Bridging the gap between payer and provider perspectives

THE AMERICAN JOURNAL OF MANAGED CARE®

Special Issue

Volume 20
Special Issue 3

Evidence-Based Oncology

Exclusive Conference Coverage From

Patient-Centered Oncology Care: Real-World Perspectives 2013

Baltimore, MD | November 14-15

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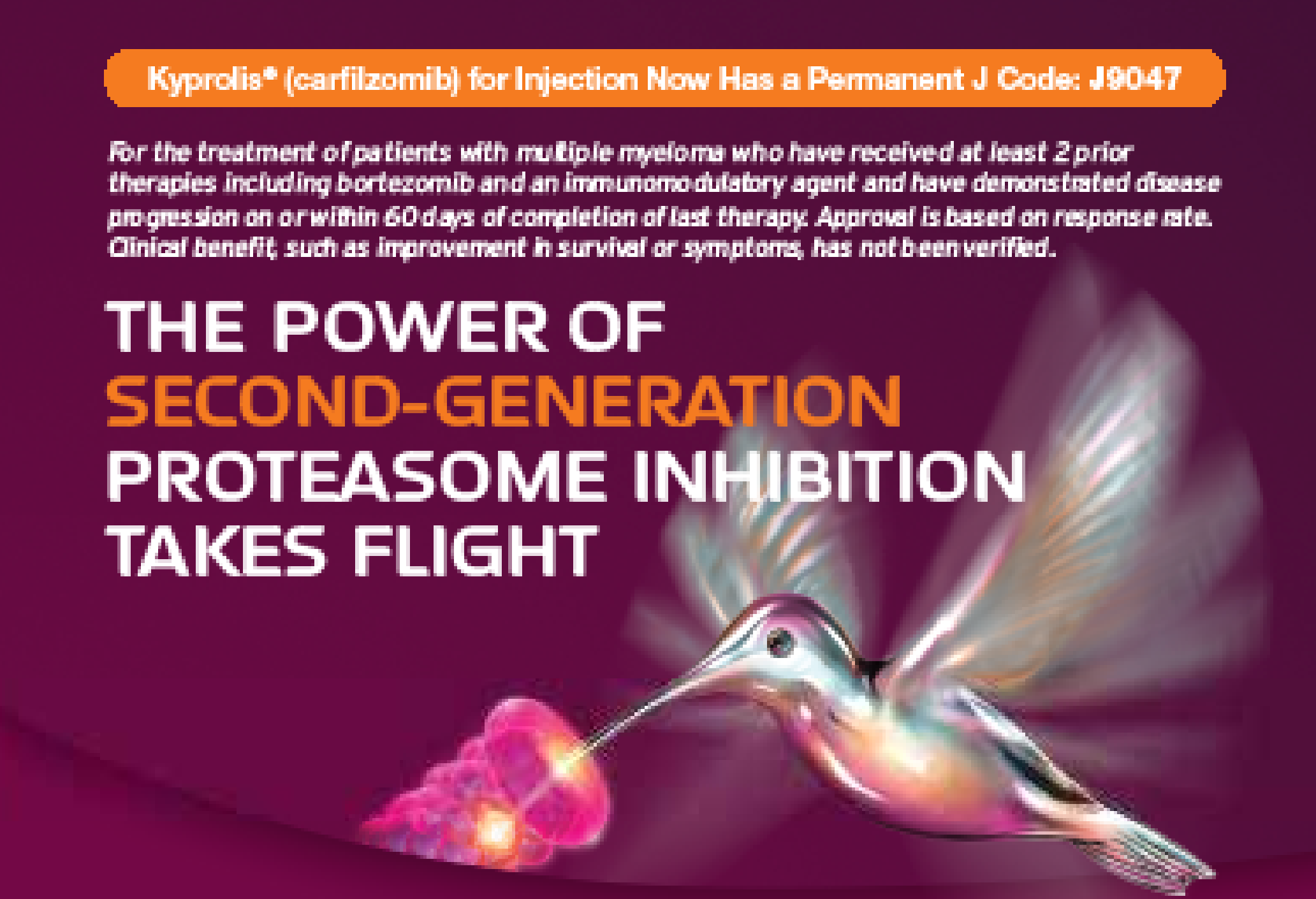
Kyprolis® (carfilzomib) for Injection Now Has a Permanent J Code: J9047

For the treatment of patients with multiple myeloma who have received at least 2 prior therapies including bortezomib and an immunomodulatory agent and have demonstrated disease progression on or within 60 days of completion of last therapy. Approval is based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

THE POWER OF SECOND-GENERATION PROTEASOME INHIBITION TAKES FLIGHT



Important Safety Information

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

The safety of KYPROLIS was evaluated in clinical studies of 526 patients with relapsed and/or refractory multiple myeloma.

Cardiac Arrest, Congestive Heart Failure, Myocardial Ischemia: Death due to cardiac arrest has occurred within a day of KYPROLIS administration. New onset or worsening of pre-existing congestive heart failure with decreased left ventricular function or myocardial ischemia have occurred following administration of KYPROLIS. Cardiac failure events (e.g., cardiac failure congestive, pulmonary edema, ejection fraction decreased) were reported in 7% of patients. Monitor for cardiac complications and manage promptly. Withhold KYPROLIS for Grade 3 or 4 cardiac events until recovery and consider whether to restart KYPROLIS based on a benefit/risk assessment. Patients with New York Heart Association Class III and IV heart failure, myocardial infarction in the preceding 6 months, and conduction abnormalities uncontrolled by medications may be at greater risk for cardiac complications.

Pulmonary Hypertension: Pulmonary arterial hypertension (PAH) was reported in 2% of patients treated with KYPROLIS and was Grade 3 or greater in less than 1% of patients. Evaluate with cardiac imaging and/or other tests as indicated. Withhold KYPROLIS for pulmonary hypertension until resolved or returned to baseline and consider whether to restart KYPROLIS based on a benefit/risk assessment.

Pulmonary Complications: Dyspnea was reported in 35% of patients enrolled in clinical trials. Grade 3 dyspnea occurred in 5%; no Grade 4 events; and 1 death (Grade 5) was reported. Monitor and manage dyspnea immediately; interrupt KYPROLIS until symptoms have resolved or returned to baseline.

Infusion Reactions: Infusion reactions were characterized by a spectrum of systemic symptoms including fever, chills, arthralgia, myalgia, facial flushing, facial edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina. These reactions can occur immediately following infusion or up to 24 hours after administration of KYPROLIS. Administer dexamethasone prior to KYPROLIS to reduce the incidence and severity of reactions. Inform patients of the risk and symptoms, and to contact physician if symptoms of an infusion reaction occur.

Tumor Lysis Syndrome: Tumor lysis syndrome (TLS) occurred following KYPROLIS administration in < 1% of patients. Patients with multiple myeloma and a high tumor burden should be considered to be at greater risk for TLS. Prior to receiving KYPROLIS, ensure that patients are well hydrated. Monitor for evidence of TLS during treatment, and manage promptly. Interrupt KYPROLIS until TLS is resolved.

KYPROLIS is engineered for selective inhibition[1]

- Single-agent KYPROLIS phase 2 study results[2,a]
  - Overall response rate (ORR) of 22.9% in PX-171-003 study (95% CI: 18.0, 28.5)
  - Median duration of response of 7.8 months (95% CI: 5.6, 9.2)
- Most patients across all phase 2 studies (85%) did not need to discontinue therapy due to an adverse event
  - Adverse reactions leading to discontinuation included congestive heart failure (2%), cardiac arrest, dyspnea, increased blood creatinine, and acute renal failure (1% each)

ADVERSE REACTIONS

The safety of KYPROLIS was evaluated in clinical trials of 526 patients with relapsed and/or refractory multiple myeloma.

- Serious adverse reactions were reported in 45% of patients. The most common were pneumonia (10%), acute renal failure (4%), pyrexia (3%), and congestive heart failure (3%)
- The most common adverse reactions (incidence ≥ 30%) were fatigue (56%), anemia (47%), nausea (45%), thrombocytopenia (36%), dyspnea (35%), diarrhea (33%), and pyrexia (30%)

[a]Study PX-171-003 was a single-arm, multicenter clinical trial of KYPROLIS in 266 patients with relapsed multiple myeloma and whose disease had a ≤ 25% response to the most recent therapy or had disease progression during or within 60 days of the most recent therapy. At the time of study entry, patients had received a median of 5 prior lines of therapy. The primary endpoint was ORR. Response was determined by Independent Review Committee assessment using International Myeloma Working Group criteria.

References: 1. Demo SD, Kirk CJ, Aujay MA, et al. Antitumor activity of PR-171, a novel irreversible inhibitor of the proteasome. Cancer Res. 2007;67(13):6383-6391. 2. KYPROLIS [prescribing information]. South San Francisco, CA: Onyx Pharmaceuticals, Inc; 2012.

Kyprolis (carfilzomib)

Thrombocytopenia: KYPROLIS causes thrombocytopenia with platelet nadirs occurring around Day 8 of each 28-day cycle and recovery to baseline by the start of the next 28-day cycle. In patients with multiple myeloma, 36% of patients experienced thrombocytopenia, including Grade 4 in 10%. Thrombocytopenia following KYPROLIS administration resulted in a dose reduction in 1% of patients and discontinuation of treatment with KYPROLIS in < 1% of patients. Monitor platelet counts frequently during treatment with KYPROLIS. Reduce or interrupt dose as clinically indicated.

