are presented with their options, they are not making decisions based on cost.

Instead, providers should ensure patients are aware of options like social workers and financial assistance programs, which, she believes, can reduce the patient's stress earlier and improve their ability to manage costs down the line. Both Shrank and Klein agreed with the importance of having a robust case management system to help patients navigate the day-to-day challenges of oncology care. According to Klein, however, the lack of reimbursement for case management remains a challenge.

Shifting the conversation back to cost sharing, Klein talked about the need to educate policy makers that patients with serious illness should not be treated the same as a "regular patient," where cost sharing is used as a tool to keep premiums low or to get patients to choose less expensive treatment options. Patients with cancer will not want to be asked questions about treatment choices, as they instead look to their healthcare provider to direct them to the best treatment.

Shrank agreed that current formularies are not constructed with the unique needs of cancer patients in mind. It may also be more difficult to quantitatively demonstrate to payers the effectiveness of eliminating cost sharing because the oncology medications are expensive and will not be able to prevent subsequent hospitalizations. Instead, payers are more likely to respond to the argument that eliminating cost sharing will result in better quality of care and improved patient experience.

To wrap up the panel discussion, Klein looked to the future, saying that those looking to overhaul the healthcare system need to "understand that not being thoughtful in the near term could leave a lot of people with challenges in terms of getting access to their treatment." He encouraged providers, payers, and patients to work together to increase education and transparency, encourage a rational benefit system, and maintain critical safety nets. ◆

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# Integrating Patient-Centered Outcomes in APMs

*Surabhi Dangi-Garimella, PhD*

**HEALTH PLANS ARE INCREASINGLY CREATING** contracts with providers that tie the quality of care to payment decisions, a trend that has already made its mark in oncology with bundled and episodic payments. While most find it difficult to move away from process measures, clinics are transitioning toward more meaningful quality-of-care measures. But do these measures really improve patient care?

At the 5th annual Patient-Centered Oncology Care® meeting in Baltimore, which was held on November 17-18, 2016, moderator Bruce Feinberg, DO, was joined by Bhuvana Sagar, MD, national medical director, Cigna Healthcare; Ted Okon, MBA, executive director, Community Oncology Alliance; and Stuart Goldberg, MD, chief medical officer, Cancer Outcomes Tracking and Analysis (COTA), John Theurer Cancer Center, for the panel discussion, "How Patient-Centered Are Payment Models?"

Feinberg asked the panel, "How patient-centered is medicine today?"

Goldberg explained that everyone defines value as the ratio of outcomes to cost, the most important part of which is defining the outcomes that are important. "At COTA, we track all the outcomes and costs. But what we can argue is, 'What does the patient see as value… survival or quality?'" Goldberg thinks that the field has so far been unsuccessful in adequately defining patient-centered outcomes.

Referencing Cigna's value-based models, Sagar pointed out that the patient constitutes the core of their medical home model, adding, "But we want to ensure that the provider is capable of delivering the required care." Sagar iterated that information sharing, shared decision making, early palliation, and addressing emotional and physical symptoms are some of the tenets of their patient-centered medical home model. "We also offer case managers to help providers and patients navigate the care journey."

She echoed Goldberg's thoughts, saying that the focus should be patient outcomes, not just process measures. "We need to navigate patients through other aspects of their care, such as financial processes. However, we are currently a little stuck in our journey toward value-based care."

Okon told the audience that at the recent Community Oncology Alliance (COA) Payer Summit,[1] "We had a lot of focus on the [Oncology Care Model (OCM)]. We are big proponents of the OCM, but part of the problem is that anyone involved in the OCM model knows it is process-centric."


" What does the patient see as value?" asked Stuart Goldberg, MD.
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Speaking to the exhaustive reporting requirements of the various new alternative payment models, Goldberg said that the time that a care provider has to spend in documenting data is increasing. "At our community centers, we are constantly moving patients around our network…but it's tough. It's hard to measure quality metrics and outcomes when you are in the blind with the kind of patients you are treating."

Okon said that he believes it's time for care providers and payers to move on to the next iteration of the OCM. He believes that CMS' Innovation Center, which developed the OCM, needs to change its focus. "They should ask the provider, 'Where are you going with your treatment…curative, palliative, or recurrence?' COA is in conversation with CMS about OCM 2.0—to move away from processes and make it really patient-centered."

Coming from a health plan, Sagar believes in giving this transition some more time. "Value-based care is a step in the right direction…there will be a lot of learning and implementing for both payers and providers." She believes, however, that although better survival is the outcome that care providers and payers want for their patient, "We also want to improve their care journey."

This was the idea rooted in COA's Oncology Medical Home (OMH),[2] Okon told the audience. "When we initiated OMH 5 years back, Dr Bruce Gould spearheaded the project," he said. Gould connected with other providers, payers, and patients, and developed patient focus groups to collect information on what patients' value most and what they expect from their cancer care. "Turned out, all 3 groups were interested in outcomes. Then it diverged a little bit, but their interests were similar," Okon said.

"Our focus is to ensure that patients have all the information they need, they get evidence-based guidelines, and they have access to their doctor," Sagar said. She added that patients being treated for cancer are a difficult population to manage, primarily because of the complexity of the disease at hand. "So, we look at centers of excellence and other options. We want to make sure they are getting their treatment. We just want to identify the ideal place to receive care while managing costs…and keeping those costs down."

On their end, providers are working to identify the sources of variance, so they can try to limit them while preventing waste within the system. "The OCM model, for us, is the first step toward the value model," Goldberg told the audience. "There's a lot of waste or lower-value care being delivered, plus variability in care delivered within the same center. We are trying to identify this variance." ◆

OKON

GOLDBERG

SAGAR

**"OUR FOCUS IS TO ENSURE THAT PATIENTS HAVE ALL THE INFORMATION THEY NEED, THEY GET EVIDENCE-BASED GUIDELINES, AND THEY HAVE ACCESS TO THEIR DOCTOR."**

—Bhuvana Sagar, MD

REFERENCES

1. COA Payer Exchange Summit 2016. *The American Journal of Managed Care®* website. http://www.ajmc.com/conferences/coa-payer-exchange-summit-2016. Published October 25-26, 2016. Accessed November 23, 2016.

2. Oncology Medical Home website. http://www.medicalhomeoncology.org/. Accessed November 23, 2016.

# Providers Have Power to Make Health IT Work for Them, Panel Says

*Mary Caffrey*

BELINSON

HIRSCH

STRICKER

**WHEN MODERATOR BRUCE FEINBERG, DO,** described the "unfulfilled promise" of healthcare information technology (IT) during Patient-Centered Oncology Care® (PCOC®), he was being kind.

