Highlights of This Issue 2017

SPECIAL FEATURES

CCR Translations

2019 New Approaches but the Same Flaws in the Search for Prognostic Signatures
Ramon Salazar and Josep Taberner
See related article, p. 2159

2023 Emerging Immunologic Biomarkers: Setting the (TNM-Immune) Stage
Janis M. Taube
See related article, p. 2147

2026 SETting OP449 into the PP2A-Activating Drug Family
Paolo Neviani and Danilo Perrotti
See related article, p. 2092

CCR Perspectives in Drug Approval

2029 U.S. Food and Drug Administration Approval: Crizotinib for Treatment of Advanced or Metastatic Non–Small Cell Lung Cancer That Is Anaplastic Lymphoma Kinase Positive

CCR Drug Updates

2035 Dabrafenib and Trametinib, Alone and in Combination for BRAF-Mutant Metastatic Melanoma
Alexander M. Menzies and Georgina V. Long

Molecular Pathways

2044 Molecular Pathways: Interleukin-15 Signaling in Health and in Cancer
Anjali Mishra, Laura Sullivan, and Michael A. Caligiuri

2051 Molecular Pathways: Molecular Basis for Sensitivity and Resistance to JAK Kinase Inhibitors
Sara C. Meyer and Ross L. Levine

Reviews

2060 Molecular Biomarkers in Advanced Renal Cell Carcinoma
Pablo Maroto and Brian Rini

2072 Hepatocellular Carcinoma: Reasons for Phase III Failure and Novel Perspectives on Trial Design
Josep M. Llovet and Virginia Hernandez-Gea

HUMAN CANCER BIOLOGY

2080 High-Throughput Detection of Clinically Relevant Mutations in Archived Tumor Samples by Multiplexed PCR and Next-Generation Sequencing
Richard Bourgon, Shan Lu, Yibing Yan, Mark R. Lackner, Weiru Wang, Victor Weigman, David Wang, Yinghui Guan, Lisa Ryner, Hartmut Koeppen, Rajesh Patel, Garret M. Hampton, Lukas C. Amier, and Yulei Wang

CANCER THERAPY: PRECLINICAL

2092 Antagonism of SET Using OP449 Enhances the Efficacy of Tyrosine Kinase Inhibitors and Overcomes Drug Resistance in Myeloid Leukemia
Anupriya Agarwal, Ryan J. MacKenzie, Raffaella Fippa, Christopher A. Eide, Jessica Oddo, Jeffrey W. Tyner, Rosalie Sears, Michael P. Vitek, María D. Otero, Dale J. Christensen, and Brian J. Druker
See related article, p. 2026

2104 Rational Combination Therapy of Vintafolide (EC145) with Commonly Used Chemotherapeutic Drugs
Joseph A. Reddy, Ryan Norton, Alicia Bloomfield, Melissa Nelson, Marilynn Vetzel, John Guan, and Christopher P. Leamon

2115 Inhibition of RET Increases the Efficacy of Antiestrogen and Is a Novel Treatment Strategy for Luminal Breast Cancer
Philip M. Spanheimer, Jung-Min Park, Ryan W. Askeland, Mikhail V. Kulak, George W. Woodfield, James P. De Andrade, Anthony R. Cyr, Sonia L. Sugg, Alexandra Thomas, and Ronald J. Weigel
A Peptide-Based Positron Emission Tomography Probe for In Vivo Detection of Caspase Activity in Apoptotic Cells
Matthew R. Hight, Yiu-Yin Cheung, Michael L. Nickels, Eric S. Dawson, Ping Zhao, Samir Saleh, Jason R. Buck, Dewei Tang, M. Kay Washington, Robert J. Coffey, and H. Charles Manning

A Distinct Metabolic Signature of Human Colorectal Cancer with Prognostic Potential
Yunping Qiu, Guoxiang Cai, Bingsen Zhou, Dan Li, Aihua Zhao, Guoxiang Xie, Houkai Li, Sanjun Cai, Dong Xie, Changzhi Huang, Weiting Ge, Zhanxiang Zhou, Lisa X. Xu, Weiping Jia, Shu Zheng, Yun Ren, and Wei Jia

Occurrence of Tertiary Lymphoid Tissue Is Associated with T-Cell Infiltration and Predicts Better Prognosis in Early-Stage Colorectal Cancers
Giuseppe Di Caro, Francesca Bergomas, Fabio Grizzi, Andrea Doni, Paolo Bianchi, Alberto Malesci, Luigi Laghi, Paola Allavena, Alberto Mantovani, and Federica Marchesi
See related article, p. 2023