Hepatic Toxicity and Hepatic Failure: Cases of hepatic failure, including fatal cases, have been reported (< 1%). KYPROLIS can cause elevations of serum transaminases and bilirubin. Withhold KYPROLIS in patients experiencing Grade 3 or greater elevations of transaminases, bilirubin, or other liver enzyme abnormalities until resolved or returned to baseline. After resolution, consider if restarting KYPROLIS is appropriate. Monitor liver enzymes frequently.

Embryo-fetal Toxicity: KYPROLIS can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. There are no adequate and well-controlled studies in pregnant women using KYPROLIS. Carfilzomib caused embryo-fetal toxicity in pregnant rabbits at doses that were lower than in patients receiving the recommended dose. Females of reproductive potential should be advised to avoid becoming pregnant while being treated with KYPROLIS.

ADVERSE REACTIONS

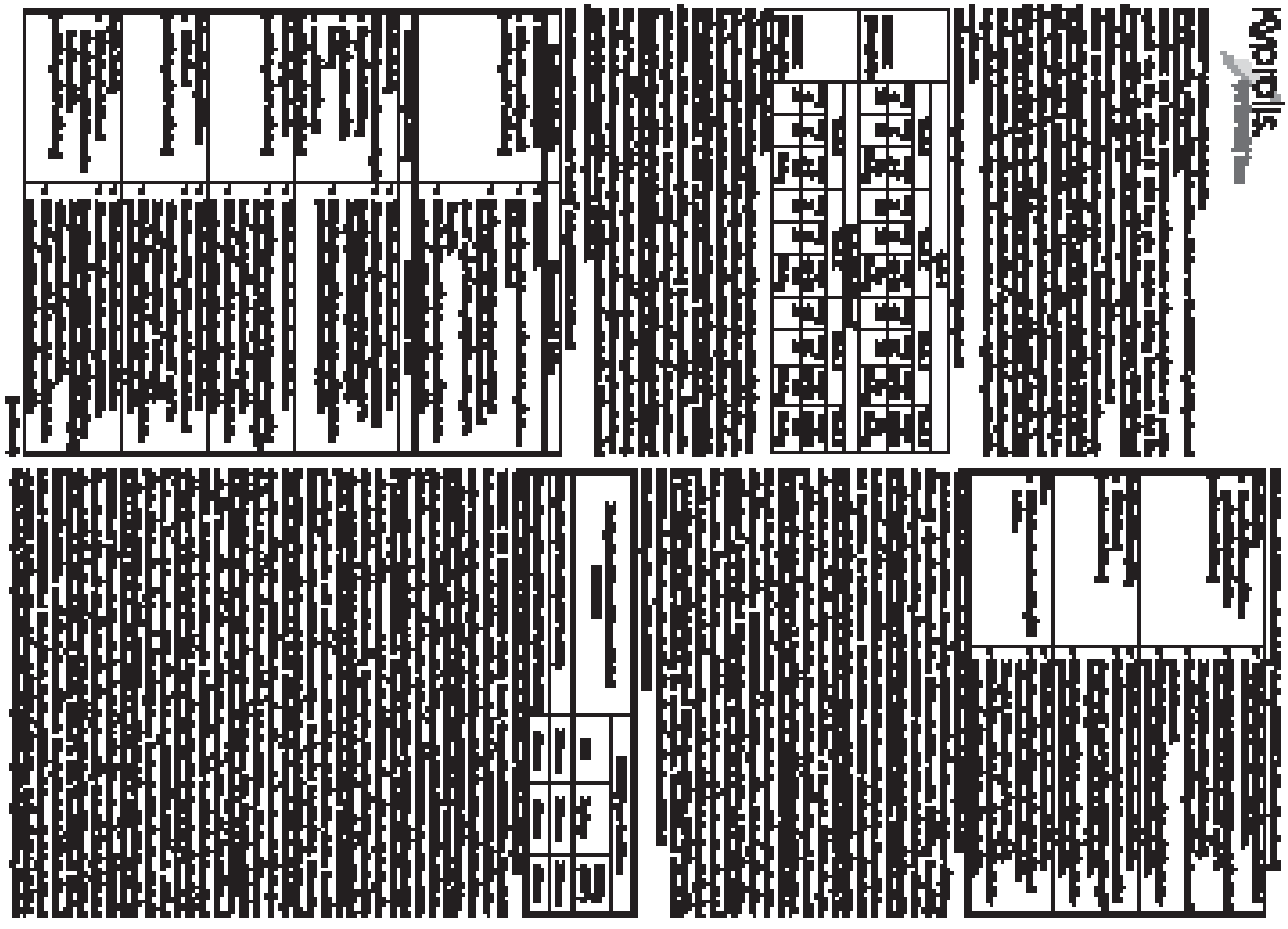
Serious adverse reactions were reported in 45% of patients. The most common serious adverse reactions were pneumonia (10%), acute renal failure (4%), pyrexia (3%), and congestive heart failure (3%). Adverse reactions leading to discontinuation of KYPROLIS occurred in 15% of patients and included congestive heart failure (2%), cardiac arrest, dyspnea, increased blood creatinine, and acute renal failure (1% each).

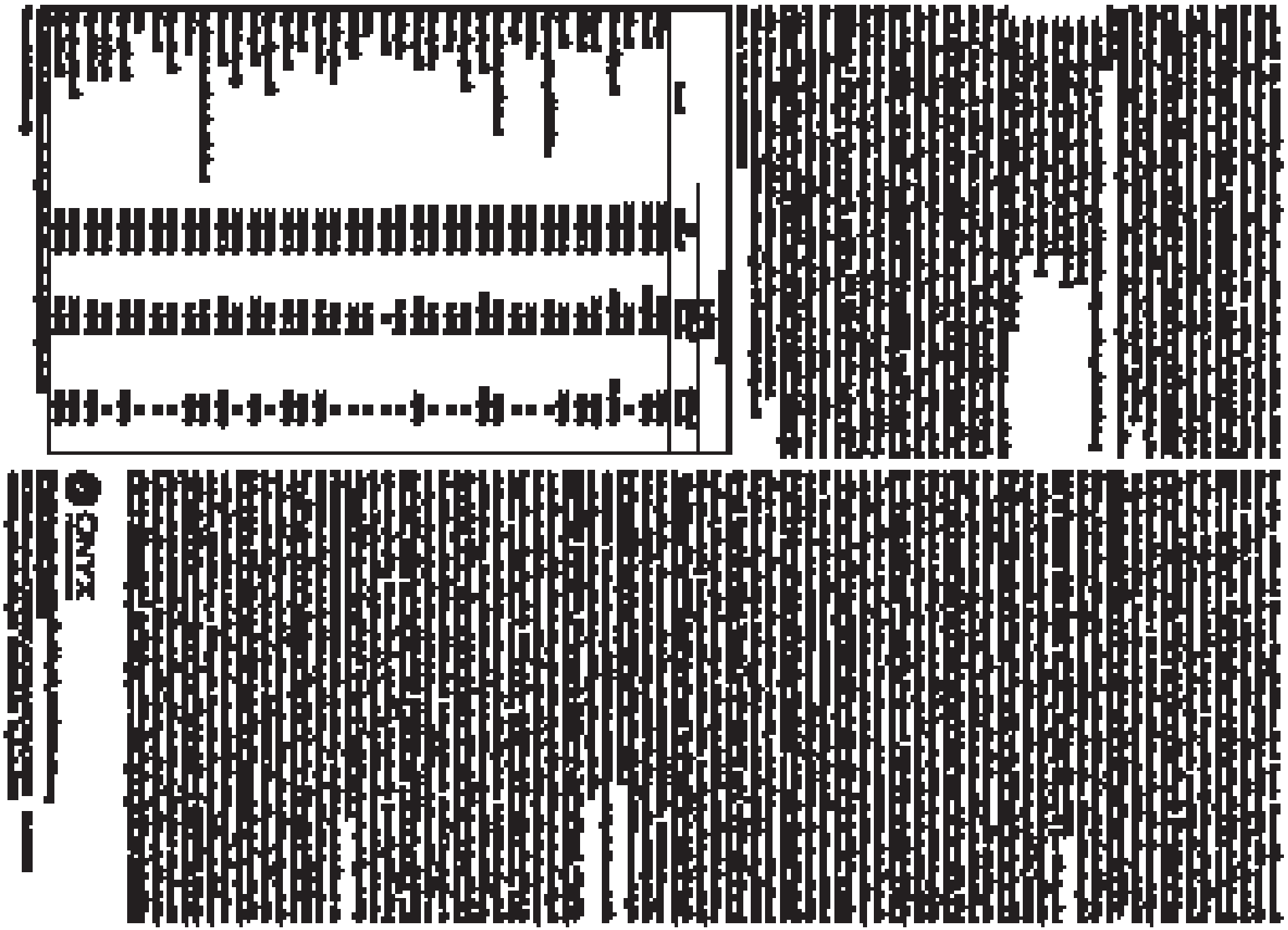
The most common adverse reactions (incidence ≥ 30%) were fatigue (56%), anemia (47%), nausea (45%), thrombocytopenia (36%), dyspnea (35%), diarrhea (33%), and pyrexia (30%).