During the panel discussion, "Surmounting Health IT Challenges in Oncology Care," Jonathan Hirsch, MSc, founder and president of Sypase, had much harsher terms for the software most doctors use in electronic health records (EHRs).

Feinberg, an oncologist whose former practice was an early adopter of health IT, expressed dismay at the thought that the systems into which providers have sunk fortunes don't give providers what they need. He was not happy about the thought of a solution that would take more time from the work day. "You're not going to fix this thing that's broken by making me do more things to overcome what's broken," he said.

"That's the tragedy of how IT has unfolded in healthcare," said Hirsch, who later described the frustration that doctors and nurses experience having to cut and paste notes multiple times or having to extract data from systems.

But Hirsch and fellow panelists Suzanne Belinson, PhD, MPH, executive director of the Center for Clinical Effectiveness at the Blue Cross and Blue Shield Association (BCBSA), and Carrie Tompkins Stricker, PhD, RN, AOCN, of Carevive Systems, had advice for attendees: the EHR vendors who make money selling their data need providers as much as providers need them, and by being smarter consumers, they can leverage better solutions, greater interoperability, and more results from their systems.

Thus far, health IT has fallen short of its mission of connecting providers in ways that allow faster, evidence-based decisions at the point of care. The rocky start for a new EHR system was cited in January reports that MD Anderson Cancer Center, in Houston, would cut up to 1000 jobs.[1] And in an interview with *Vox* about his healthcare record, President Barack Obama, cited challenges with EHRs as something that didn't go as well as the administration had hoped.[2]

**"AS PROVIDERS ARE TAKING ON MORE RISK, THEY NEED EVIDENCE AT THEIR FINGERTIPS."**

—Suzanne Belinson, PhD, MPH

Obama cited some of the same concerns voiced by the PCOC® panelists: the interests of technology providers may not align with long-term goals like interoperability—the ability of different health IT systems to talk to each other. "I'm optimistic that, over time, it's eventually going to get better," Obama said. "It's been a lot slower than I would have expected."

During the November 17-18, 2016, conference in Baltimore, Hirsch, Belinson, and Stricker agreed. But they portrayed a landscape that is about to change, as forces that Hirsch called "wedges" are about to compel interoperability.

The term "wedges," Hirsch said, refers to a crack in the system that will allow things to break open. In this case, he sees the arrival of genomics as forcing a revolution of health IT in cancer care. Oncology has been one of the worst practice areas for health IT, he said, because patients have so many encounters with so many parts of the health system, over an extended period.

"We don't need to junk everything," said Stricker, in response to Feinberg's question of whether healthcare would have to "start over" with IT. She and the other panelists said what's coming are complementary systems that will overlay what doctors are using now, but will finally give doctors what they need at the point of care. In cancer care, she said, CMS' Oncology Care Model will require data sharing from radiology, palliative care, and survivorship care.

As valued-based care takes hold, Hirsch said, the question arises, "How are you going to track patient outcomes on an individual level—and tie to treatments?"

Besides precision medicine, Belinson said, payment reform will compel change because oncologists will demand up-to-date evidence. "As providers are taking on more risk, they need evidence at their fingertips," she said. "That evidence evolves at a faster rate than any one person can consume."

These overlay products, she said, must be "agnostic" to whatever EHR the provider is using. While entrepreneurs are working hard to repair what's not working, Belinson said, "We have to collaborate now in a way that we may have never collaborated in the past. Stakeholder engagement means more than just bringing a patient and provider together," as payers, pharmaceutical companies, and multiple levels of providers all need to be connected.

Feinberg was skeptical that providers would share their enthusiasm. Hirsch said providers must be their own "wedge" and use their power to force EHR vendors to give them what they need. Do practices ask the question of whether their vendor is selling their data? If that's happening, what are practices getting in exchange? During the question-and-answer period, speakers discussed the same problem that Obama would mention weeks later—that vendors don't want to share data because they've built a business out of charging clients to get it back.

"Providers don't realize the power they have to enforce interoperability," Hirsch said.

The final wedge, Stricker said, is patient engagement—using data to compel better care coordination and ensure that "the care team interacts at the right time," when the patient needs it. The patients and their families need to be given tools to join in decisions, she said.

Feinberg was not thrilled that a bottom-up, grassroots push for interoperability was needed after all the time and dollars spent on EHRs. He wondered when health systems would see the value in investing on better IT instead of pushing this cost on to practices. Some of this type of investment is happening, the panelists said, but demand from providers was key. "It's the grassroots that will break down the silos of information," Belinson said.

The panelists said that major health IT vendors are gaining business by starting to line up their processes with the way doctors practice. Feinberg was still skeptical. Whether future systems are called EHR or something else, he said. "That workflow tool needs to work. And it doesn't today." ◆



REFERENCES

1. Ackerman T. MD Anderson set to announce layoffs today. *Houston Chronicle* website. http://www.chron.com/news/houston-texas/article/MD-Anderson-set-to-announce-layoffs-today-10837056.php. Published and accessed January 6, 2017.

2. Watch: President Obama on the future of Obamacare. *Vox* website. http://www.vox.com/policy-and-politics/2017/1/6/14182458/obama-interview-obamacare-health-vox. Published and accessed January 6, 2017.

# Specialty Pharmacies Transforming Cancer Care

*Surabhi Dangi-Garimella, PhD*

AS THE MODEL OF COLLABORATIVE HEALTHCARE expands and grows, every person who participates in patient care will have a distinct role to play to improve patient outcomes. Specialty pharmacies are increasingly bearing the charge of dispensing, distribution reimbursement, case management, and other services that serve a patient's specific disease needs.[1]

From adherence management to communicating with physicians, coordinating financial assistance, and managing prior authorization, specialty pharmacies offer patients a variety of comprehensive services. At the Patient-Centered Oncology Care® meeting, held November 17-18, 2016, in Baltimore, J. Ike Nicoll, President, The Morrison Group, and Joshua A. Rademacher, MBA, executive vice president, Enterprise Solutions and Business Development, at Avella Specialty Pharmacy, spoke to pairing novel cancer treatments with high-touch and high-technology support.

Introducing the 2 speakers, Joseph Alvarnas, MD, editor-in-chief of *Evidence-Based Oncology*™ and co-moderator of the meeting, said, "If we are talking about patient-centered care or financially sustainable care, the mindset that goes behind that has to evolve." He pointed out that when caring for patients, the idea often gets lost or isolated, which, he said, meetings such as PCOC® can help bring to the forefront by inviting diverse stakeholders to participate. Alvarnas pointed out that a partnership with individuals who can help navigate the issue of complex, potentially toxic drugs that are typically very expensive, and ensure that patients have adequate knowledge and capacity to receive the information in an equitable way, can also help.

