

March 15, 2014 • Volume 20 • Number 6

Highlights of This Issue 1399

SPECIAL FEATURES

CCR Translations

- 1401** Myeloid Suppressors Decrease Melanoma Survival by Abating Tumor-Fighting T Cells
Rolf Kiessling, Yumeng Mao, and Yago Pico de Coaña
See related article, p. 1601

Statistics in Clinical Cancer Research

- 1404** Getting More Out of Survival Data by Using the Hazard Function
Kenneth R. Hess and Victor A. Levin

Molecular Pathways

- 1410** Molecular Pathways: HER3 Targeted Therapy
Kinisha Gala and Sarat Chandarlapaty

CCR Focus

- 1418** It's All About the Test: The Complexity of Companion Diagnostic Co-development in Personalized Medicine
Susan E. Bates
- 1419** Developing Precision Medicine in a Global World
Eric H. Rubin, Jeffrey D. Allen, Jan A. Nowak, and Susan E. Bates
- 1428** Evidence of Clinical Utility: An Unmet Need in Molecular Diagnostics for Patients with Cancer
David R. Parkinson, Robert T. McCormack, Susan M. Keating, Steven I. Gutman, Stanley R. Hamilton, Elizabeth A. Mansfield, Margaret A. Piper, Patricia DeVerka, Felix W. Frueh, J. Milburn Jessup, Lisa M. McShane, Sean R. Tunis, Caroline C. Sigman, and Gary J. Kelloff
- 1445** Similarities and Differences in the Oncology Drug Approval Process between FDA and European Union with Emphasis on *In Vitro* Companion Diagnostics
Adrian M. Senderowicz and Otmar Pfaff
- 1453** FDA Perspective on Companion Diagnostics: An Evolving Paradigm
Elizabeth A. Mansfield

- 1458** Cancer Drug Development and the Evolving Regulatory Framework for Companion Diagnostics in the European Union
Francesco Pignatti, Falk Ehmann, Robert Hemmings, Bertil Jonsson, Micha Nuebling, Marisa Papaluca-Amati, Martin Posch, and Guido Rasi

- 1469** The Health Technology Assessment of Companion Diagnostics: Experience of NICE



Sarah K. Byron, Nick Crabb, Elisabeth George, Mirella Marlow, and Adrian Newland

HUMAN CANCER BIOLOGY

- 1477** FOXM1c Promotes Pancreatic Cancer Epithelial-to-Mesenchymal Transition and Metastasis via Upregulation of Expression of the Urokinase Plasminogen Activator System
Chen Huang, Dacheng Xie, Jiujiu Cui, Qi Li, Yong Gao, and Keping Xie
- 1489** DNA Topoisomerase III Alpha Regulates p53-Mediated Tumor Suppression
Mei-Yi Hsieh, Jia-Rong Fan, Han-Wen Chang, Hsiang-Chin Chen, Tang-Long Shen, Shu-Chun Teng, Yen-Hsiu Yeh, and Tsai-Kun Li
- 1502** hERG1 Channels Regulate VEGF-A Secretion in Human Gastric Cancer: Clinicopathological Correlations and Therapeutical Implications
Olivia Crociani, Elena Lastraioli, Luca Boni, Serena Pillozzi, Maria Raffaella Romoli, Massimo D'Amico, Matteo Stefanini, Silvia Crescioli, Antonio Taddei, Lapo Bencini, Marco Bernini, Marco Farsi, Stefania Beghelli, Aldo Scarpa, Luca Messerini, Anna Tomezzoli, Carla Vindigni, Paolo Morgagni, Luca Saragoni, Elisa Giommoni, Silvia Gasperoni, Francesco Di Costanzo, Franco Roviello, Giovanni De Manzoni, Paolo Bechi, and Annarosa Arcangeli
- 1513** Calcium/Calmodulin-Dependent Protein Kinase II and Its Endogenous Inhibitor α in Medullary Thyroid Cancer
Eleonora Russo, Marcella Salzano, Valentina De Falco, Caterina Mian, Susi Barollo, Agnese Secondo, Maurizio Bifulco, and Mario Vitale


Table of Contents

- 1521** High-Resolution Array CGH and Gene Expression Profiling of Alveolar Soft Part Sarcoma
Shamini Selvarajah, Saumyadipta Pyne, Eleanor Chen, Ramakrishna Sompallae, Azra H. Ligon, Gunnlaugur P. Nielsen, Glenn Dranoff, Edward Stack, Massimo Loda, and Richard Flavin
- 1531** TGF- β -Induced Upregulation of *malat1* Promotes Bladder Cancer Metastasis by Associating with *suz12*
Yu Fan, Bing Shen, Mingyue Tan, Xinyu Mu, Yan Qin, Fang Zhang, and Yong Liu

