Highlights of This Issue 937

SPECIAL FEATURES

CCR 20th Anniversary Commentary

939 CCR 20th Anniversary Commentary: In the Beginning, There Was PS-341
Beverly A. Teicher and Kenneth C. Anderson

942 CCR 20th Anniversary Commentary: Preclinical Study of Proteasome Inhibitor Bortezomib in Head and Neck Cancer
Clint T. Allen, Barbara Conley, John B. Sunwoo, and Carter Van Waes

CCR Translations

944 Immunomodulatory Antibody Therapy of Cancer: The Closer, the Better
Roxana S. Dronca and Haidong Dong
See related articles, p. 1115 and p. 1127

947 Moving from Evaluation to Value in Cancer Care
Richard L. Schilsky
See related article, p. 1036

CCR Perspectives in Drug Approval

950 FDA Approval: Siltuximab for the Treatment of Patients with Multicentric Castleman Disease
Albert Deisseroth, Chia-Wen Ko, Lei Nie, Jeanne F. Zirkelbach, Liang Zhao, Julie Bullock, Nitin Mehta, Pedro Del Valle, Haleh Saber, Christopher Sheth, Brenda Gehrze, Robert Justice, Ann Farrell, and Richard Pazdur

Molecular Pathways

955 Molecular Pathways: Translational and Therapeutic Implications of the Notch Signaling Pathway in Cancer
Rebecca A. Previs, Robert L. Coleman, Adrian L. Harris, and Anil K. Sood

962 Molecular Pathways: Linking Tumor Microenvironment to Epithelial–Mesenchymal Transition in Metastasis
Hae-Yun Jung, Laurent Fattet, and Jing Yang

Reviews

969 Zebrafish: A New Companion for Translational Research in Oncology
Jorge Barriuso, Raghavendra Nagaraju, and Adam Hurlstone

976 Cancer Immunotherapy: A Future Paradigm Shift in the Treatment of Non–Small Cell Lung Cancer
Valsamo K. Anagnostou and Julie R. Brahmer

CANCER THERAPY: CLINICAL

985 A Phase I Study of Oral ARRY-614, a p38 MAPK/Tie2 Dual Inhibitor, in Patients with Low or Intermediate-1 Risk Myelodysplastic Syndromes
Guillermo Garcia-Manero, Hanna J. Khoury, Elias Jabbour, Jeffrey Lancet, Shannon L. Winski, LouAnn Cable, Selena Rush, Sara Maloney, Grant Hogeland, Mike Ptasynski, Monica Cabrero Calvo, Zach Bohannan, Alan List, Hagop Kantarjian, and Rami Komrokji

995 CDK 4/6 Inhibitor Palbociclib (PD0332991) in Rb⁺ Advanced Breast Cancer: Phase II Activity, Safety, and Predictive Biomarker Assessment
Angela DeMichele, Amy S. Clark, Kay See Tan, Daniel F. Heitjan, Kristi Gamlich, Maryann Gallagher, Priti Lal, Michael Feldman, Paul Zhang, Christopher Colameco, David Lewis, Melissa Langer, Noah Goodman, Susan Domchek, Kerrihi Gogineni, Mark Rosen, Kevin Fox, and Peter O’Dwyer

1002 Phase I Dose-Escalation Trial of the Oral Investigational Hedgehog Signaling Pathway Inhibitor TAK-441 in Patients with Advanced Solid Tumors

1010 Angiogenic Cytokines Are Antibody Targets During Graft-versus-Leukemia Reactions
A Pilot Trial Using Lymphocytes Genetically Engineered with an NY-ESO-1–Reactive T-cell Receptor: Long-term Follow-up and Correlates with Response
Paul F. Robbins, Sadik H. Kassim, Thai L.N. Tran, Jessica S. Crystal, Richard A. Morgan, Steven A. Feldman, James C. Yang, Mark E. Dudley, John R. Wunderlich, Richard M. Sherry, Udal S. Kammula, Marybeth S. Hughes, Nicholas P. Restifo, Mark Raffeld, Chyi-Chia R. Lee, Yong F. Li, Mona El-Gamil, and Steven A. Rosenberg