Nicoll, who has worked with oncologists, as they try to navigate the healthcare system and changes within it, said that his company strives to provide physicians with the infrastructure that can help them guide the cost, as well as the quality of therapy. "We would like to create a case and show how specialty pharmacy can help oncologists and providers as they provide care outside of their walls."

The complexity of cancer care, the daily innovations in the field of diagnostics and drug development, and the high cost, "Have resulted in a lot of visibility for cancer in the payer community," Nicoll said. Referencing a presentation by Michael Kolodziej, MD, when he was the national medical director for oncology, at Aetna, Nicoll showed a slide that provided insight into the top cost drivers of oncology care for Aetna. The data, presented in 2014, showed that Aetna's annual drug spend in oncology was $1.5 billion represented a 30.8% growth in spending. Inpatient spending and radiology followed at a close second, at $1.1 billion each.

Nicoll pointed out that standard cost-saving strategies used by health plans—such as lowering physician payments, increasing prior authorization requirements, creating narrow formularies and choosing generics as the preferred option, utilizing pharmacy benefit managers and specialty pharmacies, and shifting the payment burden to patients by increasing co-pays and deductibles—have had only a limited effect on bending the cost curve in oncology. "They have, however, had a significant effect on the way we coordinate and deliver care," Nicoll added.

Coming back to where healthcare stands today, Nicoll said that we are at a point where we need to choose our path between value-based treatments and the traditional volume-based care. "We have seen a number of value-based models and a great deal being done with medical homes, bundled payments, and some early forms of ACOs [accountable care organizations]," he said, adding that we are now rethinking the paradigm of how we deliver and finance care.

Nicoll indicated that as payers shift responsibility onto patients and align it more with financial responsibility, the problems arise with inherent capabilities that exist or are required, with practices and academic medical centers taking up financial risk. This has shifted the landscape for providers in terms of what is "required" in the delivery of patient-centered care, he said, because it forces physicians to think about care delivery in the broader context of the total cost of care.

"It would require clinical organizations to develop capabilities to manage their patient not just inside, but also outside their walls, to create a patient-centered experience," Nicoll added. Providers and their organizations would need to effectively engage, educate, and support the patient and their caregivers to:

- Define, direct, and manage care across the entire care continuum
- Identify issues in real time and effectively intervene to manage the patient
- Collect, evaluate, and report the key clinical and financial data necessary to demonstrate high- quality patient care

Specialty pharmacies, according to Nicoll, can play an important role in this integrated approach since this model builds upon many of the necessary functions that he and his team perform every day, including:

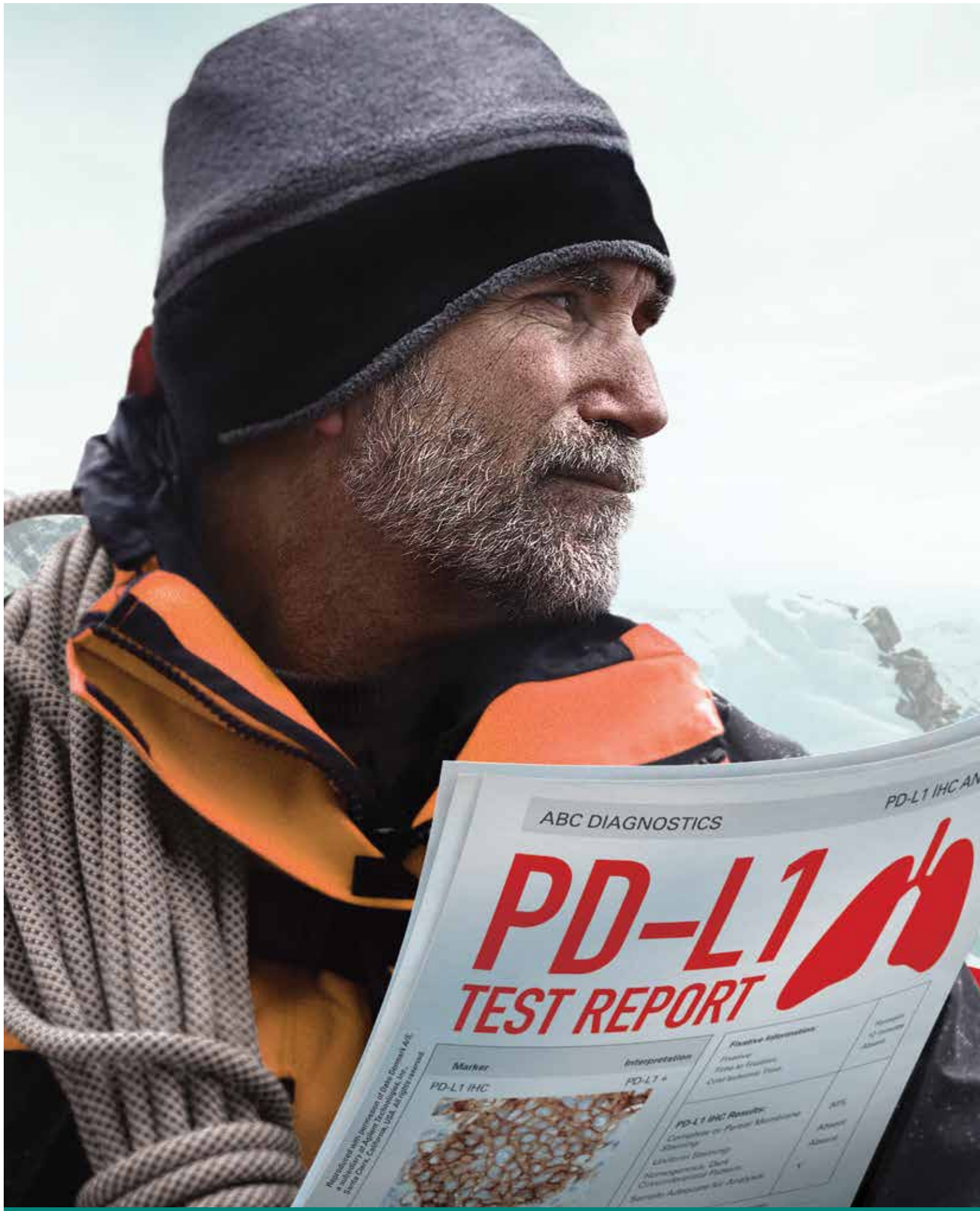
- Patient outreach/triage
- Clinical guidelines/quality
- Care management/coordination
- Technology/data analytics »

NICOLL

RADEMACHER


J. Ike Nicoll believes that the landscape has shifted for providers on what "patient-centered care" is.
© Dave McIntosh/Patient-Centered Oncology Care® 2016

Acknowledging the tremendous job that clinical teams strive to achieve with tracking and monitoring not just inpatients, but also their outpatients, Nicoll said that clinics might not always be systematic with the way things are managed. Specialty pharmacies, on the other hand, have honed these capabilities with the models they have built around these operations. While existing reimbursement models are an impediment to the collaboration between a specialty pharmacy and a clinic, value-based models could alter »



physician payment. "When it is the clinician's role to manage the patient and to be compensated based on the quality, the outcome, and the total cost of care, then you'd develop the capabilities to accommodate that," he added.