USE IN SPECIFIC POPULATIONS

Since dialysis clearance of KYPROLIS concentrations has not been studied, the drug should be administered after the dialysis procedure.

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





In This Issue...

THE AMERICAN JOURNAL OF MANAGED CARE

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The American Journal of Managed Care ISSN 1088-0224 (print) & ISSN 1936-2692 (online) is published monthly by Managed Care & Healthcare Communications, LLC, 666 Plainsboro Rd, Bldg. 300, Plainsboro, NJ 08536.

On November 14-15, 2013, more than 200 attendees gathered at the Royal Sonesta Harbor Court in Baltimore, Maryland, for the second annual, Patient Centered Oncology Care: Real-World Perspectives conference. *Evidence-Based Oncology,* a publication of *The American Journal of Managed Care,* sponsored this meeting to bring together stakeholders across the spectrum of cancer care. Our keynote speaker, Amy Berman, BS, RN, a senior program officer at The John A. Hartford Foundation, is a nurse who chose palliative care after learning she had stage IV breast cancer. She embodied the challenges that face providers and payers as they try to deliver appropriate care to patients, who on the whole are older and have more comorbidities than in years past. Berman's account of making an educated decision to decline the most aggressive treatment—and saving her insurance company an estimated $500,000—stood in contrast to the problems Bruce A. Feinberg, DO, later highlighted: even when physicians are presented with evidence that calls for a less intense approach, Feinberg said, the "culture of medicine" still propels many to embrace "now over later, new over old, and more over less."

Bruce A. Feinberg, DO, says even when the evidence calls for a less intense approach to cancer care, the "culture of medicine" still propels many to embrace "now over later, new over old, and more over less."

Among the take-aways from Patient-Centered Oncology Care: Real-World Perspectives 2013:

- Patients may not know what is realistic, because honest conversations about cost, side effects, and survival rates of new therapies may not be taking place. However, according to Berman, patients choose less aggressive forms of treatment "when they truly understand their options."
- The concept of sharing risk in prescribing breakthrough cancer therapies—where the cost is shared among health plans, providers, and pharmaceutical companies—was discussed as a way to potentially lower drug costs and prevent health plans from being cast as villains for not wanting to fund expensive, unproven treatments.
- Genetic testing creates opportunities not only for more precise, cost-effective treatment but also profit-driven abuses if consumers do not receive adequate counseling. Karen Lewis, MS, MM, CGC, a genetic counselor for Priority Health, cited research that showed 33% of genetic tests were inappropriate.

Feedback has been tremendous, and we encourage both those who attended and those who could not to reserve November 13-14, 2014, for the third annual conference. Kindly review this supplement and give us ideas on what issues we should address when we meet again.

Thank you for reading,

Brian Haug
Publisher

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.

Peter B. Bach, MD, MAPP
Director, Center for Health Policy and Outcomes
Memorial Sloan-Kettering Cancer Center

Dr Bach's main research interests cover healthcare policy, particularly as it relates to Medicare, racial disparities in cancer care quality, and lung cancer epidemiology. A former senior adviser to the administrator of the Centers for Medicare & Medicaid Services (CMS), he serves on several national committees, including the Institute of Medicine's National Cancer Policy Forum and the Committee on Performance Measurement of the National Committee on Quality Assurance. He chairs the Technical Expert Panel that is developing measures of cancer care quality for CMS.

See pages SP70, SP71
www.ajmc.com/ajmc-tv/live/pcoc13/Bach

Ethan Basch, MD
Director of Cancer Outcomes Research
University of North Carolina Chapel Hill

Dr Basch is a practicing oncologist and director of the Cancer Outcomes Research Program at the University of North Carolina in Chapel Hill. His research focuses on patient-reported outcomes in clinical trials, comparative effectiveness, and quality-of-care assessments. He is a member of the Methodology Committee of the Patient-Centered Outcomes Research Institute (PCORI), a member of the Board of Scientific Advisors of the National Cancer Institute, chairs the Health Outcomes Committee of the Alliance for Clinical Trials in Oncology, and serves on the Board of Directors of the International Society for Quality of Life Research.

See page SP75, SP76
www.ajmc.com/ajmc-tv/live/pcoc13/Basch

Jan Berger, MD, MJ
President, CEO
Health Intelligence Partners

Dr Berger founded Health Intelligence Partners 6 years ago as a healthcare consultancy that blends more than 25 years of both business and clinical experience. Prior to founding Health Intelligence Partners, Dr Berger served as senior vice president and chief clinical officer for CVS Caremark. She presently sits on the boards of Care Core National (committees: finance, compensation, search, mergers & acquisitions, and strategic directions), Meals to Heal, The University of Arizona School of Pharmacy, RxAnte, and Midwest Business Group on Health. Dr Berger is the editor-in-chief of *The American Journal of Pharmacy Benefits*.

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www.ajmc.com/ajmc-tv/live/pcoc13/Discussion5

Amy Berman, BS, RN
Senior Program Officer
The John A. Hartford Foundation

Berman is a senior program officer with the John A. Hartford Foundation. She heads the Foundation's development and dissemination of innovative, cost-effective models of care that improve health outcomes for older adults. She works to advance palliative care and to reduce avoidable readmissions. Berman also works on collaborations with federal partners, including the Centers for Medicare & Medicaid Innovation, the Office of the National Coordinator for Health Information Technology, and the Administration for Community Living. She has openly shared her experiences living with stage IV breast cancer, presenting to the Institute on Medicine.

See pages SP69, SP70, SP71, SP75, SP85, SP88
www.ajmc.com/ajmc-tv/live/pcoc13/Keynote

Michael E. Chernew, PhD
Co-Editor-in-Chief
The American Journal of Managed Care

Dr Chernew is the Leonard D. Schaeffer Professor of Health Care Policy at Harvard Medical School. His research activities focus on several areas, most notably the causes and consequences of growth in healthcare expenditures, geographic variation in medical spending, and use of Value-Based Insurance Design. Dr Chernew is vice chair of the Medicare Payment Advisory Commission, an independent agency established to advise the US Congress on issues affecting the Medicare program. He is also a member of the Congressional Budget Office's Panel of Health Advisors. In 2010, Dr Chernew was elected to the Institute of Medicine of the National Academy of Sciences; he served on the Committee on the Determination of Essential Health Benefits.

See pages SP91, SP92
www.ajmc.com/ajmc-tv/live/pcoc13/Discussion7

Jerry Conway
VP of Reimbursement & Payer Strategy
Foundation Medicine, Inc

Conway joined Foundation Medicine Inc in May 2012 with over 22 years of sales and executive management experience in the routine clinical and esoteric laboratory marketplaces. His experience includes payer contracting and reimbursement in a wide range of business environments, including Fortune 500 and start-up companies. He has previously worked for Metamark Genetics Inc, a national provider of cancer prognostic tests and services, as vice president of reimbursement and payer contracting.

See pages SP88, SP90
www.ajmc.com/ajmc-tv/live/pcoc13/Conway

Jeffrey D. Dunn, PharmD, MBA
Senior Vice President
VRx Pharmacy

Dr Dunn is senior vice president at VRx, an integrated pharmacy services management company. VRx incorporates PBM functions, pharmacy & therapeutics (P&T)/formulary management, medication therapy management (MTM)/integrated care management (ICM), and government functions for commercial and Medicare Part D employer groups and health plans. Dr Dunn is a board member at VRx and oversees all clinical responsibilities. He manages the P&T process and formularies for commercial and Medicare Part D, as well as all MTM/ICM activities. He is an active member of the Academy of Managed Care Pharmacy, the American Society of Health-System Pharmacists, and the Utah Pharmaceutical Association. He is a reviewer for the *Journal of Managed Care Pharmacy* and *Managed Care Interface*, an editor for the International Scholarly Research Network and *Oncology Business News*, and sits on the editorial board of *The American Journal of Managed Care*.

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www.ajmc.com/ajmc-tv/live/pcoc13/Discussion7

Kirby Eng, RPh
Director, Oncology Medical Pharmacy Management
CVS Caremark

Eng is responsible for the development and implementation of oncology specialty drug management strategies for CVS Caremark health plan and employer clients. He has more than 16 years of broad oncology experience in specialty pharmacy, manufacturing, sales and market strategic planning, group purchasing, oncology drug distribution, and provider network management. Before CVS Caremark, he held positions with CuraScript Specialty Pharmacy, US Oncology, Oncology Therapeutics Network (McKesson Specialty), Sicor (Teva), and Eli Lilly and Co. He has been an active participant on National Comprehensive Cancer Network task forces involving oral chemotherapy, specialty pharmacy, and risk evaluation and mitigation strategies.

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www.ajmc.com/ajmc-tv/live/pcoc13/Discussion7

Bruce A. Feinberg, DO
Vice President and Chief Medical Officer
Cardinal Health Specialty Solutions, Clinical Pathways

Dr Feinberg is a leading oncologist recognized for his expertise in oncology and the business of specialty healthcare. He serves as vice president and chief medical officer for the Clinical Pathways business of Cardinal Health Specialty Solutions. Prior to joining the Cardinal Health team, Dr Feinberg was instrumental in establishing Georgia Cancer Specialists (GCS), the largest and first integrated oncologic specialty practice in the southeast. As CEO and president of GCS, he expanded community access to oncology care by bringing the latest cancer treatments, technologies, and clinical trials closer to the patient. In 2012, Specialty Solutions launched PathWare™ Decision Transaction Solutions, a software technology that Dr Feinberg was instrumental in designing, to improve the work flow process for payers and physicians. He is the author of the best-selling *Breast Cancer Answers* and its follow-up book, *Colon Cancer Answers*.

