Highlights of This Issue 1819

SPECIAL FEATURES

CCR Translations

1821 The Antitumor Immunity of Ipilimumab: (T-cell) Memories to Last a Lifetime? Michael A. Postow, Margaret K. Callahan, and Jedd D. Wolchok See article p. 2039

1824 Second-Line Therapies in Hepatocellular Carcinoma: Emergence of Resistance to Sorafenib Augusto Villanueva and Josep M. Llovet See article p. 2090

1827 In Search of a Real "Targeted" Therapy for Thyroid Cancer Marcia S. Brose See article p. 2056

CCR New Strategies

1830 New Strategies for Advanced Neuroendocrine Tumors in the Era of Targeted Therapy Mei Dong, Alexandria T. Phan, and James C. Yao

Statistics in Clinical Cancer Research

1837 Statistical Issues and Recommendations for Noninferiority Trials in Oncology: A Systematic Review Shiro Tanaka, Yousuke Kinjo, Yoshiki Kataoka, Kenichi Yoshimura, and Satoshi Teramukai

CCR Drug Updates

1848 Abiraterone in Prostate Cancer: A New Angle to an Old Problem Mark N. Stein, Susan Goodin, and Robert S. DiPaola

Molecular Pathways


HUMAN CANCER BIOLOGY

Molecular Pathways: Regulation and Therapeutic Implications of Multidrug Resistance Kevin G. Chen and Branimir I. Sikic

1870 Immune Thrombocytopenia in Patients with Chronic Lymphocytic Leukemia Is Associated with Stereotyped B-cell Receptors Carlo Visco, Francesco Maura, Giacomo Tuana, Luca Agnelli, Marta Lionetti, Sonia Fabris, Elisabetta Novella, Ilaria Giaretta, Gianluigi Reda, Wilma Barcellini, Luca Baldini, Antonino Neri, Francesco Rodeghiero, and Agostino Cortecezzi

1879 MAPKAP Kinase 2 Overexpression Influences Prognosis in Gastrointestinal Stromal Tumors and Associates with Copy Number Variations on Chromosome 1 and Expression of p38 MAP Kinase and ET1

1888 Protein Kinase CK2 Protects Multiple Myeloma Cells from ER Stress–Induced Apoptosis and from the Cytotoxic Effect of HSP90 Inhibition through Regulation of the Unfolded Protein Response Sabrina Manni, Alessandra Brancalion, Laura Quotti Tubi, Anna Colpo, Laura Pavan, Anna Cabrelle, Elisa Ave, Fortunato Zaffino, Giovanni Di Maia, Maria Ruzzene, Fausto Adami, Renato Zamollo, Maria Rita Pitiari, Pierfrancesco Tassone, Lorenzo A. Pinna, Carmela Gurrieri, Gianpiero Semenzato, and Francesco Piazza

1901 Glioblastoma Stem–like Cell Lines with Either Maintenance or Loss of High-Level EGFR Amplification, Generated via Modulation of Ligand Concentration Alexander Schulte, Hauke S. Gunther, Tobias Martens, Svenja Zapf, Sabine Riethdorf, Clemens Wulffing, Malgorzata Stoupiec, Manfred Westphal, and Katrin Lamszus
L1 Cell Adhesion Molecule Promotes Tumorigenicity and Metastatic Potential in Non–Small Cell Lung Cancer
Josephine Hai, Chang-Qi Zhu, Bizhan Bandarchi, Yu-Hui Wang, Roya Navab, Frances A. Shepherd, Igor Jurisica, and Ming-Sound Tsao

Immune Suppression in Premalignant Respiratory Papillomas: Enriched Functional CD4+ Foxp3+ Regulatory T Cells and PD-1/PD-L1/L2 Expression
Lynda J. Hatam, James A. DeVoti, David W. Rosenthal, Fung Lam, Allan L. Abramson, Bettie M. Steinberg, and Vincent R. Bonagura

Integrative Genomics Identified RFC3 As an Amplified Candidate Oncogene in Esophageal Adenocarcinoma