Rademacher then came up on stage to speak about the various services offered by his company. These include:

1. **Initial assessment.** Patient profile, adherence and persistence risk, predictive, and criteria-based cadence of Avella interventions. »

2. **Clinical assessment.** Patient history, concomitant and co-morbid conditions, disease-specific criteria, depression screening, social support, and disease progression rates.
3. **Clinical services**. Nursing assessments, patient education, nursing and pharmacist criteria-based cadence of interventions, and side effects and adverse events (AEs).
4. **Follow-on care support.** Clinician follow-up for AEs and/or side effects management, patient self-management tools, persistence and compliance, and documentation and shared information.

**"IT WOULD REQUIRE CLINICAL ORGANIZATIONS TO DEVELOP CAPABILITIES TO MANAGE THEIR PATIENT, NOT JUST INSIDE, BUT ALSO OUTSIDE THEIR WALLS, TO CREATE A PATIENT-CENTERED EXPERIENCE."**

—J. Ike Nicoll

Being the point of integration and clinical coordination with our oncology partners, "We make significant investments in technology, to deliver both provider-specific and patient-specific applications, such as patient portals, mobile applications, and data analytics," Rademacher said. He went on to describe some of the tools and portals that have been developed by Avella to monitor patient compliance and send feedback to providers.

Rademacher said that patients who receive counseling have, on average, a 7.8% greater medication possession ratio than those who opt out of the counseling that is provided by Avella. A successful case study for Avella was the improved adherence observed among patients with HIV using a mobile app developed by Avella—these patients presented a 49% improvement in adherence compared with the national standard.

AdhereTech and Proteus Discover are 2 technologies that the company has developed for tracking patient adherence. AdhereTech is a wireless pill bottle that gathers patient adherence information, populates and analyzes the data, and sends custom alerts to patients—all to improve patient adherence to treatment. Proteus Discover involves encapsulating an ingestible sensor into a pill or tablet to monitor adherence and also track outcomes.

Rademacher concluded that specialty pharmacy best practices, such as adherence strategies, patient engagement, and data sharing between providers and pharmacists will be critical components of value-based care delivery models. These, he believes, will force providers and pharmacies to rethink their traditional relationships and move toward true collaboration. ◆

## REFERENCES

1. Moore CD. Cancer care: the role of specialty pharmacy. *Pharmacy Times* website. http://www.pharmacytimes.com/publications/issue/2015/july2015/cancer_care. Published July 21, 2015. Accessed January 12, 2017.

# TAIHO ONCOLOGY PATIENT SUPPORT

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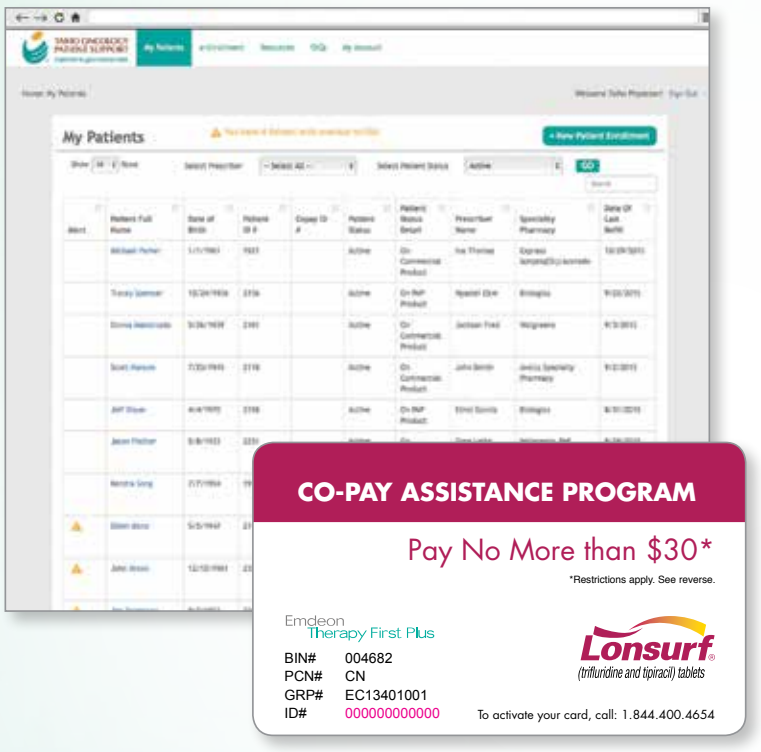


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**Please see Important Safety Information and brief summary of Prescribing Information on the following pages.**

Lonsurf®
(trifluridine and tipiracil) tablets

TAIHO ONCOLOGY

Lonsurf®
*(trifluridine and tipiracil) tablets*

## Indication

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

## Important Safety Information

### WARNINGS AND PRECAUTIONS

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

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

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

### USE IN SPECIFIC POPULATIONS

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

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

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

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

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

### ADVERSE REACTIONS

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

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

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

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

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

**Learn more at LONSURFhcp.com**



TAIHO ONCOLOGY

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

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

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

## 4 CONTRAINDICATIONS
None.

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

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

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

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

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

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

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

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

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

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

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

**Table 2 Laboratory Test Abnormalities**

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

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

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

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

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

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

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

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

*Data*

*Animal Data*

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

**8.2 Lactation**

*Risk Summary*

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

*Data*

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

**8.3 Females and Males of Reproductive Potential**

*Contraception*

Females

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

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

Males

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

**8.4 Pediatric Use**

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

Animal Data

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

**8.5 Geriatric Use**

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

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

**8.6 Hepatic Impairment**

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

**8.7 Renal Impairment**

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

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

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

**8.8 Ethnicity**

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

**10 OVERDOSAGE**

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

There is no known antidote for LONSURF overdosage.