See page SP85, SP86
www.ajmc.com/ajmc-tv/live/pcoc13/Feinberg

A. Mark Fendrick, MD
Professor, Division of General Medicine, Department of Internal Medicine and Department of Health Management and Policy
University of Michigan

Dr Fendrick is a professor of internal medicine in the School of Medicine and a professor of health management and policy in the School of Public Health at the University of Michigan. He currently directs the Center for Value-Based Insurance Design at the University of Michigan, the leading advocate for development, implementation, and evaluation of innovative health benefit plans. Dr Fendrick's research focuses on the clinical and economic assessment of medical interventions, with special attention to how technological innovation influences clinical practice, benefit design, and healthcare systems. He is the co-editor-in-chief of *The American Journal of Managed Care*.

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www.ajmc.com/ajmc-tv/live/pcoc13/Discussion2

John L. Fox, MD, MHA
Senior Medical Director, and Associate Vice President, Medical Affairs
Priority Health

Dr Fox is the senior medical director and associate vice president of medical affairs for Priority Health, a provider-sponsored health plan with 640,000 members. He is responsible for technology assessment (medical and pharmaceutical) and utilization and case management. He is engaged in new program development including physician profiling, pay-for-performance programs, integrated specialty pharmacy, and value-based benefit designs. He is currently involved in development of payment reform strategies, including the oncology medical home.

See pages SP76, SP88, SP90, SP92
www.ajmc.com/ajmc-tv/live/pcoc13/Discussion8

Bo Gamble
Director of Strategic Practice Initiatives
Community Oncology Alliance

Gamble joined Community Oncology Alliance in May 2011 as the director of strategic practice initiatives. He has a diverse range of cancer and other healthcare experience at the national and local levels. His experience includes serving 13 years as administrator of a multiphysician, multi-location oncology practice in eastern North Carolina. In his other 17 years of healthcare experience, he has served as an independent consultant for hospital patient accounting and IT implementation projects, national director of client support for a healthcare software company, and business office manager for a 300+ bed hospital. He has served as the president and legislative chairperson for the North Carolina oncology practice management society, a member of the COA Board of Directors, and the co-chair of the national COA Administrators' Network.

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www.ajmc.com/ajmc-tv/live/pcoc13/Discussion8

Cliff Goodman, PhD
Senior Vice President & Principal
The Lewin Group

Dr Goodman is senior vice president and principal at The Lewin Group, a healthcare policy and human services consulting firm based in Falls Church, Virginia. He has 30 years of experience in such areas as health technology assessment, evidence-based healthcare, comparative effectiveness research, health economics, and studies pertaining to healthcare innovations, regulation, and payment. He directs studies and projects for an international range of government agencies; pharmaceutical, biotechnology, and medical device companies; healthcare provider institutions; and professional, industry, and patient advocacy groups. Dr Goodman served as chair of the Medicare Evidence Development & Coverage Advisory Committee for the Centers for Medicare & Medicaid Services (2009-2012). He is president of the professional society, Health Technology Assessment International, and is a fellow of the American Institute for Medical and Biological Engineering.

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www.ajmc.com/ajmc-tv/live/pcoc13/Discussion1

Ira M. Klein, MD, MBA, FACP
Chief of Staff, Office of the Chief Medical Officer
Aetna, Inc

Dr Klein is a national medical director in the Office of the Chief Medical Officer, holding the position of clinical thought leadership, responsible for core program development across the enterprise. He recently transitioned from his previous role of almost 2 years as chief of staff to the chief medical officer at Aetna, having been in this role since 2011, and remains as part of the team responsible for communicating and deploying the strategic efforts of the CMO in multiple areas, including leveraging of business acquisitions, clinical integration, and clinical program development.

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www.ajmc.com/ajmc-tv/live/pcoc13/Discussion2

Michael A. Kolodjiez, MD
National Medical Director, Oncology Strategies
Aetna, Inc

Dr Kolodjiez is the national medical director, oncology solutions, Office of the Chief Medical Officer, Aetna. He joined New York Oncology in the winter of 1998, and was a partner in the practice until December 2012. He was an active member of the US Oncology Pharmacy and Therapeutics committee, on the executive committee from 2002 to 2011, and chairman from 2004 to 2011. He served as medical director for oncology services for US Oncology from 2007 to 2011. In this role, he helped direct the implementation of the USON clinical pathways initiative, the integration of the USON EMR into this program, and the development of the USON disease management and advanced care planning programs, now known as Innovent Oncology.

See pages SP87, SP88, SP90
www.ajmc.com/ajmc-tv/live/pcoc13/Discussion5

Karen Lewis, MS, MM, CGC
Medical Policy and Technology Administrator
Priority Health

Lewis oversees medical policy development and works with the medical directors for medical necessity review and grievance and appeals cases. She has been involved in many grant projects, including sudden cardiovascular death in the young, genetics education for healthcare providers, and is currently the insurance champion for a collaborative agreement between the Centers for Disease Control and Prevention and the Michigan Department of Community Health, evaluating cancer genomics best practices. In addition to her genetics activities, Lewis is an adjunct professor at the Michigan State College of Human Medicine in ethics and humanities.

See pages SP86, SP87
www.ajmc.com/ajmc-tv/live/pcoc13/Lewis

Ellen Matloff, MS
Director, Cancer Genetic Counseling
Yale Cancer Center

Matloff is a research scientist in the Department of Genetics and the director of Cancer Genetic Counseling at Yale Cancer Center/Yale School of Medicine in New Haven, Connecticut. She came to Yale in 1995 to start the Cancer Genetic Counseling program, which is now one of the largest in the country. She has received several research grants, has lectured internationally on cancer genetics, and has published extensively on the topic of cancer genetic counseling and testing. Matloff was also a plaintiff in the well-known BRCA patent case against Myriad Genetic Laboratories, in which gene patents were banned by a unanimous Supreme Court decision in June 2013.

See page SP67

Lee N. Newcomer, MD, MHA
Senior Vice President, Oncology, Genetics and Women's Health
UnitedHealthcare

At UnitedHealthcare (UHC), Dr Newcomer has strategic responsibility for oncology, genetics, and women's health. A board-certified medical oncologist, he began his management career as a medical director for Cigna Health Care of Kansas City in 1990. From 1991 to 2000, Dr Newcomer was the chief medical officer at UHC, where his work emphasized the development of performance measures and incentives to improve clinical care. Dr Newcomer was a founding executive of Vivius, a consumer-directed venture that allowed consumers to create their own personalized health plans. He returned to UHC in 2006 to focus on combining clinical, financial, and administrative incentives for improved and affordable cancer care.

See pages SP77, SP85, SP88, SP90
www.ajmc.com/ajmc-tv/live/pcoc13/Newcomer

Scott D. Ramsey, MD, PhD
Director, Cancer Technology Assessment Group
Fred Hutchinson Cancer Research Center

Dr Ramsey is a general internist and health economist. He is a full member in the Cancer Prevention Program, Public Health Sciences Division at the Fred Hutchinson Cancer Research Center, where he directs the Hutchinson Institute for Cancer Outcomes Research, a multidisciplinary team devoted to clinical and economic evaluations of new and existing cancer prevention, screening, and treatment technologies. In addition, Dr Ramsey is a professor in the School of Medicine, School of Pharmacy, and the Institute for Public Health Genetics at the University of Washington.

See pages SP88, SP90, SP91
www.ajmc.com/ajmc-tv/live/pcoc13/Ramsey

Dennis Scanlon, PhD
Professor of Health Policy and Administration
Pennsylvania State University

Dr Scanlon is a professor of health policy and administration at The Pennsylvania State University, College of Health and Human Development. He serves as principal investigator for the Robert Wood Johnson Foundation's Aligning Forces for Quality evaluation and is a consultant on an Agency for Healthcare Research and Quality study, "Assessing a Statewide Multi-Stakeholder Chronic Care Model Implementation." Scanlon also serves on the editorial boards of several journals.

See pages SP71, SP75, SP77, SP85
www.ajmc.com/ajmc-tv/live/pcoc13/Discussion1

Manasi A. Tirodkar, PhD, MS
Research Scientist
The National Committee for Quality Assurance

Dr Tirodkar is a research scientist at the National Committee for Quality Assurance. With a background in medical anthropology and health services research, she has extensive experience with survey and case study methodology as well as health systems and practice transformation. She has worked on measure development projects spanning different disease conditions and populations (cardiovascular, cancer, geriatrics) and directs projects related to evaluations of the patient-centered medical home and shared decision making. She recently completed directing a mixed-methods AHRQ-funded project on PCMH practice transformation. She recently started a new project to evaluate the impact of patient-centered oncology care in a pilot funded by PCORI.

