Highlights of This Issue 2593

SPECIAL FEATURES

CCR Translations

2595  Oncolytic Virotherapy Needs Trials, Not Access Programs
Kevin J. Harrington
See article, p. 2734

Molecular Pathways

2598  Molecular Pathways: Tumor-Derived Microvesicles and Their Interactions with Immune Cells In Vivo
Ferdinando Pucci and Mikael J. Pittet

CCR Focus

2606  PFS: The Endpoint We Love and Love to Hate
Susan E. Bates

2607  Overview: Progression-Free Survival as an Endpoint in Clinical Trials with Solid Tumors
Ronald L. Korn and John J. Crowley

2613  Missing Data and Measurement Variability in Assessing Progression-Free Survival Endpoint in Randomized Clinical Trials
Rajeshwari Sridhara, Sumithra J. Mandrekar, and Lori E. Dodd

2621  The Imaging Viewpoint: How Imaging Affects Determination of Progression-Free Survival
Daniel Carl Sullivan, Lawrence H. Schwartz, and Binsheng Zhao

2629  The Clinical Viewpoint: Definitions, Limitations of RECIST, Practical Considerations of Measurement
Liza C. Villaruz and Mark A. Socinski

2637  Assessment of Audit Methodologies for Bias Evaluation of Tumor Progression in Oncology Clinical Trials
Jenny J. Zhang, Lifujun Zhang, Huanyu Chen, Anthony J. Murgo, Lori E. Dodd, Richard Pazdur, and Rajeshwari Sridhara

HUMAN CANCER BIOLOGY

2657  Aberrant BAF57 Signaling Facilitates Prometastatic Phenotypes
Sucharitha Balasubramaniam, Clay E.S. Comstock, Adam Ertel, Kwang Won Jeong, Michael R. Stallcup, Sankar Addya, Peter A. McCue, William F. Ostrander Jr, Michael A. Augello, and Karen E. Knudsen

2668  Relapsed Classic E-Cadherin (CDH1)–Mutated Invasive Lobular Breast Cancer Shows a High Frequency of HER2 (ERBB2) Gene Mutations

CANCER THERAPY: PRECLINICAL

2677  Potent Antimyeloma Activity of a Novel ERK5/CDK Inhibitor
Stela Álvarez-Fernández, María Jesús Ortiz-Ruiz, Tracy Parrott, Sara Zaknoen, Enrique M. Ocío, Jesús San Miguel, Francis J. Burrows, Azucena Esparís-Ogando, and Atanasio Pandiella

2688  Concomitant BRAF and PI3K/mTOR Blockade Is Required for Effective Treatment of BRAF<sup>VDel</sup> Colorectal Cancer

Contents

The Journal of Clinical and Translational Research

The Journal of Clinical and Translational Research iii www.aacrjournals.org

May 15, 2013 • Volume 19 • Number 10

Modeling the Relationship between Progression-Free Survival and Overall Survival: The Phase II/III Trial
Mary W. Redman, Bryan H. Goldman, Michael LeBlanc, Anne Schott, and Laurence H. Baker

Modeling the Relationship between Progression-Free Survival and Overall Survival: The Phase II/III Trial
Mary W. Redman, Bryan H. Goldman, Michael LeBlanc, Anne Schott, and Laurence H. Baker
Temozolomide-Mediated DNA Methylation in Human Myeloid Precursor Cells: Differential Involvement of Intrinsic and Extrinsic Apoptotic Pathways

Inhibition of Melanoma Growth by Small Molecules That Promote the Mitochondrial Localization of ATF2

Identification of Prognosis-Relevant Subgroups in Patients with Chemoresistant Triple-Negative Breast Cancer
Ke-Da Yu, Rui Zhu, Ming Zhan, Angel A. Rodriguez, Wei Yang, Stephen Wong, Andreas Makris, Brian D. Lehmann, Xi Chen, Ingrid Mayer, Jennifer A. Pietenpol, Zhi-Ming Shao, W. Fraser Symmans, and Jenny C. Chang

Antiviral and Antitumor T-cell Immunity in Patients Treated with GM-CSF–Coding Oncolytic Adenovirus

Molecular Profiling of Aromatase Inhibitor–Treated Postmenopausal Breast Tumors Identifies Immune-Related Correlates of Resistance

Correction: Chromosome 5q Loss in Colorectal Flat Adenomas

Sorafenib or Placebo with Either Gemcitabine or Capecitabine in Patients with HER-2–Negative Advanced Breast Cancer That Progressed during or after Bevacizumab

Neoadjuvant Chemotherapy with or without Zoledronic Acid in Early Breast Cancer—A Randomized Biomarker Pilot Study
Matthew C. Winter, Caroline Wilson, Stuart P. Syddall, Simon S. Cross, Alyson Evans, Christine E. Ingram, Ingrid J. Jolley, Matthew Q. Hatton, Jennifer V. Freeman, Stefano Mori, Ingunn Holen, and Robert E. Coleman

Phase I Study of the Hedgehog Pathway Inhibitor IPI-926 in Adult Patients with Solid Tumors

Molecular Profiling of Aromatase Inhibitor–Treated Postmenopausal Breast Tumors Identifies Immune-Related Correlates of Resistance

Correction: Chromosome 5q Loss in Colorectal Flat Adenomas
ABOUT THE COVER

This image is taken from a bone metastasis in a patient with stage IV relapsed invasive CDH1 mutated lobular carcinoma of the breast. The tumor was negative for ERBB2 (HER2) amplification (FISH). The targeted next generation sequencing assay used in this study found an ERBB2-GRB7 putative gene fusion that has not been previously reported. The fusion retains the kinase domain of ERBB2 (uniprot.org) which suggests that it could result in ERBB2 activation. The 17q12-21 amplicon which includes both ERBB2 and GRB7 is frequently amplified in breast cancer and preclinical studies suggest that it may be a recombination hotspot. An expression screening study has reported that GRB7 can function as an ERBB2-dependent oncogene. GRB7 encodes an adaptor protein that interacts with ERBB2 and has been shown in a preclinical study to enhance its transformative capacity and increase ERBB2 phosphorylation in fibroblasts. For details, see the article by Ross and colleagues on page 2668 of this issue.

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