Frequency of Driver Mutations in Lung Adenocarcinoma from Female Never-Smokers Varies with Histologic Subtypes and Age at Diagnosis
Yang Zhang, Yihua Sun, Yunjian Pan, Chenguang Li, Lei Shen, Yuan Li, Xiaoyang Luo, Ting Ye, Rui Wang, Haichuan Hu, Hang Li, Lei Wang, William Pao, and Haiquan Chen

Impaired Cognitive Function and Hippocampal Neurogenesis following Cancer Chemotherapy
Lori-Ann Christie, Munjal M. Acharya, Vipan K. Parihar, Anna Nguyen, Vahan Martirosian, and Charles L. Limoli

Cyclin-Dependent Kinase 7/9 Inhibitor SNS-032 Abrogates FIP1-like-1 Platelet-Derived Growth Factor Receptor α and Bcr-Abl Oncogene Addiction in Malignant Hematologic Cells
Yongbin Wu, Chun Chen, Xiaoyang Sun, Xianping Shi, Bei Jin, Ke Ding, Sai-Ching Jim Yeung, and Jingxuan Pan

ON 01910.Na Is Selectively Cytotoxic for Chronic Lymphocytic Leukemia Cells through a Dual Mechanism of Action Involving PI3K/AKT Inhibition and Induction of Oxidative Stress
Colby M. Chapman, Xiameng Sun, Mark Roschewski, Georg Aue, Mohamed Farooqui, Lawrence Stennett, Federica Gibellini, Diane Arthur, Patricia Pérez-Galán, and Adrian Wiestner

Serum Autoantibody Signature of Ductal Carcinoma In Situ Progression to Invasive Breast Cancer
Alain Mangé, Jérôme Lacombe, Caroline Bascoul-Mollevi, Marta Jarlier, Pierre-Jean Lamy, Philippe Rouanet, Thierry Maudelonde, and Jérôme Solassol

Copy Number Gain of 1q25 Predicts Poor Progression-Free Survival for Pediatric Intracranial Ependymomas and Enables Patient Risk Stratification: A Prospective European Clinical Trial Cohort Analysis on Behalf of the Children’s Cancer Leukaemia Group (CCLG), Société Française d’OncoLOGie Pédiatrique (SFOP), and International Society for Pediatric Oncology (SIOP)

A Three-Gene Expression Signature Model for Risk Stratification of Patients with Neuroblastoma
Idoia Garcia, Gemma Mayol, José Rios, Gema Domenech, Nai-Kong V. Cheung, André Oberthuer, Matthias Fischer, John M. Maris, Garrett M. Brodeur, Barbara Hero, Eva Rodríguez, Mariona Suñol, Patricia Galvan, Carmen de Torres, Jaume Mora, and Cinzia Lavarino

¹⁸F-FDG-PET/CT Imaging as an Early Survival Predictor in Patients with Primary High-Grade Soft Tissue Sarcomas Undergoing Neoadjuvant Therapy
A Panel of Four miRNAs Accurately Differentiates Malignant from Benign Indeterminate Thyroid Lesions on Fine Needle Aspiration

Xavier M. Keutgen, Filippo Filicori,
Michael J. Crowley, Yongchun Wang,
Theresa Scognamiglio, Rana Hoda,
Daniel Buitrago, David Cooper,
Martha A. Zeiger, Rasa Zarnegar,
Oliver Elemento, and Thomas J. Fahey III

Phase I/II Trial of Carboplatin and Paclitaxel Chemotherapy in Combination with Intravenous Oncolytic Reovirus in Patients with Advanced Malignancies

Eleni M. Karapanagiotou, Victoria Roulstone,
Katie Twigger, Merced Ball, MaryAnne Tanay,
Chris Nutting, Kate Newbold, Martin E. Gore,
James Larkin, Konstantinos N. Syrigos,
Matt Coffey, Brad Thompson, Karl Mettiger,
Richard G. Vile, Hardev S. Pandha,
Geoff D. Hall, Alan A. Melcher, John Chester,
and Kevin J. Harrington