CANCER THERAPY: PRECLINICAL

- 1542** Preclinical Activity of the Oral Proteasome Inhibitor MLN9708 in Myeloma Bone Disease
Antonio Garcia-Gomez, Dalia Quwaider, Miriam Canavese, Enrique M. Ocio, Ze Tian, Juan F. Blanco, Allison J. Berger, Carlos Ortiz-de-Solorzano, Teresa Hernández-Iglesias, Anton C.M. Martens, Richard W.J. Groen, Joaquín Mateo-Urdiales, Susana Fraile, Miguel Galarraga, Dharminder Chauhan, Jesús F. San Miguel, Noopur Raje, and Mercedes Garayoa
- 1555** Temozolomide Does Not Impair Gene Therapy-Mediated Antitumor Immunity in Syngeneic Brain Tumor Models
Marianela Candolfi, Kader Yagiz, Mia Wibowo, Gabrielle E. Ahlzadeh, Mariana Puntel, Homayon Ghiasi, Neha Kamran, Christopher Paran, Pedro R. Lowenstein, and Maria G. Castro
- 1566** Hedgehog–GLI Signaling Inhibition Suppresses Tumor Growth in Squamous Lung Cancer
Lingling Huang, Vonn Walter, D. Neil Hayes, and Mark Onaitis
- 1576** The Nedd8-Activating Enzyme Inhibitor MLN4924 Thwarts Microenvironment-Driven NF- κ B Activation and Induces Apoptosis in Chronic Lymphocytic Leukemia B Cells
J. Claire Godbersen, Leigh Ann Humphries, Olga V. Danilova, Peter E. Kebbekus, Jennifer R. Brown, Alan Eastman, and Alexey V. Danilov
- 1590** Rapid Induction of Androgen Receptor Splice Variants by Androgen Deprivation in Prostate Cancer
Ziyang Yu, Sen Chen, Adam G. Sowalsky, Olga S. Voznesensky, Elahe A. Mostaghel, Peter S. Nelson, Changmeng Cai, and Steven P. Balk

IMAGING, DIAGNOSIS, PROGNOSIS

- 1601** Myeloid-Derived Suppressor Cells Predict Survival of Patients with Advanced Melanoma: Comparison with Regulatory T Cells and NY-ESO-1- or Melan-A–Specific T Cells
Benjamin Weide, Alexander Martens, Henning Zelba, Christina Stutz, Evelyn Derhovanessian, Anna Maria Di Giacomo, Michele Maio, Antje Sucker, Bastian Schilling, Dirk Schadendorf, Petra Büttner, Claus Garbe, and Graham Pawelec
See related article, p. 1401
- 1610** Radiation-Enhanced Lung Cancer Progression in a Transgenic Mouse Model of Lung Cancer Is Predictive of Outcomes in Human Lung and Breast Cancer 
Oliver Delgado, Kimberly G. Batten, James A. Richardson, Xian-Jin Xie, Adi F. Gazdar, Aadil A. Kaisani, Luc Girard, Carmen Behrens, Milind Suraokar, Gail Fasciani, Woodring E. Wright, Michael D. Story, Ignacio I. Wistuba, John D. Minna, and Jerry W. Shay
- 1623** EASL- and mRECIST-Evaluated Responses to Combination Therapy of Sorafenib with Transarterial Chemoembolization Predict Survival in Patients with Hepatocellular Carcinoma
Lei Liu, Weijuan Wang, Hui Chen, Yan Zhao, Wei Bai, Zhanxin Yin, Chuangye He, Jia Jia, Man Yang, Jielai Xia, Daiming Fan, and Guohong Han
- 1632** Positron Emission Tomography Imaging with ¹⁸F-Labeled Z_{HER2:2891} Affibody for Detection of HER2 Expression and Pharmacodynamic Response to HER2-Modulating Therapies
Sebastian Trousil, Susan Hoppmann, Quang-Dé Nguyen, Maciej Kaliszczak, Giampaolo Tomasi, Peter Iveson, Duncan Hiscock, and Eric O. Aboagye

CANCER THERAPY: CLINICAL

- 1644** A Phase I, Pharmacokinetic, and Pharmacodynamic Study of Panobinostat, an HDAC Inhibitor, Combined with Erlotinib in Patients with Advanced Aerodigestive Tract Tumors
Jhanelle E. Gray, Eric Haura, Alberto Chiappori, Tawee Tanvetyanon, Charles C. Williams, Mary Pinder-Schenck, Julie A. Kish, Jenny Krehling, Richard Lush, Anthony Neuger, Leticia Tetteh, Angela Akar, Xiuhua Zhao, Michael J. Schell, Gerold Bepler, and Soner Altioek



