Highlights of This Issue vii

SPECIAL FEATURES

1085 Finding the Right Dose for Cancer Therapeutics—Can We Do Better? Eric H. Rubin and Keaven M. Anderson See article p. 1289

1088 Targeting the Cytoprotective Chaperone, Clusterin, for Treatment of Advanced Cancer Amina Zoubeidi, Kim Chi, and Martin Gleave

1094 Targeting the RB-pathway in Cancer Therapy Erik S. Knudsen and Jean Y.J. Wang

Perspectives

1100 A New Therapy Paradigm for Prostate Cancer Founded on Clinical Observations Eleni Efstratiou and Christopher J. Logothetis

HUMAN CANCER BIOLOGY


1140 X-Linked Ectodermal Dysplasia Receptor Is Downregulated in Breast Cancer via Promoter Methylation Vasu Punj, Hittu Matta, and Preet M. Chaudhary

CANCER THERAPY: PRECLINICAL


1159 AZD8931, an Equipotent, Reversible Inhibitor of Signaling by Epidermal Growth Factor Receptor, ERBB2 (HER2), and ERBB3: A Unique Agent for Simultaneous ERBB Receptor Blockade in Cancer D. Mark Hickinson, Teresa Klinowska, Georgina Speake, John Vincent, Cath Trigwell, Judith Anderton, Sarah Beck, Gayle Marshall, Sara Davenport, Rowena Callis, Elizabeth Mills, Konstantina Grosios, Paul Smith, Bernard Barba, Robert W. Wilkinson, and Donald Ogilvie

1170 Blockade of the Extracellular Signal-Regulated Kinase Pathway Enhances the Therapeutic Efficacy of Microtubule-Destabilizing Agents in Human Tumor Xenograft Models Kazushi Watanabe, Susumu Tanimura, Aya Uchiyama, Toshiaki Sakamoto, Takumi Kawabata, Kei-ichi Ozaki, and Michiaki Kohno
Low-Molecular-Weight Cyclin E Can Bypass Letrozole-Induced G1 Arrest in Human Breast Cancer Cells and Tumors
Said Akli, Tuyen Bui, Hannah Wingate, Anna Biernacka, Stacy Moulder, Susan L. Tucker, Kelly K. Hunt, and Khandan Keyomarsi

Anti–Transforming Growth Factor β Receptor II Antibody Has Therapeutic Efficacy against Primary Tumor Growth and Metastasis through Multieffects on Cancer, Stroma, and Immune Cells

MutS Homologue 2 and the Long-term Benefit of Adjuvant Chemotherapy in Lung Cancer

Metastatic Renal Cell Carcinoma Treated with Sunitinib: Early Evaluation of Treatment Response Using Dynamic Contrast-Enhanced Ultrasonography
Nathalie Lassau, Serge Koscielny, Laurence Albige, Linda Chami, Baya Benatsou, Mohamed Chebil, Alain Roche, and Bernard J. Escudier

Tobacco Use in Human Papillomavirus–Positive Advanced Oropharynx Cancer Patients Related to Increased Risk of Distant Metastases and Tumor Recurrence

A 3′-Untranslated Region Polymorphism in IGF1 Predicts Survival of Non–Small Cell Lung Cancer in a Chinese Population
Mingfeng Zhang, Zhibin Hu, Jinlin Huang, Yongqian Shu, Juncheng Dai, Guanglu Jin, Rong Tang, Jing Dong, Yijiang Chen, Lin Xu, Xinen Huang, and Hongbing Shen

Low Levels of Phosphorylated Epidermal Growth Factor Receptor in Nonmalignant and Malignant Prostate Tissue Predict Favorable Outcome in Prostate Cancer Patients
Peter Hammarsten, Amar Karali, Andreas Josefsson, Stina Hägghström Rudolfsson, Pernilla Wikström, Lars Egevad, Torvald Granfors, Pär Stattin, and Anders Bergh

A Phase I Safety and Pharmacokinetic Study of the Death Receptor 5 Agonistic Antibody PRO95780 in Patients with Advanced Malignancies
D. Ross Camidge, Roy S. Herbst, Michael S. Gordon, S. Gail Eckhardt, Razelle Kurzrock, Blythe Durbin, Josephine Ing, Tanyifor M. Tohnya, Jason Sager, Avi Ashkenazi, Gordon Bray, and David Mendelson