CANCER THERAPY: CLINICAL

CTLA-4 Blockade with Ipilimumab: Long-term Follow-up of 177 Patients with Metastatic Melanoma

Peter A. Prieto, James C. Yang,
Richard M. Sherry, Marybeth S. Hughes,
Udai S. Kammula, Donald E. White,
Catherine L. Levy, Steven A. Rosenberg, and
Giao Q. Phan

See commentary p. 1821

Phase I Study of Rigosertib, an Inhibitor of the Phosphatidylinositol 3-Kinase and Polo-like Kinase 1 Pathways, Combined with Gemcitabine in Patients with Solid Tumors and Pancreatic Cancer

Wen Wee Ma, Wells A. Messersmith,
Grace K. Dy, Colin D. Weekes,
Amy Whitworth, Chen Ren, Manoj Maniar,
Francois Wilhelms, S. Gail Eckhardt,
Alex A. Adjei, and Antonio Jimeno

Phase II Efficacy and Pharmacogenomic Study of Selumetinib (AZD6244; ARRY-142886) in Iodine-131 Refractory Papillary Thyroid Carcinoma with or without Follicular Elements

D. Neil Hayes, Amy S. Lucas,
Tawee Tanvetyanon,
Monika K. Krzyzanowska,
Christine H. Chung, Barbara A. Murphy,
Jill Gilbert, Ranee Mehra, Dominic T. Moore,
Arif Sheikh, Janelle Hoskins,
Michele C. Hayward, Ni Zhao,
Wendi O’Connor, Karen E. Week,
Roger B. Cohen, and Ezra E.W. Cohen

See commentary p. 1827

Phase II, Open-Label Study of Brivanib as Second-Line Therapy in Patients with Advanced Hepatocellular Carcinoma

Richard S. Finn, Yoon-Koo Kang,
Mary Mulcahy, Blase N. Polite, Ho Yeong Lim,
Ian Walters, Christine Baudelet,
Demetrios Manekas, and Joong-Won Park

See commentary p. 1824

Sorafenib Is an Inhibitor of UGT1A1 but Is Metabolized by UGT1A9: Implications of Genetic Variants on Pharmacokinetics and Hyperbilirubinemia

Cody J. Peer, Tristan M. Sissung, AeRang Kim,
Lokesh Jain, Sukyung Woo, Erin R. Gardner,
C. Tyler Kirkland, Sarah M. Troutman,
Bevin C. English, Emily D. Richardson,
Joel Federjpg, David Venzon,
William Dahut, Elise Kohn,
Shivaani Kummar, Robert Yarchoan,
Giuseppe Giaccone, Brigitte Widemann, and
William D. Figg

PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE

Tumor Hypoxia Predicts Biochemical Failure following Radiotherapy for Clinically Localized Prostate Cancer

Michael Milosevic, Padraig Warde,
Cynthia Menard, Peter Chung, Ants Toi,
Adriana Ishkanian, Michael McLean,
Melania Pintilie, Jenna Sykes,
Mary Gospodarowicz, Charles Catton,
Richard P. Hill, and Robert Bristow

CORRECTIONS

Correction: Molecular Imaging of TGFβ-Induced Smad2/3 Phosphorylation Reveals a Role for Receptor Tyrosine Kinases in Modulating TGFβ Signaling
ABOUT THE COVER

High-level EGFR gene amplification can be retained in glioblastoma stem-like cell lines established and propagated without recombinant EGF. In contrast, high-level amplification is lost in parallel cell lines from the same tumors established with EGF supplementation. Cell lines with high-level EGFR amplification produce highly aggressive xenograft tumors in the brains of nude mice, retaining the EGFR amplification as shown in the cover figure, whereas counterpart cell lines, lacking high-level amplification, are either nontumorigenic or grow significantly more slowly in vivo. For details, see the article by Schulte and colleagues on page 1901 of this issue.