## Highlights of This Issue 4917

### SPECIAL FEATURES

#### CCR Translations

4919  
**Why Is This Effective HSP90 Inhibitor Not Being Developed in HER2+ Breast Cancer?**  
Carlos L. Arteaga  
*See article p. 5132*

#### CCR New Strategies

4922  
**New Strategies in Metastatic Melanoma: Oncogene-Defined Taxonomy Leads to Therapeutic Advances**  
Keith T. Flaherty and David E. Fisher

#### Editor's Note

4929  
**Introducing CCR Perspectives in Drug Approval**  
James L. Abbruzzese

#### CCR Perspectives in Drug Approval

4930  
**The National Institute for Health and Clinical Excellence and Its Role in Assessing the Value of New Cancer Treatments in England and Wales**  
Rebecca Trowman, Helen Chung, Carole Longson, Peter Littlejohns, and Peter Clark

### Molecular Pathways

4936  
**Stem Cell Quiescence**  
Ling Li and Ravi Bhataia

4942  
**Cancer Stem Cells and Chemosensitivity**  
Marcello Mauger-Saccà, Paolo Vigneri, and Ruggero De Maria

### Review

4948  
**Exploring Breast Cancer Estrogen Disposition: The Basis for Endocrine Manipulation**  
Per E. Lønning, Ben P. Haynes, Anne H. Straume, Anita Dunbier, Hildegunn Helle, Stian Knappskog, and Mitch Dowsett

#### Perspective

4959  
**To DNA or not to DNA? That is the Question, When It Comes to Molecular Subtyping for the Clinic!**  
Serge J. Smeets, Ulrike Harjes, Wessel N. van Wieringen, Daoudieh Ste, Rund H. Braekenhoff, Gerrit A. Meijer, and Bauke Ylstra

### HUMAN CANCER BIOLOGY

4965  
**Epigenetic Silencing of MicroRNA-34b/c Plays an Important Role in the Pathogenesis of Malignant Pleural Mesothelioma**  
Takafumi Kubo, Shinichi Toyooka, Kazunori Tsukuda, Masakiyo Sakaguchi, Takuya Fukazawa, Junichi Soh, Hiroaki Asano, Tsuyoshi Ueno, Takayuki Muraoka, Hiromasa Yamamoto, Yasutomo Nasu, Takumi Kishimoto, Harvey I. Pass, Hideki Matsui, Nam-ho Huh, and Shinichiro Miyoshi

4975  
**Interleukin-7 Inhibits Tumor-Induced CD27CD28 Suppressor T Cells: Implications for Cancer Immunotherapy**  
Yue Zhang, Lukas W. Pfannenstiel, Elzbieta Boleska, Carolina L. Montes, Xiaoyu Zhang, Andrei I. Chapoval, Ronald B. Gartenhaus, Scott E. Strome, and Brian R. Gastman

### CANCER THERAPY: PRECLINICAL

4987  
**Adoptive Transfer of Tumor Reactive B Cells Confers Host T-Cell Immunity and Tumor Regression**  
Qiao Li, Xiangming Lan, Qiu Pan, Ning Ning, Ji Yet, Yingxin Xu, Shengping Li, and Alfred E. Chang
Targeting GPCR-Mediated p70S6K Activity May Improve Head and Neck Cancer Response to Cetuximab

Neil E. Bhola, Sufi M. Thomas, Maria Freilino, Sonali Joyce, Anirban Sahu, Jessica Maxwell, Athanasios Argeris, Raja Seethala, and Jennifer R. Grandis

Enhanced Metastasis Suppression by Targeting TRAIL Receptor 2 in a Murine Model of Triple-Negative Breast Cancer

Dmitry Malin, Feng Chen, Carol Schiller, Jennifer Koblinski, and Vincent L. Cryns

Fibroblast Growth Factor Receptors Are Components of Autocrine Signaling Networks in Head and Neck Squamous Cell Carcinoma Cells

Marianne E. Marshall, Trista K. Hinz, Scott A. Kono, Katherine R. Singleton, Brady Bichon, Kathryn E. Ware, Lindsay Marek, Barbara A. Fredericks, David Raben, and Lynn E. Heasley

Mitoxantrone Inhibits HIF-1α Expression in a Topoisomerase II-Independent Pathway

Yng-Min Toh and Taisai-Kun Li

Enhancement of 5-Fluorouracil-induced In Vitro and In Vivo Radiosensitization with MEK Inhibition

Mary Ellen Urick, Eun Joo Chung, William P. Shield, III, Naamit Gerber, Ayla White, Anastasia Sowers, Angela Thetford, Kevin Camp Hansen, James Mitchell, and Deborah E. Critir

The Efficacy of IGF-1 Receptor Monoclonal Antibody against Human Gastrointestinal Carcinomas is Independent of k-ras Mutation Status

Mary Ellen Urick, Eun Joo Chung, William P. Shield, III, Naamit Gerber, Ayla White, Anastasia Sowers, Angela Thetford, Kevin Camp Hansen, James Mitchell, and Deborah E. Critir