**17 PATIENT COUNSELING INFORMATION**

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

Severe Myelosuppression:

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

Gastrointestinal toxicity:

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

Administration Instructions:

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

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

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

Embryo-Fetal Toxicity:

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

Lactation:

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



TAIHO ONCOLOGY, INC.

# The Future of Oncology Care: 2017 and Beyond

*Christina Mattina*

**THE 5TH ANNUAL PATIENT-CENTERED ONCOLOGY CARE® (PCOC®)** meeting, hosted by *The American Journal of Managed Care®*, November 17-18, 2016, in Baltimore, concluded with a panel discussion on oncology care in 2017. Bruce A. Feinberg, DO, moderated the discussion that featured panelists Robert Carlson, MD, chief executive officer of the National Comprehensive Cancer Network (NCCN); Scott Gottlieb, MD, resident fellow at the American Enterprise Institute; Ted Okon, MBA, executive director of Community Oncology Alliance; and Kavita Patel, MD, nonresident fellow at the Brookings Institute.

Feinberg began by asking, "Has value-based care realigned incentives, so that providers look for the minimum acceptable quality of care? The panelists said, "No," with Patel replying that because quality measures are hard to grasp for cancer care, the evolution to quality and value is not yet complete.

According to Carlson, lack of access is the greater problem because quality care is impossible without access. He said he hopes that the 20 million individuals who have gained coverage under the Affordable Care Act (ACA) will be able to keep their access even if the ACA is repealed. Gottlieb, an ACA critic, said that although the law has increased access, that access is not always sufficient. He predicted that the ACA would be replaced by a number of smaller bills that will target patients who are disadvantaged under the current system. Patel and Okon agreed that if the ACA is dismantled, there will be a need for laws with bipartisan support so that access is not disrupted.

The conversation then shifted to pathways and guidelines for preferred regimens, which could be a way to maintain quality. Carlson said that the NCCN guidelines were more comprehensive than most pathways, which he pointed out focus primarily on drug spending. He described preferred regimens as those "that should be used the vast majority of the time, and they would typically be the regimens that you would find on a pathway system."

Feinberg mentioned the problem of low health literacy in the United States, asking the panelists how patient-centered oncology could let patients make their own decisions when they may not even understand the implications of these choices. Patel said that many of her patients still don't understand the basics of insurance and can be blindsided by surprise out-of-network bills, which she called "really unconscionable."

Gottlieb, meanwhile, argued that although there will always be some patients who are confused, the average patient deserves more credit. "We shouldn't try to regulate toward the consumer who's going to be confused in the market. I think we need to regulate toward a more average consumer who's capable, with the right tools and the right education, of making these kinds of decisions," he said.

Feinberg asked the panel if value-based care is here for good, despite all the changes likely to occur in the next year. Okon affirmed that "right side of the aisle, left side of the aisle, yes, yes, yes. It's just a matter of how we implement it and go about it, but I think that everybody wants value." Gottlieb agreed that payment reforms would continue as a "secular trend."

The panel wrapped up with a question from an audience member on each expert's personal definition of value. Okon and Patel both defined the concept of "value" as a combination of quality and cost, but Carlson drew laughs when he replied that value is "whatever the patient tells me it is." ◆


CARLSON


GOTTLIEB


OKON


PATEL

**SIDEBAR**

## Cassidy, Collins Unveil Details to ACA Replacement Proposal

LAURA JOSZT

**NEW HEALTHCARE REFORM** legislation was introduced January 23, 2017, by Senators Bill Cassidy, MD (R-LA), and Susan Collins (R-ME). The proposed Patient Freedom Act1 (S.191) would not fully repeal the Affordable Care Act (ACA), but would instead place more power in the hands of the states by giving them the option of staying with the ACA or making another choice.

The proposal eliminates mandates, preserves consumer protections, requires price transparency, and could auto-enroll people who are eligible for tax credits. In a press conference to unveil the details of the plan, Cassidy noted that the Freedom Act includes limited options to cover everyone and take care of people with preexisting conditions without raising costs or having mandates, which is what President Donald J. Trump has made clear he wants.

States that choose to stay with the ACA under the Patient Freedom Act would continue to receive subsidies and tax credits for residents, but would be bound by the individual and employee mandates of the ACA. "California, New York—you love Obamacare, you can keep it," Cassidy said. He added that Maine and Louisiana, which have seen premiums rise by double-digit percentages year to year, would be able to opt for something different.

States that choose the alternative—which Collins believes most states will choose—would cover their uninsured populations with a standard, high-deductible plan with basic pharmaceutical coverage and some preventive care; this plan would be financed through a health savings account (HSA). States also would receive the same amount in federal dollars they would have received under the ACA, plus what they would have received for expanding Medicaid—even if they hadn't. However, individuals could opt out of the state plan and choose more generous health insurance coverage, using their HSA to finance it. The HSAs would phase out at certain income levels, Collins explained.

Cassidy said he believed that this plan could cover more people than the ACA since states have the opportunity to auto-enroll people. "If someone is eligible for a credit, she or he would be enrolled automatically unless they choose otherwise," he said. "Automatic enrollment, if you will, much like when I turn 65, I'm on Medicare. There's no mandate—I'm on Medicare. I may call up and say 'I don't wish to be,' but, as a rule, folks remain on Medicare."

The final option for states would be to design an alternative solution, but without receiving federal assistance. "Significant changes are going to need to be made in order to prevent the individual market from going into a tailspin," Collins said. "Our goal is to increase the number of people who are insured, to help restrain the growth of premiums, and to give consumers more choices."

**REFERENCE**

Patient Freedom Act: better choices for affordable health care. Bill Cassidy, MD, website. http://www.cassidy.senate.gov/imo/media/doc/One%20Pager%20(1.20.17)%20(002).pdf. Accessed January 24, 2017.

## TAGRISSO™ (osimertinib) tablets, for oral use

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

### INDICATIONS AND USAGE

TAGRISSO is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

This indication is approved under accelerated approval based on tumor response rate and duration of response *[see Clinical Studies (14) in full Prescribing Information]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

### DOSAGE AND ADMINISTRATION

#### Patient Selection

Confirm the presence of a T790M EGFR mutation in tumor or, in the absence of tumor, plasma specimens prior to initiation of treatment with TAGRISSO *[see Indications and Usage (1) and Clinical Studies (14) in full Prescribing Information]*. Testing for the presence of the mutation in plasma specimens is recommended only in patients for whom a tumor biopsy cannot be obtained. If this mutation is not detected in a plasma specimen, re-evaluate the feasibility of biopsy for tumor tissue testing. Information on FDA-approved tests for the detection of T790M mutations is available at http://www.fda.gov/companiondiagnostics.