Table of Contents

1656 Phase I Study of Oral Rigosertib (ON 01910. Na), a Dual Inhibitor of the PI3K and Plk1 Pathways, in Adult Patients with Advanced Solid Malignancies

Daniel W. Bowles, Jennifer R. Diamond, Elaine T. Lam, Colin D. Weekes, David P. Astling, Ryan T. Anderson, Stephen Leong, Lia Gore, Marileila Varella-Garcia, Brian W. Vogler, Stephen B. Keyzar, Elizabeth Freas, Dara L. Aisner, Chen Ren, Aik-Chook Tan, Francois Wilhelm, Manoj Maniar, S. Gail Eckhardt, Wells A. Messersmith, and Antonio Jimeno

1666 Phase I Dose-Escalation Study of Onartuzumab as a Single Agent and in Combination with Bevacizumab in Patients with Advanced Solid Malignancies

Ravi Salgia, Premal Patel, John Bothos, Wei Yu, Steve Eppler, Priti Hegde, Shuang Bai, Surinder Kaur, Ihsan Nijem, Daniel V.T. Catenacci, Amy Peterson, Mark J. Ratain, Blase Polite, Janice M. Mehnert, and Rebecca A. Moss

PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE

1676 Inactivation of the *CDKN2A* Tumor-Suppressor Gene by Deletion or Methylation Is Common at Diagnosis in Follicular Lymphoma and Associated with Poor Clinical Outcome

Abdulmohsen Alhejaily, Andrew G. Day, Harriet E. Feilotter, Tara Baetz, and David P. LeBrun

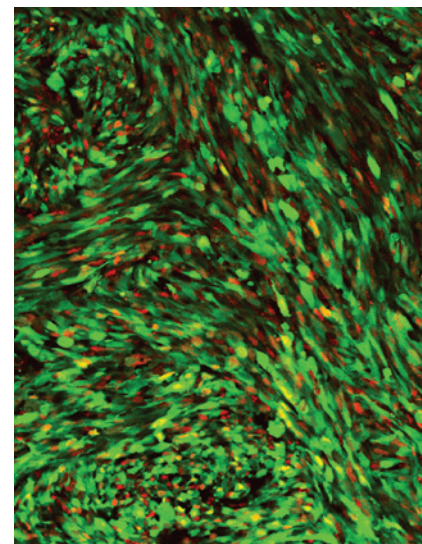
 AC icon indicates Author Choice

 CME icon indicates that this article is available for continuing medical education credit at <http://cme.aacrjournals.org>

For more information please visit www.aacrjournals.org

ABOUT THE COVER

The cover shows a section of an intracranial glioblastoma (GBM); GBM cells express the fluorescent protein citrine (green) and the High-mobility group protein B1 (HMGB1) fused to the red fluorescent protein cherry. In living cells HMGB1 is located in the nucleus; upon cell death, HMGB1 is translocated to the cytoplasm and is eventually secreted. Circulating levels of HMGB1 may constitute a noninvasive surrogate biomarker of therapeutic efficacy. For details, see the article by Candolfi and colleagues on page 1555 of this issue.



1687 A Functional Germline Variant in *GLI1* Implicates Hedgehog Signaling in Clinical Outcome of Stage II and III Colon Carcinoma Patients

Joanna Szkandera, Martin Pichler, Gudrun Absenger, Michael Stotz, Melanie Weissmueller, Hellmut Samonigg, Martin Asslaber, Sigurd Lax, Gerhard Leitner, Thomas Winder, Wilfried Renner, and Armin Gerger

1698 Noninvasive Detection of Response and Resistance in *EGFR*-Mutant Lung Cancer Using Quantitative Next-Generation Genotyping of Cell-Free Plasma DNA

Geoffrey R. Oxnard, Cloud P. Paweletz, Yanan Kuang, Stacy L. Mach, Allison O'Connell, Melissa M. Messineo, Jason J. Luke, Mohit Butaney, Paul Kirschmeier, David M. Jackman, and Pasi A. Jänne

CORRECTION

1706 Correction: Carbonic Anhydrase IX Promotes Tumor Growth and Necrosis *In Vivo* and Inhibition Enhances Anti-VEGF Therapy

Clinical Cancer Research

20 (6)

Clin Cancer Res 2014;20:1399-1706.

Updated version Access the most recent version of this article at:
<http://clincancerres.aacrjournals.org/content/20/6>

E-mail alerts [Sign up to receive free email-alerts](#) related to this article or journal.

Reprints and Subscriptions To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions To request permission to re-use all or part of this article, use this link <http://clincancerres.aacrjournals.org/content/20/6>.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.