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www.ajmc.com/ajmc-tv/live/pcoc13/Discussion1

Phyllis Torda
Vice President, Quality Solutions Group
The National Committee for Quality Assurance

Torda is vice president for the Quality Solutions Group at the National Committee for Quality Assurance (NCQA). In that capacity, she leads NCQA's efforts to work with federal and state governments and private organizations on quality assessment issues. In her 17 years at NCQA, Torda has led a wide variety of activities related to performance measurement, quality assessment, and reporting. She is the principal investigator for NCQA's contract with the Centers for Medicare & Medicaid Services (CMS) to develop performance measures for the Medicare population and to evaluate Medicare Special Needs Plans. She has also led NCQA's activities to develop measures of inpatient psychiatric care and cancer care for CMS and to develop measures for reporting from electronic health records for CMS and the Office of the National Coordinator for Health IT.

See pages SP77, SP85
www.ajmc.com/ajmc-tv/live/pcoc13/Discussion3

IN MBC, ONCOLOGISTS ARE CONSISTENTLY
EXTENDING THE CONTINUUM OF MEANINGFUL CARE[1-3]

With MBC treatment potentially extending to 6 lines and beyond, third-line chemotherapy can still be early in the fight for some patients[2]

MBC=metastatic breast cancer.

Indication

Halaven is indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

Important Safety Information

Neutropenia

- Monitor complete blood counts prior to each dose, and increase the frequency of monitoring in patients who develop Grade 3 or 4 cytopenias. Delay administration and reduce subsequent doses in patients who experience febrile neutropenia or Grade 4 neutropenia lasting longer than 7 days
- Severe neutropenia (ANC <500/mm^3) lasting more than 1 week occurred in 12% (62/503) of patients. Patients with elevated liver enzymes >3 × ULN and bilirubin >1.5 × ULN experienced a higher incidence of Grade 4 neutropenia and febrile neutropenia than patients with normal levels
- Grade 3 and Grade 4 neutropenia occurred in 28% and 29%, respectively, of patients who received Halaven. Febrile neutropenia occurred in 5% of patients and two patients (0.4%) died from complications

Peripheral Neuropathy

- Patients should be monitored closely for signs of peripheral motor and sensory neuropathy
- Grade 3 peripheral neuropathy occurred in 8% of patients, and Grade 4 in 0.4% of patients who received Halaven. Delay administration of Halaven until resolution to Grade 2 or less
- Neuropathy lasting more than 1 year occurred in 5% of patients. Twenty-two percent of patients developed a new or worsening neuropathy that had not recovered within a median follow-up duration of 269 days (range 25-662 days)
- Peripheral neuropathy (5%) was the most common adverse reaction resulting in discontinuation

Pregnancy Category D

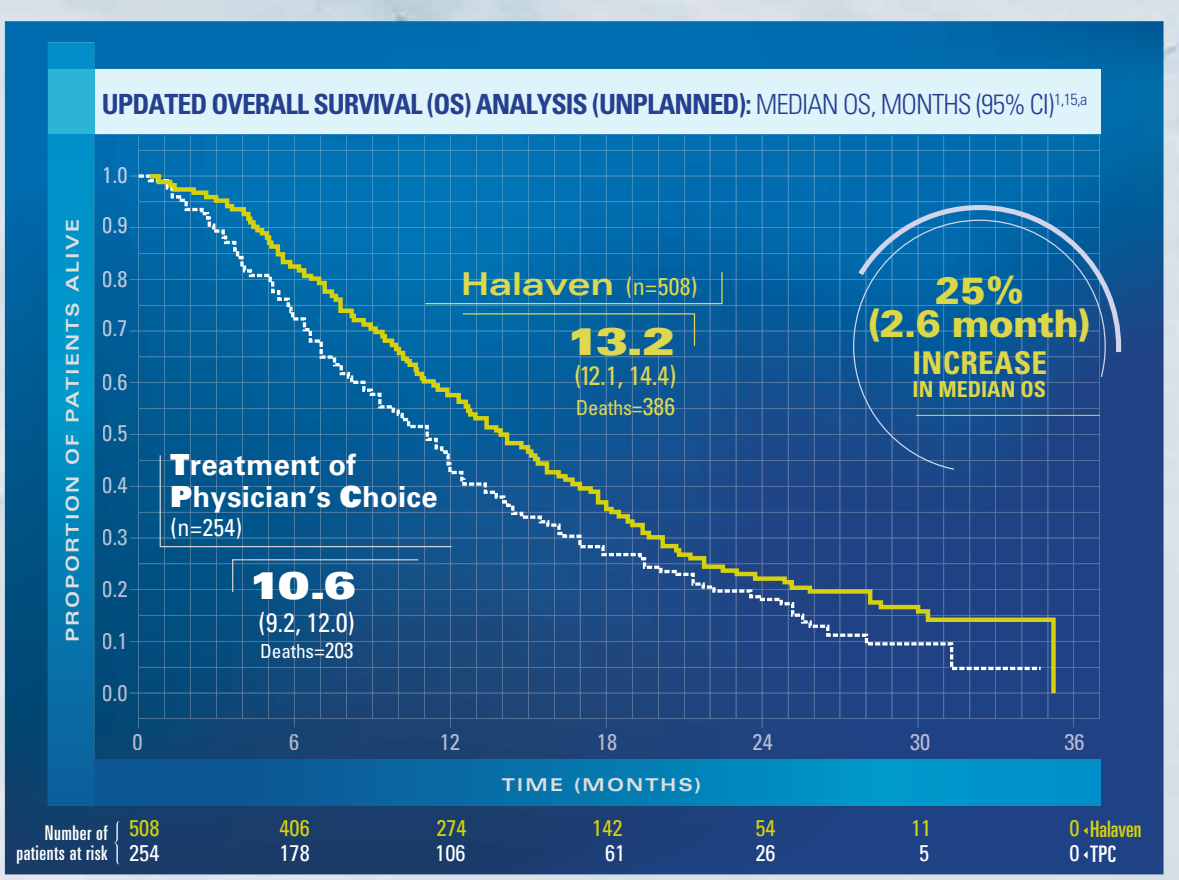
- Halaven is expected to cause fetal harm when administered to a pregnant woman and patients should be advised of these risks

QT Prolongation

- In an uncontrolled ECG study in 26 patients, QT prolongation was observed on Day 8, independent of eribulin concentration, with no prolongation on Day 1. ECG monitoring is recommended for patients with congestive heart failure; bradyarrhythmias;

GIVE YOUR PATIENTS AN OPPORTUNITY FOR MORE LIFE

The FIRST and ONLY single agent that significantly extended OVERALL SURVIVAL in third-line MBC[7-14]



Results from an updated, unplanned survival analysis of the Phase III, randomized, open-label, multicenter, multinational Eisai Metastatic Breast Cancer Study Assessing Physician's Choice versus E7389 (Eribulin) (EMBRACE) trial of Halaven versus Treatment of Physician's Choice (TPC) in patients with MBC (N=762), conducted when 77% of events (deaths) had been observed. The primary endpoint was OS. Patients were randomized (2:1) to receive either Halaven 1.4 mg/m^2 intravenously for 2 to 5 minutes on Days 1 and 8 of a 21-day cycle, or any single-agent therapy, selected prior to randomization. At baseline, all patients had received ≥2 prior chemotherapeutic regimens for metastatic disease and demonstrated disease progression within 6 months of their last chemotherapeutic regimen. All patients received prior anthracycline- and taxane-based chemotherapy, unless contraindicated. Therapies in the TPC arm consisted of 97% chemotherapy (26% vinorelbine, 18% gemcitabine, 18% capecitabine, 16% taxanes [included paclitaxel, docetaxel, nab-paclitaxel, and ixabepilone], 9% anthracyclines, 10% other chemotherapy), and 3% hormonal therapy.

CI=confidence interval.
[a]Conducted in the intent-to-treat population.

The updated OS analysis was consistent with the primary analysis[7]

- The primary analysis, conducted when ~50% of events (deaths) had been observed, demonstrated a median OS for Halaven vs TPC of 13.1 months (95% CI: 11.8, 14.3) vs 10.6 months (95% CI: 9.3, 12.5), hazard ratio=0.81 (95% CI: 0.66, 0.99) (*P*=0.041)[7,15]

concomitant use of drugs that prolong QT interval, including Class Ia and III antiarrhythmics; and electrolyte abnormalities

- Correct hypokalemia or hypomagnesemia prior to initiating Halaven and monitor electrolytes periodically during therapy. Avoid in patients with congenital long QT syndrome

Hepatic and Renal Impairment

- For patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic and/or moderate (CrCl 30-50 mL/min) renal impairment, a reduction in starting dose is recommended

Most Common Adverse Reactions

- Most common adverse reactions (≥25%) reported in patients receiving Halaven were neutropenia (82%), anemia (58%), asthenia/fatigue (54%), alopecia (45%), peripheral neuropathy (35%), nausea (35%), and constipation (25%)
- The most common serious adverse reactions reported in patients receiving Halaven were febrile neutropenia (4%) and neutropenia (2%)

References: 1. Dufresne A, et al. *Breast Cancer Res Treat.* 2008;107(2):275-279. **2.** Planchat E, et al. *Breast.* 2011;20(6):574-578. **3.** Ray S, et al. In: *J Clin Oncol.* San Francisco, CA: ASCO Breast Cancer Symposium; 2012. Abstract 116. **4.** Cardoso F, et al. *Ann Oncol.* 2002;13(2):197-207. **5.** Seah DS, et al. Poster presented at: 2012 ASCO Annual Meeting; June 1–5, 2012; Chicago, IL. Abstract 6089. **6.** Lin NU, et al. *Lancet.* 2011;377(9769):878-880. **7.** Halaven [package insert]. Woodcliff Lake, NJ: Eisai Inc; 2013. **8.** Saad ED, et al. *J Clin Oncol.* 2010;28(11):1958-1962. **9.** Slamon DJ, et al. *N Engl J Med.* 2001;344(11):783-792. **10.** Geyer CE, et al. *N Engl J Med.* 2006;355(26):2733-2743. **11.** von Minckwitz G, et al. *J Clin Oncol.* 2009;27(12):1999-2006. **12.** Miller K, et al. *N Engl J Med.* 2007;357(26):2666-2676. **13.** Robert NJ, et al. *J Clin Oncol.* 2011;29(10):1252-1260. **14.** Sparano JA, et al. *J Clin Oncol.* 2010;28(20):3256-3263. **15.** Cortes J, et al. *Lancet.* 2011;377(9769):914-923.