#### Recommended Dosage Regimen

The recommended dose of TAGRISSO is 80 mg tablet once a day until disease progression or unacceptable toxicity. TAGRISSO can be taken with or without food.

If a dose of TAGRISSO is missed, do not make up the missed dose and take the next dose as scheduled.

#### Administration to Patients Who Have Difficulty Swallowing Solids

Disperse tablet in 60 mL (2 ounces) of non-carbonated water only. Stir until tablet is dispersed into small pieces (the tablet will not completely dissolve) and swallow immediately. Do not crush, heat, or ultrasonicate during preparation. Rinse the container with 120 mL to 240 mL (4 to 8 ounces) of water and immediately drink.

If administration via naso-gastric tube is required, disperse the tablet as above in 15 mL of non-carbonated water, and then use an additional 15 mL of water to transfer any residues to the syringe. The resulting 30 mL liquid should be administered as per the nasogastric tube instructions with appropriate water flushes (approximately 30 mL).

#### Dosage Modification

Adverse Reactions

**Table 1 Recommended Dose Modifications for TAGRISSO**

| Target Organ | Adverse Reaction[a] | Dose Modification |
|---|---|---|
| *Pulmonary* | Interstitial lung disease (ILD)/Pneumonitis | Permanently discontinue TAGRISSO. |
| *Cardiac* | QTc[†] interval greater than 500 msec on at least 2 separate ECGs[b] | Withhold TAGRISSO until QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then resume at 40 mg dose. |
| | QTc interval prolongation with signs/ symptoms of life-threatening arrhythmia | Permanently discontinue TAGRISSO. |
| | Asymptomatic, absolute decrease in LVEF[c] of 10% from baseline and below 50% | Withhold TAGRISSO for up to 4 weeks.<br>• If improved to baseline LVEF, resume.<br>• If not improved to baseline, permanently discontinue. |
| | Symptomatic congestive heart failure | Permanently discontinue TAGRISSO. |
| *Other* | Grade 3 or higher adverse reaction | Withhold TAGRISSO for up to 3 weeks. |
| | If improvement to Grade 0-2 within 3 weeks | Resume at 80 mg or 40 mg daily. |
| | If no improvement within 3 weeks | Permanently discontinue TAGRISSO. |

[a] Adverse reactions graded by the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 (NCI CTCAE v4.0).
[b] ECGs = Electrocardiograms
[c] LVEF = Left Ventricular Ejection Fraction
[†] QTc = QT interval corrected for heart rate

Drug Interactions

*Strong CYP3A4 Inducers*

If concurrent use is unavoidable, increase TAGRISSO dosage to 160 mg daily when coadministering with a strong CYP3A inducer. Resume TAGRISSO at 80 mg 3 weeks after discontinuation of the strong CYP3A4 inducer *[see Drug Interactions (7), and Clinical Pharmacology (12.3) in full Prescribing Information]*.

### CONTRAINDICATIONS

None.

### WARNINGS AND PRECAUTIONS

#### Interstitial Lung Disease/Pneumonitis

Across clinical trials, interstitial lung disease (ILD)/pneumonitis occurred in 3.3% (n=27) of TAGRISSO treated patients (n=813); 0.5% (n=4) were fatal.

Withhold TAGRISSO and promptly investigate for ILD in any patient who presents with worsening of respiratory symptoms which may be indicative of ILD (e.g., dyspnea, cough and fever). Permanently discontinue TAGRISSO if ILD is confirmed *[see Dosage and Administration (2.4) and Adverse Reactions (6) in full Prescribing Information]*.

#### QTc Interval Prolongation

The heart rate-corrected QT (QTc) interval prolongation occurs in patients treated with TAGRISSO. Of the 411 patients in Study 1 and Study 2, one patient (0.2%) was found to have a QTc greater than 500 msec, and 11 patients (2.7%) had an increase from baseline QTc greater than 60 msec *[see Clinical Pharmacology (12.2) in full Prescribing Information]*.

In Study 1 and 2, patients with baseline QTc of 470 msec or greater were excluded. Conduct periodic monitoring with ECGs and electrolytes in patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval. Permanently discontinue TAGRISSO in patients who develop QTc interval prolongation with signs/symptoms of life-threatening arrhythmia *[see Dosage and Administration (2.4) in full Prescribing Information]*.

#### Cardiomyopathy

Across clinical trials, cardiomyopathy (defined as cardiac failure, pulmonary edema, ejection fraction decreased or stress cardiomyopathy) occurred in 1.4% (n=11) of TAGRISSO treated patients (n=813); 0.2% (n=2) were fatal.

In Study 1 and Study 2, Left Ventricular Ejection Fraction (LVEF) decline >10% and a drop to <50% occurred in 2.4% (9/375) of patients who had baseline and at least one follow-up LVEF assessment.

Assess LVEF by echocardiogram or multigated acquisition (MUGA) scan before initiation of TAGRISSO and then at 3 month intervals while on treatment. Withhold treatment with TAGRISSO if ejection fraction decreases by 10% from pretreatment values and is less than 50%. For symptomatic congestive heart failure or persistent, asymptomatic LV dysfunction that does not resolve within 4 weeks, permanently discontinue TAGRISSO *[see Dosage and Administration (2.4) in full Prescribing Information]*.

#### Embryo-Fetal Toxicity

Based on data from animal studies and its mechanism of action, TAGRISSO can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, osimertinib caused post-implantation fetal loss when administered during early development at a dose exposure 1.5 times the exposure at the recommended human dose. When males were treated prior to mating with untreated females, there was an increase in preimplantation embryonic loss at plasma exposures of approximately 0.5-times those observed in patients at the 80 mg dose level.

Advise pregnant women of the potential risk to a fetus.

Advise females of reproductive potential to use effective contraception during treatment with TAGRISSO and for 6 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception for 4 months after the final dose *[see Use in Specific Populations (8.1), (8.3) and Clinical Pharmacology (12.3) in full Prescribing Information]*.

### ADVERSE REACTIONS

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

Interstitial Lung Disease/Pneumonitis *[see Warnings and Precautions (5.1) in full Prescribing Information]*

QTc Interval Prolongation *[see Warnings and Precautions (5.2) in full Prescribing Information]*

#### Clinical Trials Experience

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

The data described below reflect exposure to TAGRISSO (80 mg daily) in 411 patients with EGFR T790M mutation-positive non-small cell lung cancer who received prior EGFR TKI therapy, in two single-arm studies, Study 1 and Study 2. Patients with a past medical history of ILD or radiation pneumonitis that required steroid treatment, serious arrhythmia or baseline QTc interval greater than 470 ms were excluded from Study 1 and Study 2. Baseline patient and disease characteristics were: median age 63 years, 13% of patients were ≥75 years old, female (68%), White (36%), Asian (60%), metastatic (96%), sites of brain metastases (39%), World Health Organization (WHO) performance status of 0 (37%) or 1 (63%), 1 prior line of therapy [EGFR-TKI treatment only, second line, chemotherapy-naïve (31%)], 2 or more prior lines of therapy (69%). Of the 411 patients, 333 patients were exposed to TAGRISSO for at least 6 months; 97 patients were exposed for at least 9 months; however, no patient was exposed to TAGRISSO for 12 months.