Hypoxia-Driven Gene Expression Is an Independent Prognostic Factor in Stage II and III Colon Cancer Patients
Jeroen Dekervel, Daphne Hompes, Hannah van Malenstein, Dusan Popovic, Xavier Sagaert, Bart De Moor, Eric Van Cutsem, André D’Hoore, Chris Verslype, and Jos van Pelt
See related article, p. 2019

Hypermethylation of the GABRE~miR-452~miR-224 Promoter in Prostate Cancer Predicts Biochemical Recurrence after Radical Prostatectomy
Helle Kristensen, Christa Haldrup, Siri Strand, Kamilla Mundbjerg, Martin M. Mortensen, Kasper Thorsen, Marie Stampe Ostenfeld, Peter J. Wild, Christian Arsov, Wolfgang Goering, Tapio Visakorpi, Lars Egevad, Johan Lindberg, Henrik Grønberg, Sören Høyer, Michael Borre, Torben F. Ørntoft, and Karina D. Sørensen

Imaging the Norepinephrine Transporter in Neuroblastoma: A Comparison of [18F]-MFBG and 123I-MIBG
Hanwen Zhang, Ruimin Huang, Nai-Kong V. Cheung, Hongfen Guo, Pat B. Zanzonico, Howard T. Thaler, Jason S. Lewis, and Ronald G. Blasberg

A Phase I/II, Multiple-Dose, Dose-Escalation Study of Siltuximab, an Anti-Interleukin-6 Monoclonal Antibody, in Patients with Advanced Solid Tumors
Eric Angevin, Josep Tabernero, Elena Elez, Steven J. Cohen, Rastilav Bahleda, Jean-Luc van Laethem, Christian Ottensmeier, Jose A. Lopez-Martín, Sally Clive, Florence Joly, Isabelle Ray-Coquard, Luc Driix, Jean-Pascal Machiels, Neil Steven, Manjula Reddy, Brett Tall, Thomas A. Puchalski, Rajesh Bandekar, Helgi van de Velde, Brenda Tromp, Jessica Vermeulen, and Razelle Kurzrock

First-In-Human Phase I Study of Lurbinectedin (PM01183) in Patients with Advanced Solid Tumors
María Elena Elez, Josep Tabernero, David Geary, Teresa Macarrulla, S. Peter Kang, Carmen Kahatt, Arturo Soto-Matos Pita, Carlos Fernandez Teruel, Mariano Siguero, Martin Cullell-Young, Sergio Zyldergemaju, and Mark J. Ratain

Ultra Low-Dose IL-2 for GVHD Prophylaxis after Allogeneic Hematopoietic Stem Cell Transplantation Mediates Expansion of Regulatory T Cells without Diminishing Antiviral and Antileukemic Activity

Preclinical and Early Clinical Evaluation of the Oral AKT Inhibitor, MK-2206, for the Treatment of Acute Myelogenous Leukemia
Marina Y. Konopleva, Roland B. Walter, Stefan H. Faderl, Elias J. Jabbour, Zhihong Zeng, Gautam Borthakur, Xuelin Huang, Tapan M. Kadia, Peter P. Ruvolo, Jennie B. Feliu, Hongbo Lu, LaKiesha Debose, Jan A. Burger, Michael Andreoff, Wenbin Liu, Keith A. Baggerly, Steven M. Kornblau, L. Austin Doyle, Elihu H. Estey, and Hagop M. Kantarjian
LETTERS TO THE EDITOR

2236 Proteomic Markers of DNA Repair and PI3K Pathway Activation Predict Response to the PARP Inhibitor BMN 673 in Small Cell Lung Cancer—Letter
Haifeng Qiu

2237 Proteomic Markers of DNA Repair and PI3K Pathway Activation Predict Response to the PARP Inhibitor BMN 673 in Small Cell Lung Cancer—Response
Robert J.G. Cardnell and Lauren A. Byers

ABOUT THE COVER

The cover shows a class of recurrent hotspot mutations in PIK3R1 and PIK3CA from endometrial cancer patients that are clustered at the interface between the ISH2 domain of PIK3R1 and the C2 domain of PIK3CA. Alteration of some of these crucial amino acids has been shown to be sufficient to disrupt the inhibitory contact by PIK3R1 and may represent a novel mechanism of oncogenic activation of PIK3CA. For details, see the article by Bourgon and colleagues on page 2080 of this issue.