Please see accompanying brief summary of Halaven full Prescribing Information.

Visit **www.halaven.com/hcp.aspx**

Halaven®
(eribulin mesylate) Injection
ADVANCING SURVIVAL

HALAVEN® (eribulin mesylate) Injection BRIEF SUMMARY – See package insert for full prescribing information.

2.2 Dose Modification

Assess for peripheral neuropathy and obtain complete blood cell counts prior to each dose.

Recommended dose delays

- Do not administer HALAVEN on Day 1 or Day 8 for any of the following:
  - ANC <1,000/mm^3
  - Platelets <75,000/mm^3
  - Grade 3 or 4 non-hematological toxicities.
- The Day 8 dose may be delayed for a maximum of 1 week.
  - If toxicities do not resolve or improve to ≤ Grade 2 severity by Day 15, omit the dose.
  - If toxicities resolve or improve to ≤ Grade 2 severity by Day 15, administer HALAVEN at a reduced dose and initiate the next cycle no sooner than 2 weeks later.

Recommended dose reductions

- If a dose has been delayed for toxicity and toxicities have recovered to Grade 2 severity or less, resume HALAVEN at a reduced dose as set out in Table 1.
- Do not re-escalate HALAVEN dose after it has been reduced.

Table 1 Recommended Dose Reductions

Event Description	Recommended HALAVEN Dose
Permanently reduce the 1.4 mg/m^2 HALAVEN dose for any of the following:	1.1 mg/m^2
ANC <500/mm^3 for >7 days	
ANC <1,000 /mm^3 with fever or infection	
Platelets <25,000/mm^3	
Platelets <50,000/mm^3 requiring transfusion	
Non-hematologic Grade 3 or 4 toxicities	
Omission or delay of Day 8 HALAVEN dose in previous cycle for toxicity	
Occurrence of any event requiring permanent dose reduction while receiving 1.1 mg/m^2	0.7 mg/m^2
Occurrence of any event requiring permanent dose reduction while receiving 0.7 mg/m^2	Discontinue HALAVEN

ANC = absolute neutrophil count.

Toxicities graded in accordance with National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.

5 WARNINGS AND PRECAUTIONS

5.1 Neutropenia

Severe neutropenia (ANC <500/mm^3) lasting more than one week occurred in 12% (62/503) of patients in Study 1, leading to discontinuation in <1% of patients. Patients with alanine aminotransferase or aspartate aminotransferase >3 × ULN (upper limit of normal) experienced a higher incidence of Grade 4 neutropenia and febrile neutropenia than patients with normal aminotransferase levels. Patients with bilirubin >1.5 × ULN also had a higher incidence of Grade 4 neutropenia and febrile neutropenia.

Monitor complete blood counts prior to each dose; increase the frequency of monitoring in patients who develop Grade 3 or 4 cytopenias. Delay administration of HALAVEN and reduce subsequent doses in patients who experience febrile neutropenia or Grade 4 neutropenia lasting longer than 7 days. Clinical studies of HALAVEN did not include patients with baseline neutrophil counts below 1,500/mm^3.

5.2 Peripheral Neuropathy

Grade 3 peripheral neuropathy occurred in 8% (40/503) of patients, and Grade 4 in 0.4% (2/503) of patients in Study 1. Peripheral neuropathy was the most common toxicity leading to discontinuation of HALAVEN (5% of patients; 24/503). Neuropathy lasting more than one year occurred in 5% (26/503) of patients. Twenty-two percent (109/503) of patients developed a new or worsening neuropathy that had not recovered within a median follow-up duration of 269 days (range 25-662 days). Monitor patients closely for signs of peripheral motor and sensory neuropathy. Withhold HALAVEN in patients who experience Grade 3 or 4 peripheral neuropathy until resolution to Grade 2 or less.

5.3 Embryo-Fetal Toxicity

There are no adequate and well-controlled studies of HALAVEN in pregnant women. HALAVEN is a microtubule inhibitor; therefore, it is expected to cause fetal harm when administered to a pregnant woman. Embryo-fetal toxicity and teratogenicity occurred in rats that received eribulin mesylate at approximately half of the recommended human dose based on body surface area. If this drug is used during pregnancy, or if a patient becomes pregnant while taking this drug, she should be apprised of the potential hazard to the fetus.

5.4 QT Prolongation

In an uncontrolled open-label ECG study in 26 patients, QT prolongation was observed on Day 8, independent of eribulin concentration, with no QT prolongation observed on Day 1. ECG monitoring is recommended if therapy is initiated in patients with congestive heart failure, bradyarrhythmias, drugs known to prolong the QT interval, including Class Ia and III antiarrhythmics, and electrolyte abnormalities. Correct hypokalemia or hypomagnesemia prior to initiating HALAVEN and monitor these electrolytes periodically during therapy. Avoid HALAVEN in patients with congenital long QT syndrome.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

• Neutropenia • Peripheral neuropathy • QT interval prolongation

The most common adverse reactions (≥25%) reported in patients receiving HALAVEN were neutropenia, anemia, asthenia/fatigue, alopecia, peripheral neuropathy, nausea, and constipation. The most common serious adverse reactions reported in patients receiving HALAVEN were febrile neutropenia (4%) and neutropenia (2%). The most common adverse reaction resulting in discontinuation of HALAVEN was peripheral neuropathy (5%).

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

In clinical trials, HALAVEN has been administered to 1,222 patients with multiple tumor types, including 240 patients exposed to HALAVEN for 6 months or longer. The majority of the 1,222 patients were women (82%) with a median age of 58 years (range: 26 to 91 years). The racial and ethnic distribution was Caucasian (83%), Black (5%), Asian (2%), and other (5%).

The adverse reactions described in Table 2 were identified in 750 patients treated in Study 1. In Study 1, patients were randomized (2:1) to receive either HALAVEN (1.4 mg/m^2 on Days 1 and 8 of a 21-day cycle) or single agent treatment chosen by their physician (control group). A total of 503 patients received HALAVEN, and 247 patients in the control group received therapy consisting of chemotherapy [total 97% (anthracyclines 10%, capecitabine 18%, gemcitabine 19%, taxanes 15%, vinorelbine 25%, other chemotherapies 10%)] or hormonal therapy (3%). The median duration of exposure was 118 days for patients receiving HALAVEN and 63 days for patients receiving control therapy. Table 2 reports the most common adverse reactions occurring in at least 10% of patients in either group.

Table 2 Adverse Reactions with a Per-Patient Incidence of at Least 10% in Study 1

MedDRA ver 10.0	HALAVEN (n=503)		Control Group (n=247)	
	All Grades	≥ Grade 3	All Grades	≥ Grade 3
Blood and Lymphatic System Disorders[a]				
Neutropenia	82%	57%	53%	23%
Anemia	58%	2%	55%	4%
Nervous system disorders				
Peripheral neuropathy[b]	35%	8%	16%	2%
Headache	19%	<1%	12%	<1%
General disorders and administrative site conditions				
Asthenia/Fatigue	54%	10%	40%	11%
Mucosal inflammation	9%	1%	10%	2%
Pyrexia	21%	<1%	13%	<1%
Gastrointestinal disorders				
Constipation	25%	1%	21%	1%
Diarrhea	18%	0	18%	0
Nausea	35%	1%	28%	3%
Vomiting	18%	1%	18%	1%
Musculoskeletal and connective tissue disorders				
Arthralgia/Myalgia	22%	<1%	12%	1%
Back pain	16%	1%	7%	2%
Bone pain	12%	2%	9%	2%
Pain in extremity	11%	1%	10%	1%
Investigations				
Weight decreased	21%	1%	14%	<1%
Metabolism and nutrition disorders				
Anorexia	20%	1%	13%	1%
Respiratory, thoracic, and mediastinal disorders				
Cough	14%	0	9%	0
Dyspnea	16%	4%	13%	4%
Skin and subcutaneous tissue disorders				
Alopecia	45%	NA[c]	10%	NA[c]

Table 2 (cont'd)

MedDRA ver 10.0	HALAVEN (n=503)		Control Group (n=247)	
	All Grades	≥ Grade 3	All Grades	≥ Grade 3
Infections and Infestations				
Urinary Tract Infection	10%	1%	5%	0

[a] Based upon laboratory data.