In Studies 1 and 2, the most common (>20%) adverse reactions (all grades) observed in TAGRISSO-treated patients were diarrhea (42%), rash (41%), dry skin (31%), and nail toxicity (25%). Dose reductions occurred in 4.4% of patients treated with TAGRISSO. The most frequent adverse reactions that led to dose reductions or interruptions were: electrocardiogram QTc prolonged (2.2%) and neutropenia (1.9%). Serious adverse reactions reported in 2% or more patients were pneumonia and pulmonary embolus. There were 4 patients (1%) treated with TAGRISSO who developed fatal adverse reactions of ILD/pneumonitis. Other fatal adverse reactions occurring in more than 1 patient included pneumonia (4 patients) and CVA/cerebral hemorrhage (2 patients). Discontinuation of therapy due to adverse reactions occurred in 5.6% of patients treated with TAGRISSO. The most frequent adverse reactions that led to discontinuation were ILD/pneumonitis and cerebrovascular accidents/infarctions.

Tables 2 and 3 summarize the common adverse reactions and laboratory abnormalities observed in TAGRISSO-treated patients.

**Table 2 Adverse Reactions (>10% for all NCI CTCAE* Grades or >2% for Grades 3-4) in Study 1 and Study 2**

| Adverse Reaction | TAGRISSO N=411 | |
|---|---|---|
| | All Grades | Grade 3-4[f] |
| | % | % |
| **Gastrointestinal disorders** | | |
| Diarrhea | 42 | 1.0 |
| Nausea | 17 | 0.5 |
| Decreased appetite | 16 | 0.7 |
| Constipation | 15 | 0.2 |
| Stomatitis | 12 | 0 |
| **Skin disorders** | | |
| Rash[a] | 41 | 0.5 |
| Dry skin[b] | 31 | 0 |
| Nail toxicity[c] | 25 | 0 |
| Pruritus | 14 | 0 |
| **Eye Disorders**[d] | 18 | 0.2 |
| **Respiratory** | | |
| Cough | 14 | 0.2 |
| **General** | | |
| Fatigue | 14 | 0.5 |
| **Musculoskeletal** | | |
| Back pain | 13 | 0.7 |
| **Central Nervous System** | | |
| Headache | 10 | 0.2 |
| **Infections** | | |
| Pneumonia | 4 | 2.2 |
| **Vascular events** | | |
| Venous thromboembolism[e] | 7 | 2.4 |

* NCI CTCAE v4.0.
[a] Includes cases reported within the clustered terms for rash adverse events: Rash, rash generalized, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pustular, erythema, folliculitis, acne, dermatitis and acneform dermatitis.
[b] Includes dry skin, eczema, skin fissures, xerosis.
[c] Includes nail disorders, nail bed disorders, nail bed inflammation, nail bed tenderness, nail discoloration, nail disorder, nail dystrophy, nail infection, nail ridging, onychoclasis, onycholysis, onychomadesis, paronychia.
[d] Includes dry eye, vision blurred, keratitis, cataract, eye irritation, blepharitis, eye pain, lacrimation increased, vitreous floaters. Other ocular toxicities occurred in <1% of patients.
[e] Includes deep vein thrombosis, jugular venous thrombosis, and pulmonary embolism.
[f] No grade 4 events have been reported.

Additional clinically significant adverse reactions occurring in 2% or more of patients treated with TAGRISSO included cerebrovascular accident (2.7%).

**Table 3 Laboratory Abnormalities (≥20% for all NCI CTCAE Grades) in Study 1 and Study 2**

| Laboratory Abnormality | TAGRISSO N=411 | |
|---|---|---|
| | Change from Baseline All Grades (%) | Change from Baseline to Grade 3 or Grade 4 (%)[a] |
| **Clinical Chemistry** | | |
| Hyponatremia | 26 | 3.4 |
| Hypermagnesemia | 20 | 0.7 |
| **Hematologic** | | |
| Lymphopenia | 63 | 3.3 |
| Thrombocytopenia | 54 | 1.2[a] |
| Anemia | 44 | 0.2 |
| Neutropenia | 33 | 3.4 |

[a] The only grade 4 laboratory abnormality was 1 patient with grade 4 thrombocytopenia.

## DRUG INTERACTIONS

### Effect of Other Drugs on Osimertinib

Strong CYP3A Inducers

Coadministering TAGRISSO with a strong CYP3A4 inducer decreased the exposure of osimertinib compared to administering TAGRISSO alone *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Decreased osimertinib exposure may lead to reduced efficacy.

Avoid coadministering TAGRISSO with strong CYP3A inducers (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort) [note: effect of St. John's Wort varies widely and is preparation-dependent]. Increase the TAGRISSO dosage when coadministering with a strong CYP3A4 inducer if concurrent use is unavoidable *[see Dosage and Administration (2.4) in full Prescribing Information]*. No dose adjustments are required when TAGRISSO is used with moderate and/or weak CYP3A inducers.

### Effect of Osimertinib on Other Drugs

Coadministering TAGRISSO with a BCRP substrate increased the exposure of the BCRP substrate compared to administering the BCRP substrate alone *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Increased BCRP substrate exposure may increase the risk of exposure-related toxicity.

Monitor for adverse reactions of the BCRP substrate (e.g., rosuvastatin, sulfasalazine, topotecan), unless otherwise instructed in its approved labeling, when coadministered with TAGRISSO.

## USE IN SPECIFIC POPULATIONS

### Pregnancy

*Risk Summary*

Based on data from animal studies and its mechanism of action, TAGRISSO can cause fetal harm when administered to a pregnant woman. There are no available data on TAGRISSO use in pregnant women. Administration of osimertinib to pregnant rats was associated with embryolethality and reduced fetal growth at plasma exposures 1.5 times the exposure at the recommended human dose *[see Data]*. Advise pregnant women of the potential risk to a fetus.