Tipifarnib Plus Tamoxifen in Tamoxifen-Resistant Metastatic Breast Cancer: A Negative Phase II and Screening of Potential Therapeutic Markers by Proteomic Analysis
Florence Dalenc, Sophie F. Doisneau-Sixou, Ben C. Allal, Sabrina Marsili, Valérie Lausers-Cances, Karima Chaoui, Odile Schiltz, Bernard Monsarrat, Thomas Filleron, Nicole Renée, Emilie Malisseein, Elise Meunier, Gilles Favre, and Henri Roché

The Predictive Value of HLA Class I Tumor Cell Expression and Presence of Intratumoral Tregs for Chemotherapy in Patients with Early Breast Cancer
Leona Downey, Robert B. Livingston, Maria Koehler, Michael Arbushites, Lisa Williams, Angela Santiago, Roberta Guzman, Iovonne Villalobos, Angelo Di Leo, and Michael F. Press

Phase I Oncology Studies: Evidence That in the Era of Targeted Therapies Patients on Lower Doses Do Not Fare Worse
Rajul K. Jain, J. Jack Lee, David Hong, Maurie Markman, Jing Gong, Aung Naing, Jennifer Wheler, and Razelle Kurzrock
See commentary p. 1085

Phase I Trial of Pelvic Radiation, Weekly Cisplatin, and 3-Aminopyridine-2-Carboxaldehyde Thiosemicarbazone (3-AP, NSC #663249) for Locally Advanced Cervical Cancer
Charles A. Kunos, Steven Waggoner, Vivian von Gruenigen, Elisa Eldermire, John Pink, Afshin Dowlati, and Timothy J. Kinsella

Randomized Phase III Trial of Gefitinib versus Docetaxel in Non–Small Cell Lung Cancer Patients Who Have Previously Received Platinum-Based Chemotherapy
Dae Ho Lee, Keunchil Park, Joo Hang Kim, Jong-Seok Lee, Sang Won Shin, Jin-Hyoung Kang, Myung-Ju Ahn, Jin Seok Ahn, Cheolwon Suh, and Sang-We Kim

Phase I Clinical and Magnetic Resonance Imaging Study of the Vascular Agent NGR-hTNF in Patients with Advanced Cancers [European Organization for Research and Treatment of Cancer Study 16041]

Potential Clinical Significance of a Plasma-Based KRAS Mutation Analysis in Patients with Advanced Non–Small Cell Lung Cancer
Shuhang Wang, Tongtong An, Jie Wang, Jun Zhao, Zhijie Wang, Minglei Zhuo, Huai Bai, Lu Yang, Yan Zhang, Xin Wang, Jianchun Duan, Yuyan Wang, Qingzhi Guo, and Meina Wu

Smoking and Colorectal Cancer in Lynch Syndrome: Results from the Colon Cancer Family Registry and The University of Texas M.D. Anderson Cancer Center
Mala Pande, Patrick M. Lynch, John L. Hopper, Mark A. Jenkins, Steve Gallinger, Robert W. Haile, Loic LeMarchand, Noralane M. Lindor, Peter T. Campbell, Polly A. Newcomb, John D. Potter, John A. Baron, Marsha L. Frazier, and Christopher I. Amos

Studies of TMPRSS2-ERG Gene Fusions in Diagnostic Trans-Rectal Prostate Biopsies
Gerhardt Attard, Johann S. de Bono, Jeremy Clark, and Colin S. Cooper

Vascular Endothelial Growth Factor Concentration as a Predictive Marker: Ready for Primetime?
Peter A. Kavsak, Hal Hirte, and Sebastien J. Hotte

Correction: A First-in-Man Phase I and Pharmacokinetic Study on CHR-2797 (Tosedostat), an Inhibitor of M1 Aminopeptidases, in Patients with Advanced Solid Tumors

Correction: The Novel Expanded Porphyrin, Motexaﬁn Gadolinium, Combined with [90Y] Ibritumomab Tiuxetan for Relapsed/Refractory Non-Hodgkin's Lymphoma: Preclinical Findings and Results of a Phase I Trial
ABOUT THE COVER

Expression of the miR-34 family was found to be frequently reduced in human epithelial ovarian cancer, particularly so in tumors with p53 mutations. The figure shows miR-34a expression (dark blue) in ovarian serous adenocarcinoma as determined by in situ hybridization with locked nucleic acid–modified probes. Immunohistochemistry in serial sections revealed significant inverse correlation between miR-34a and its target MET, an oncogene commonly overexpressed in advanced stages of cancer. For details, see the article by Corney and colleagues on page 1119 of this issue.