[b] Includes neuropathy peripheral, neuropathy, peripheral motor neuropathy, polyneuropathy, peripheral sensory neuropathy, and paraesthesia.

[c] Not applicable; (grading system does not specify > Grade 2 for alopecia).

Cytopenias: Grade 3 neutropenia occurred in 28% (143/503) of patients who received HALAVEN in Study 1, and 29% (144/503) of patients experienced Grade 4 neutropenia. Febrile neutropenia occurred in 5% (23/503) of patients; two patients (0.4%) died from complications of febrile neutropenia. Dose reduction due to neutropenia was required in 12% (62/503) of patients and discontinuation was required in <1% of patients. The mean time to nadir was 13 days and the mean time to recovery from severe neutropenia (<500/mm^3) was 8 days. Grade 3 or greater thrombocytopenia occurred in 1% (7/503) of patients. G-CSF (granulocyte colony-stimulating factor) or GM-CSF (granulocyte–macrophage colony-stimulating factor) was used in 19% of patients who received HALAVEN.

Peripheral Neuropathy: In Study 1, 17% of enrolled patients had Grade 1 peripheral neuropathy and 3% of patients had Grade 2 peripheral neuropathy at baseline. Dose reduction due to peripheral neuropathy was required by 3% (14/503) of patients who received HALAVEN. Four percent (20/503) of patients experienced peripheral motor neuropathy of any grade and 2% (8/503) of patients developed Grade 3 peripheral motor neuropathy.

Liver Function Test Abnormalities: Among patients with Grade 0 or 1 ALT levels at baseline, 18% of HALAVEN-treated patients experienced Grade 2 or greater ALT elevation. One HALAVEN-treated patient without documented liver metastases had concomitant Grade 2 elevations in bilirubin and ALT; these abnormalities resolved and did not recur with re-exposure to HALAVEN.

Less Common Adverse Reactions: The following additional adverse reactions were reported in ≥5% to <10% of the HALAVEN-treated group: **Eye Disorders:** increased lacrimation; **Gastrointestinal Disorders:** dyspepsia, abdominal pain, stomatitis, dry mouth; **General Disorders and Administration Site Conditions:** peripheral edema; **Infections and Infestations:** upper respiratory tract infection; **Metabolism and Nutrition Disorders:** hypokalemia; **Musculoskeletal and Connective Tissue Disorders:** muscle spasms, muscular weakness; **Nervous System Disorders:** dysgeusia, dizziness; **Psychiatric Disorders:** insomnia, depression; **Skin and Subcutaneous Tissue Disorders:** rash.

6.2 Postmarketing Experience

The following adverse drug reactions have been identified during post-approval of HALAVEN. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. **Blood and Lymphatic System Disorders:** lymphopenia; **Gastrointestinal Disorders:** pancreatitis; **Hepatobiliary Disorders:** hepatitis; **Immune System Disorders:** drug hypersensitivity; **Infections and Infestations:** pneumonia, sepsis/neutropenic sepsis; **Metabolism and Nutrition Disorders:** hypomagnesemia, dehydration; **Respiratory, thoracic, and mediastinal disorders:** interstitial lung disease; **Psychiatric Disorders:** anxiety; **Skin and Subcutaneous Tissue Disorders:** pruritus.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Category D

There are no adequate and well-controlled studies with HALAVEN in pregnant women. HALAVEN is a microtubule inhibitor; therefore, it is expected to cause fetal harm when administered to a pregnant woman. Embryo-fetal toxicity and teratogenicity occurred in rats that received eribulin mesylate at approximately half of the recommended human dose based on body surface area. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

In a developmental toxicity study, pregnant rats received intravenous infusion of eribulin mesylate during organogenesis (Gestation Days 8, 10, and 12) at doses approximately 0.04, 0.13, 0.43 and 0.64 times the recommended human dose, based on body surface area (mg/m^2). Increased abortion and severe external or soft tissue malformations were observed in offspring at doses 0.64 times the recommended human dose based on body surface area (mg/m^2), including the absence of a lower jaw, tongue, stomach and spleen. Increased embryo-fetal death/resorption, reduced fetal weights, and minor skeletal anomalies consistent with developmental delay were also reported at or above doses of 0.43 times the recommended human dose.

Maternal toxicity of eribulin mesylate was reported in rats at or above doses of 0.43 times the recommended human dose (mg/m^2), and included enlarged spleen, reduced maternal weight gain and decreased food consumption.

8.3 Nursing Mothers

It is not known whether HALAVEN is excreted into human milk. No studies in humans or animals were conducted to determine if HALAVEN is excreted into milk. Because many drugs are excreted into human milk and because of the potential for serious adverse reactions in human milk fed infants from HALAVEN, a decision should be made whether to discontinue nursing or to discontinue HALAVEN taking into account the importance of the drug to the mother.

8.4 Pediatric Use

The safety and effectiveness of HALAVEN in pediatric patients below the age of 18 years have not been established.

8.6 Hepatic Impairment

Administration of HALAVEN at a dose of 1.1 mg/m^2 to patients with mild hepatic impairment and 0.7 mg/m^2 to patients with moderate hepatic impairment resulted in similar exposure to eribulin as a dose of 1.4 mg/m^2 to patients with normal hepatic function. Therefore, a lower starting dose of 1.1 mg/m^2 is recommended for patients with mild hepatic impairment (Child-Pugh A) and of 0.7 mg/m^2 is recommended for patients with moderate hepatic impairment (Child-Pugh B). HALAVEN was not studied in patients with severe hepatic impairment (Child-Pugh C).

8.7 Renal Impairment

For patients with moderate renal impairment (CrCl 30-50 mL/min), the geometric mean dose-normalized systemic exposure increased 2-fold compared to patients with normal renal function. A lower starting dose of 1.1 mg/m^2 is recommended for patients with moderate renal impairment. The safety of HALAVEN was not studied in patients with severe renal impairment (CrCl <30 mL/min).

10 OVERDOSAGE

Overdosage of HALAVEN has been reported at approximately 4 times the recommended dose, which resulted in Grade 3 neutropenia lasting seven days and a Grade 3 hypersensitivity reaction lasting one day.

There is no known antidote for HALAVEN overdose.

12 CLINICAL PHARMACOLOGY

12.3 Pharmacokinetics

Specific Populations

Hepatic Impairment

A study evaluated the PK of eribulin in patients with mild (Child-Pugh A; n=7) and moderate (Child-Pugh B; n=5) hepatic impairment. Compared to patients with normal hepatic function (n=6), eribulin exposure increased 1.8-fold and 2.5-fold in patients with mild and moderate hepatic impairment, respectively. Administration of HALAVEN at a dose of 1.1 mg/m^2 to patients with mild hepatic impairment and 0.7 mg/m^2 to patients with moderate hepatic impairment resulted in similar exposure to eribulin as a dose of 1.4 mg/m^2 to patients with normal hepatic function.

Renal Impairment

No formal PK trials were conducted with HALAVEN in patients with renal impairment. Available data suggests that geometric mean dose-normalized systemic exposure is similar for patients with mild renal impairment (CrCl 50-80 mL/min) relative to patients with normal renal function. However, for patients with moderate renal impairment (CrCl 30-50 mL/min), the geometric mean dose-normalized systemic exposure increased 2-fold compared to patients with normal renal function.

12.6 Cardiac Electrophysiology

The effect of HALAVEN on the QTc interval was assessed in an open-label, uncontrolled, multicenter, single-arm dedicated QT trial. A total of 26 patients with solid tumors received 1.4 mg/m^2 of HALAVEN on Days 1 and 8 of a 21-day cycle. A delayed QTc prolongation was observed on Day 8, with no prolongation observed on Day 1. The maximum mean QTcF change from baseline (95% upper confidence interval) was 11.4 (19.5) ms.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, mutagenesis, impairment of fertility

Carcinogenicity studies have not been conducted with eribulin mesylate.

Eribulin mesylate was not mutagenic in *in vitro* bacterial reverse mutation assays (Ames test). Eribulin mesylate was positive in mouse lymphoma mutagenesis assays, and was clastogenic in an *in vivo* rat bone marrow micronucleus assay.

The effects of HALAVEN on human fertility are unknown. Fertility studies have not been conducted with eribulin mesylate in humans or animals. However, nonclinical findings in repeated-dose dog and rat toxicology studies suggest that male fertility may be compromised by treatment with eribulin mesylate. Rats exhibited testicular toxicity (hypocellularity of seminiferous epithelium with hypospermia/aspermia) following dosing with eribulin mesylate at or above 0.43 times the recommended human dose (mg/m^2) given once weekly for 3 weeks, or at or above 0.21 times the recommended human dose (mg/m^2) given once weekly for 3 out of 5 weeks, repeated for 6 cycles. Testicular toxicity was also observed in dogs given 0.64 times the recommended human dose (mg/m^2) weekly for 3 out of 5 weeks, repeated for 6 cycles.

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling

- Advise patients to contact their health care provider for a fever of 100.5°F or greater or other signs or symptoms of infection such as chills, cough, or burning or pain on urination.
- Advise women of childbearing potential to avoid pregnancy and to use effective contraception during treatment with HALAVEN.