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

*Data*

Animal Data

When administered to pregnant rats prior to embryonic implantation through the end of organogenesis (gestation days 2-20) at a dose of 20 mg/kg/day, which produced plasma exposures of approximately 1.5 times the clinical exposure, osimertinib caused post-implantation loss and early embryonic death. When administered to pregnant rats from implantation through the closure of the hard palate (gestation days 6 to 16) at doses of 1 mg/kg/day and above (0.1-times the AUC observed in patients at the recommended dose of 80 mg), an equivocal increase in the rate of fetal malformations and variations was observed in treated litters relative to those of concurrent controls. When administered to pregnant dams at doses of 30 mg/kg/day during organogenesis through lactation Day 6, osimertinib caused an increase in total litter loss and postnatal death. At a dose of 20 mg/kg/day, osimertinib administration during the same period resulted in increased postnatal death as well as a slight reduction in mean pup weight at birth that increased in magnitude between lactation days 4 and 6.

### Lactation

Risk Summary

There are no data on the presence of osimertinib in human milk, the effects of osimertinib on the breastfed infant or on milk production. Administration to rats during gestation and early lactation was associated with adverse effects, including reduced growth rates and neonatal death *[see Use in Specific Populations (8.1) in full Prescribing Information]*. Because of the potential for serious adverse reactions in breastfed infants from osimertinib, advise a lactating woman not to breastfeed during treatment with TAGRISSO and for 2 weeks after the final dose.

### Females and Males of Reproductive Potential

Contraception

*Females*

Advise females of reproductive potential to use effective contraception during treatment with TAGRISSO and for 6 weeks after the final dose *[see Use in Specific Populations (8.1) in full Prescribing Information]*.

*Males*

Advise male patients with female partners of reproductive potential to use effective contraception during and for 4 months following the final dose of TAGRISSO *[see Nonclinical Toxicology (13.1) in full Prescribing Information]*.

Infertility

Based on animal studies, TAGRISSO may impair fertility in females and males of reproductive potential. The effects on female fertility showed a trend toward reversibility. It is not known whether the effects on male fertility are reversible *[see Nonclinical Toxicology (13.1) in full Prescribing Information]*.

### Pediatric Use

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

### Geriatric Use

One hundred eighty-seven (45%) of the 411 patients in clinical trials of TAGRISSO were 65 years of age and older, and 54 patients (13%) were 75 years of age and older. No overall differences in effectiveness were observed based on age. Exploratory analysis suggests a higher incidence of Grade 3 and 4 adverse reactions (32% versus 25%) and more frequent dose modifications for adverse reactions (23% versus 17%) in patients 65 years or older as compared to those younger than 65 years.

### Renal Impairment

No dose adjustment is recommended in patients with mild [creatinine clearance (CLcr) 60-89 mL/min, as estimated by the Cockcroft Gault method (C-G)] or moderate (CLcr 30-59 mL/min, as estimated by C-G) renal impairment. There is no recommended dose of TAGRISSO for patients with severe renal impairment (CLcr <30 mL/min) or end-stage renal disease *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

### Hepatic Impairment

No dose adjustment is recommended in patients with mild hepatic impairment [total bilirubin less than or equal to upper limit of normal (ULN) and AST greater than ULN or total bilirubin between 1.0 to 1.5 times ULN and any AST]. There is no recommended dose for TAGRISSO for patients with moderate or severe hepatic impairment *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

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# TAGRISSO:
# BREAK THROUGH
## THE T790M RESISTANCE BARRIER

**in patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, at progression on or after EGFR TKI therapy**

- Proven effective in two separate, global, Phase II, single-arm, open-label clinical trials in patients with metastatic EGFR T790M mutation-positive NSCLC who had progressed on or after EGFR TKI therapy[1]
  - A 59% objective response rate (95% CI: 54–64) in patients who progressed with previous EGFR TKI therapy
- In a separate dose-finding part of AURA, 63 patients with centrally confirmed T790M positive NSCLC who progressed on prior systemic therapy, including an EGFR TKI, were administered TAGRISSO 80 mg[1]:
  - 51% of patients in the 80-mg cohort had a confirmed response by BICR
  - The median DoR was 12.4 months (95% CI: 8.3, not calculable)
- Grade 3/4 adverse events occurred at <3.5%[1]
- <6% of patients in a pooled analysis (N=411) had either dose reductions or discontinuations due to adverse events[1]
- Interstitial Lung Disease (ILD)/Pneumonitis occurred in 3.3% and was fatal in 0.5% of 813 TAGRISSO patients. Withhold TAGRISSO and promptly investigate for ILD in any patient presenting with worsening of respiratory symptoms indicative of ILD (e.g., dyspnea, cough and fever). Permanently discontinue TAGRISSO if ILD is confirmed[1]
- The most common adverse events in a pooled analysis of TAGRISSO patients (N=411) were diarrhea (42%), rash (41%), dry skin (31%), and nail toxicity (25%)[1]

## IMPORTANT SAFETY INFORMATION

- There are no contraindications for TAGRISSO
- Interstitial Lung Disease (ILD)/Pneumonitis occurred in 3.3% and was fatal in 0.5% of 813 TAGRISSO patients. Withhold TAGRISSO and promptly investigate for ILD in any patient presenting with worsening of respiratory symptoms indicative of ILD (e.g., dyspnea, cough and fever). Permanently discontinue TAGRISSO if ILD is confirmed
- QTc interval prolongation occurred in TAGRISSO patients. Of the 411 patients in two Phase II studies, 0.2% were found to have a QTc greater than 500 msec, and 2.7% had an increase from baseline QTc greater than 60 msec. Conduct periodic monitoring with ECGs and electrolytes in patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval. Permanently discontinue TAGRISSO in patients who develop QTc interval prolongation with signs/symptoms of life threatening arrhythmia
- Cardiomyopathy occurred in 1.4% and was fatal in 0.2% of 813 TAGRISSO patients. Left Ventricular Ejection Fraction (LVEF) decline >10% and a drop to <50% occurred in 2.4% of (9/375) TAGRISSO patients. Assess LVEF before initiation and then at 3 month intervals of TAGRISSO treatment. Withhold TAGRISSO if ejection fraction decreases by 10% from pretreatment values and is less than 50%. For symptomatic congestive heart failure or persistent asymptomatic LV dysfunction that does not resolve within 4 weeks, permanently discontinue TAGRISSO
- Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during TAGRISSO treatment and for 6 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception for 4 months after the final dose
- The most common adverse reactions (>20%) observed in TAGRISSO patients were diarrhea (42%), rash (41%), dry skin (31%) and nail toxicity (25%)

## INDICATION

TAGRISSO is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor therapy.

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

**Please see Brief Summary of complete Prescribing Information.**

**Reference: 1.** TAGRISSO [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2015.

AstraZeneca



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