Redifferentiation of Iodine-Refractory BRAF V600E-Mutant Metastatic Papillary Thyroid Cancer with Dabrafenib
S. Michael Rothenberg, David G. McFadden, Edwin L. Palmer, Gilbert H. Daniels, and Lori J. Wirth

Raising the Bar for Antineoplastic Agents: How to Choose Threshold Values for Superiority Trials in Advanced Solid Tumors
Alberto F. Sobrero, Alessandro Pastorino, Daniel J. Sargent, and Paolo Bruzzi

A Phase I Study of PF-04449913, an Oral Hedgehog Inhibitor, in Patients with Advanced Solid Tumors
Andrew J. Wagner, Wells A. Messersmith, M. Naveed Shaik, Sherry Li, Xianxian Zheng, Karen R. McLachlan, Rossano Cesari, Rachel Courtney, Wendy J. Levin, and Anthony B. El-Khoueiry

Nottingham Clinico-Pathological Response Index (NPRI) after Neoadjuvant Chemotherapy (Neo-ACT) Accurately Predicts Clinical Outcome in Locally Advanced Breast Cancer

Longitudinal Noninvasive Imaging of Progesterone Receptor as a Predictive Biomarker of Tumor Responsiveness to Estrogen Deprivation Therapy
Szerman Ruby Chan, Amy M. Fowler, Julie A. Allen, Dong Zhou, Carmen S. Dence, Terry L. Sharp, Nicole M. Fettig, Farrokh Dehdashti, and John A. Katzenellenbogen

Correlation of PD-L1 Tumor Expression and Treatment Outcomes in Patients with Renal Cell Carcinoma Receiving Sunitinib or Pazopanib: Results from COMPARZ, a Randomized Controlled Trial
Toni K. Choueiri, David J. Figueroa, André P. Fay, Sabina Signoretti, Yuan Liu, Robert Gagnon, Keith Deen, Christopher Carpenter, Peter Benson, Thai H. Ho, Lini Pandite, Paul de Souza, Thomas Powles, and Robert J. Motzer

Gene Expression Markers of Efficacy and Resistance to Cetuximab Treatment in Metastatic Colorectal Cancer: Results from CALGB 80203 (Alliance)
Stephanie M. Cushman, Chen Jiang, Ace I. Hatch, Ivo Shterev, Alexander B. Sibley, Donna Niedzwiecki, Alan P. Venook, Kourosh Owzar, Herbert I. Hurwitz, and Andrew B. Nixon

Clinical Relevance of KRAS-Mutated Subclones Detected with Picodroplet Digital PCR in Advanced Colorectal Cancer Treated with Anti-EGFR Therapy
Pierre Laurent-Puig, Deniz Pekin, Corinne Normand, Steve K. Kostopoulou, Philippe Nizard, Karla Perez-Toralla, Rachel Rowell, Jeff Olson, Preethi Srinivasan, Delphine Le Corre, Theay Hor, Zakaria El Harrak, Xinyu Li, Darren R. Link, Olivier Bouché, Jean-François Emile, Bruno Landi, Valérie Boige, J. Brian Hutchison, and Valerie Taly

Circulating Tumor Cell Analysis in Metastatic Triple-Negative Breast Cancers

Neuregulin 1 Expression Is a Predictive Biomarker for Response to AV-203, an ERBB3 Inhibitory Antibody, in Human Tumor Models
Kristan Meetze, Sylvie Vincent, Steven Tyler, Elizabeth K. Maza, Andrea R. Delpero, Steve Bottega, Donna McIntosh, Richard Nicoletti, William M. Winston, Solly Weiler, Bin Feng, Jero Gyuris, and Zhigang Weng

The Human Agonistic CD40 Antibody ADC-1013 Eradicates Bladder Tumors and Generates T-cell–Dependent Tumor Immunity
Sara M. Mangsbo, Sissela Broos, Erika Fletcher, Niina Veijonmäki, Christina Furebring, Eva Dahlén, Per Norlén, Malin Lindstedt, Thomas H. Tötterman, and Peter Ellmark