Eisai

The Angelina Effect: Rising Interest in Genetic Testing Creates Opportunities for Patients—and Profit

Ellen T. Matloff, MS, *is a research scientist in the Department of Genetics and the director of cancer genetic counseling at Yale Cancer Center/Yale School of Medicine in New Haven, Connecticut. She has sounded the alarm on behalf of patients and families for whom a genetic mutation may be a warning sign for cancer. Matloff was a plaintiff in the case against Myriad Genetics, which prompted the US Supreme Court to end the monopoly in genetic testing. But as she has warned, this presents challenges for providers in managing patient expectations. Matloff addressed attendees at Patient-Centered Oncology Care 2013 at an evening reception November 14, 2013.*

In the small world of genetic counselors, time is now divided into Before Angelina Jolie and After Angelina Jolie.

The roughly 3000 professionals in the United States who are certified to handle the complex task of ordering genetic tests and interpreting results have experienced both the good and ill effects of a sea change in their field, thanks to a number of factors, according to **Ellen T. Matloff, MS,** who has been a genetic counselor at Yale University since 1995.

The announcement on May 14, 2013, by one of the world's most beautiful women that she had undergone prophylactic breast removal because of a faulty BRCA1 gene stunned the public and the medical community alike. Jolie's announcement, which appeared on the op-ed page of *The New York Times*,[1] set off a tidal wave of interest and inquiries about BRCA testing; calls to Matloff's clinic and others soared.[2]

Then came the June 2013 US Supreme Court ruling that said genes could not be owned, which opened the door to competition in genetic testing for the BRCA1 and BRCA2 mutations, among scores of others.

But as awareness and access have skyrocketed, so have opportunities for profit. And, as she has done repeatedly in the months since, Matloff sounded the alarm to the attendees at Patient-Centered Oncology Care 2013 on behalf of patients who, swayed by aggressive marketing, might order the wrong test or have results misinterpreted, resulting in poor medical decisions.

Harnessing the power of genetic testing to help cancer patients and families requires understanding what the tests can and cannot do, and patients are best served if their results are interpreted by a certified counselor, she said. Despite what might be believed, or portrayed in the media, most physicians have limited genetics training—a point doctors have admitted in surveys.

A positive test for a mutation does not guarantee a person will get cancer, nor does a negative result mean a person has no risk of cancer, Matloff warns. She pointed out in her presentation that only 10% of cancers are hereditary, which means 90% result from something else.

It's important to understand risk factors, such as early onset of cancer, whether multiple family members are affected, and whether there are "related" cancers in the family. Factors such as unusual presentation of the disease and ethnicity can play a role in whether one person's cancer means the rest of the family is at risk, she said.

Matloff's arrival at Yale coincided with the cloning of BRCA1 (1994) and BRCA2 (1995). BRCA1 is associated with increased risk of breast, ovarian, and prostate cancer; BRCA2 carries risks of breast, ovarian, prostate, pancreatic, and male breast cancer. Jolie's decision was driven by the presence of BRCA1, which her doctors said increased her risk of breast cancer 87%.[1] Her mother died at 56, and other women in the family had died early.

The risks are real: data that Matloff presented show that compared with an overall risk of 11 to 13% of breast cancer in the general population, BRCA1 mutations are associated with a 55 to 58% increased risk; BRCA2 risks are 50 to 80%. Ovarian cancer risk rises from 1 to 2% of the population generally to 15 to 60% with BRCA1 and 15 to 40% with BRCA2.

Jolie was the first to state that while surgery made sense for her, it was not for everyone.[1] But as Matloff reports, unfortunately, that message has not gotten through to some women, who have surgery based on "mutations of unknown significance," or who demand BRCA testing when, in fact, a better review of the family history would have resulted in testing for a different mutation.

Matloff's tale of an episode in a synagogue in her area highlights the concern: certain BRCA mutations are associated with increased rates of cancer among the Ashkenazi Jewish population, but these are very specific mutations. The local rabbi said that the congregation had been offered 100 free genetic tests and they could be handed out during the high holidays—and if "anything came up" the patients could follow up. Matloff was alarmed that testing would be done without the involvement of genetic counselors. Yet she knows that the rise of direct-to-consumer testing companies such as 23andMe makes these episodes increasingly common.

She walked the attendees through a series of examples to show just how complex the testing process can be, and how knowledge of family history prior to testing is essential. To begin with, it's important to order the right test—yet Matloff has seen cases in which patients pay for tests that won't even give them the answer they need.

Of note, within 2 weeks of Matloff's presentation, the US Food and Drug Administration ordered 23andMe[3] to halt marketing until it complied with the agency's regulatory requirements. **EBO**

References

1. Jolie A. My medical choice. *The New York Times.* May 14, 2013. http://www.nytimes.com/2013/05/14/opinion/my-medical-choice.html. Accessed January 7, 2014.

2. Beagin N. Genetic testing should come with counseling: American Cancer Society CMO, Supreme Court plaintiff among experts who warn of consumer risks. *Am J Manag Care*. 2013;19(SP13):SP441-SP452.

3. Caffrey MK. FDA tells direct-to-consumer genetic testing company to halt marketing. *Am J Manag Care.* 2013;19(SP13):SP453-SP454.

THE AMERICAN JOURNAL OF MANAGED CARE®

Friday, November 15, 2013

Time	Event	Room
7:30 AM - 8:30 AM	**Registration**	Pre-function (2nd Floor)
8:00 AM - 8:30 AM	**Breakfast and Product Theater:** Granix (tbo-filgrastim), Another Option in Short-Acting G-CSF Therapy *Sponsored by Teva Pharmaceuticals*	Whitehall Ballroom (2nd Floor)
8:30 AM - 9:15 AM	**Keynote:** Person-Centered Care: The New Business Case for Cancer *Amy Berman, BS, RN*	Whitehall Ballroom (2nd Floor)
9:15 AM - 10:45 AM	**Session 1: Patient-Centered Oncology Care: Real-World Perspectives** • **Presentation 1:** Oncology Practice in the Era of PCMHs and ACOs: Square Pegs or Round Holes? *Peter B. Bach, MD, MAPP* • **Discussion 1:** The Role of Consumerism in Deliverability of Care *Cliff Goodman, PhD; Amy Berman, BS, RN; Dennis Scanlon, PhD; Manasi A. Tirodkar, PhD MS* • **Presentation 2:** Incorporating Patient-Centered Outcomes in Clinical Trials *Ethan Basch, MD* • **Discussion 2:** Implications of Healthcare Reform: "No" Will Be Heard *Cliff Goodman, PhD; A. Mark Fendrick, MD; John L. Fox, MD, MHA; Ira M. Klein, MD, MBA, FACP*	Whitehall Ballroom (2nd Floor)
10:45 AM - 11:00 AM	**Break**	Ravenhurst & Pre-function (2nd Floor)
11:00 AM - 12:30 PM	**Session 2: Quality in Oncology** • **Presentation 3:** Defining and Measuring Quality Outcomes in Oncology *Lee N. Newcomer, MD, MHA* • **Discussion 3:** Challenges and Opportunities for Quality Measures in Oncology *Ira M. Klein, MD, MBA, FACP; Lee N. Newcomer, MD, MHA; Phyllis Torda; Dennis Scanlon, PhD* • **Presentation 4:** An Update on Clinical Pathways *Bruce A. Feinberg, DO* • **Discussion 4:** Clinical Pathways in Practice *Ira M. Klein, MD, MBA, FACP; Bruce A. Feinberg, DO; Bo Gamble; Michael Kolodjiez, MD*	Whitehall Ballroom (2nd Floor)
12:30 PM - 1:30 PM	**Lunch**	Hamptons (2nd Floor)
1:30 PM - 3:00 PM	**Session 3: Precision Medicine** • **Presentation 5:** Payer Perspectives on Genetic Counseling *Karen Lewis, MS, MM, CGC* • **Discussion 5:** Companion Diagnostics in Targeted Treatments *Ira M. Klein, MD, MBA, FACP; Jan Berger, MD, MJ; Peter B. Bach, MD, MAPP* • **Presentation 6:** The Present (and Future) of Genetic Profiling in Oncology *Jerry Conway* • **Discussion 6:** Next-Generation Genetic Sequencing in Oncology: Ready for Prime Time? *Ira M. Klein, MD, MBA, FACP; Michael Kolodjiez, MD; Lee N. Newcomer, MD, MHA; John L. Fox, MD, MHA; Jerry Conway*	Whitehall Ballroom (2nd Floor)
3:00 PM - 3:15 PM	**Break**	Ravenhurst & Pre-function (2nd Floor)
3:15 PM - 4:20 PM	**Session 4: Stakeholder Collaboration: A Focus on the Future** • **Presentation 7:** Where Does HEOR Fit in the Oncology Model? *Scott D. Ramsey, MD, PhD* • **Discussion 7:** Value-Based Pricing: The Role of Outcomes Data in Pricing Models *Cliff Goodman, PhD; Jeffrey D. Dunn, PharmD, MBA; Michael E. Chernew, PhD; Kirby Eng, RPh* • **Discussion 8:** Redefining the Role of Industry in Contemporary Healthcare *Cliff Goodman, PhD; John L. Fox, MD, MHA; Bo Gamble*	Whitehall Ballroom (2nd Floor)
4:30 PM	**Meeting Close and Departures**	