See related commentary, p. 944
1127  Curing Mice with Large Tumors by Locally Delivering Combinations of Immunomodulatory Antibodies
Min Dai, Yuen Yee Yip, Ingegerd Hellsbrohm, and Karl Erik Hellsbrohm
See related commentary, p. 944

1139  Activity of MM-398, Nanoliposomal Irinotecan (nal-IRI), in Ewing’s Family Tumor Xenografts Is Associated with High Exposure of Tumor to Drug and High SLFN11 Expression
Min H. Kang, Jing Wang, Monish R. Makena, Joo-Sang Lee, Nancy Paz, Connor P. Hall, Michael M. Song, Ruben I. Calderon, Riza E. Cruz, Ashly Hindle, Winford Ko, Jonathan B. Fitzgerald, Daryl C. Drummond, Timothy J. Triche, and C. Patrick Reynolds

1151  Radiotherapy Combined with the Immunocytokine L19-IL2 Provides Long-lasting Antitumor Effects

1161  Targeting the Metabolic Plasticity of Multiple Myeloma with FDA-Approved Ritonavir and Metformin
Sevim Dalva-Aydemir, Richa Bajpai, Maylyn Martinez, Kehinde U.A. Adekola, Irawati Kandela, Changyong Wei, Seema Singhal, Jennifer E. Koblinski, Noopur S. Raje, Steven T. Rosen, and Mala Shanmugam

1172  Patient-Derived Xenografts from Non–Small Cell Lung Cancer Brain Metastases Are Valuable Translational Platforms for the Development of Personalized Targeted Therapy

1183  Integrinβ6-Targeted Immunoliposomes Mediate Tumor-Specific Drug Delivery and Enhance Therapeutic Efficacy in Colon Carcinoma
Benjia Liang, Muhammad Shahbaz, Yang Wang, Huijie Gao, Ruiiang Fang, Zhenghuan Niu, Song Liu, Ben Wang, Qi Sun, WeiBo Niu, Enyu Liu, Jiaoyang Wang, and Jun Niu

BIOLOGY OF HUMAN TUMORS

1196  Epigenetics Markers of Metastasis and HPV-Induced Tumorigenesis in Penile Cancer
Andrew Feber, Manit Arya, Patricia de Winter, Muhammad Saqib, Raj Nigam, Peter R. Malone, Wei Shen Tan, Simon Rodney, Matthias Lechner, Alex Freeman, Charles Jameson, Asif Muneer, Stephan Beck, and John D. Kelly

1207  A Serum MicroRNA Signature Predicts Tumor Relapse and Survival in Triple-Negative Breast Cancer Patients
Kristine Kleivi Sahlberg, Giulia Bottai, Bjorn Naume, Barbara Burwinkel, George A. Calin, Anne-Lise Berresen-Dale, and Libero Santarpia

1215  Sonic Hedgehog and Gli1 Expression Predict Outcome in Resected Pancreatic Adenocarcinoma
Raphael Maréchal, Jean-Baptiste Bachet, Annabelle Calomme, Pieter Demetter, Jean Robert Delpero, Magali Svrek, Jérôme Cros, Armelle Bardier-Dupas, Francesco Puleo, Geneviève Monges, Pascal Hammel, Christophe Louvet, François Paye, Philippe Bachelier, Yves Patrice Le Trec, Jean-Christophe Vaillant, Alain Sauvanet, Thierry André, Isabelle Salmon, Jacques Devière, Jean-François Emile, and Jean-Luc Van Laethem

1225  Direct Serum Assay for Cell-Free Bmi-1 mRNA and Its Potential Diagnostic and Prognostic Value for Colorectal Cancer
Xin Zhang, Xiaoyun Yang, Yanli Zhang, Xinfeng Liu, Guixi Zheng, Yongmei Yang, Lili Wang, Lutao Du, and Chuanxin Wang
ABOUT THE COVER

The cover shows a section of a tumor biopsy from mice with the SW1 melanoma, which were treated with an anti-CTLA4/PD-1/CD137 mAb combination. Immunohistochemical staining shows a dramatic decrease of tumor-infiltrating CD19 cells. For details, see the article by Dai and colleagues on page 1127 of this issue.