Pertuzumab in Combination with Trastuzumab Shows Significantly Enhanced Antitumor Activity in HER2-Positive Human Gastric Cancer Xenograft Models

Yoriko Yamashita-Kashima, Shigeyuki Iijima, Keigo Yorozu, Koh Furugaki, Mitsue Kurasawa, Masateru Ohta, and Kaori Fujimoto-Ouchi

HER2-Affitoxin: A Potent Therapeutic Agent for the Treatment of HER2-Overexpressing Tumors

Rafal Zielinski, Ilya Lyakhov, Moinuddin Hassan, Monika Kuban, Kimberly Shafei-Weaver, Amir Gandjkhahche, and Jacek Capala

High ALK Receptor Tyrosine Kinase Expression Supersedes ALK Mutation as a Determining Factor of an Unfavorable Phenotype in Primary Neuroblastoma

Johannes H. Schulte, Hagen S. Bachmann, Bent Brockmeyer, Katleen DePreter, André Oertelt, Sandra Ackermann, Yvonne Kahlert, Kristian Pagtler, Jessica Theissen, Frank Westermann, Jo Vandesompele, Frank Speelman, Frank Berthold, Angelika Eggert, Benedikt Brors, Barbara Hero, Alexander Schramm, and Matthias Fischer

FDG-PET as a Potential Tool for Selecting Patients with Advanced Non–Small Cell Lung Cancer Who May Be Spared Maintenance Therapy after First-Line Chemotherapy

Dok Hyun Yoon, Sora Baek, Chang-Min Choi, Dae Ho Lee, Cheolwon Suh, Jin-Sook Ryu, Dae Hyuk Moon, Jung Shin Lee, and Sang-We Kim

Treatment-Induced Oxidative Stress and Cellular Antioxidant Capacity Determine Response to Bortezomib in Mantle Cell Lymphoma

Marc A. Weniger, Edwin D. Rizzatti, Patricia Perez-Galan, Delong Liu, Quyan Wang, Peter J. Munson, Nalini Raghavachari, Therese White, Megan M. Tew, Kieron Dunleavy, Yihong Ye, Wyndham H. Wilson, and Adrian Wiesttner

Phase I and Pharmacokinetic Study of Sunitinib in Pediatric Patients with Refractory Solid Tumors: A Children’s Oncology Group Study

Steven G. DuBois, Suzanne Shusterman, Azeez M. Ingle, Charlotte H. Ahern, Joel M. Reid, Bing Wu, Sylvain Baruchel, Julia Glade-Bender, Percy Ivy, Holcombe E. Grier, Peter C. Adamson, and Susan M. Blaney

Multihistology, Target-Driven Pilot Trial of Oral Topotecan as an Inhibitor of Hypoxia-Inducible Factor-1α in Advanced Solid Tumors

Shivaani Kummar, Mark Raffeld, Lamin Juwara, Yvonne Hornemeyer, Agnes Strassberger, Deborah Allen, Seth M. Steinberg, Annamaria Rapisarda, Shawn D. Spencer, William D. Figg, Xiaohong Chen, Ismail Baris Turkbey, Peter Choyke, Anthony J. Murgo, James H. Doroshow, and Giovanni Melillo
HSP90 Inhibition Is Effective in Breast Cancer: A Phase II Trial of Tanespimycin (17-AAG) Plus Trastuzumab in Patients with HER2-Positive Metastatic Breast Cancer Progressing on Trastuzumab
Shanu Modi, Alison Stopeck, Hannah Linden, David Solit, Sarat Chandarlapaty, Neal Rosen, Gabriella D'Andrea, Maura Dickler, Mary E. Moynahan, Steven Sugarman, Weinig Ma, Sujata Patil, Larry Norton, Alison L. Hannah, and Clifford Hudis
See commentary p. 4919

Comparison of Clinical and Immunological Effects of Intravenous and Intradermal Administration of α-GalactosylCeramide (KRN7000)-Pulsed Dendritic Cells
Andrew J. Nicol, Andrea Tazbirkova, and Mie Nieda

Clinical, Pharmacodynamic, and Pharmacokinetic Evaluation of BNC105P: A Phase I Trial of a Novel Vascular Disrupting Agent and Inhibitor of Cancer Cell Proliferation
Danny Rischin, David C. Bibby, Geoff Chong, Gabriel Kremmidiotis, Annabel F. Leske, Clayton A. Matthews, Shirley S. Wong, Mark A. Rosen, and Jayesh Desai

EGF61 Polymorphism Predicts Complete Pathologic Response to Cetuximab-Based Chemoradiation Independent of KRAS Status in Locally Advanced Rectal Cancer Patients

p53 Expression in Node-Positive Breast Cancer Patients: Results from the Cancer and Leukemia Group B 9344 Trial (159905)

Circulating Cell-Free DNA in Plasma of Never Smokers with Advanced Lung Adenocarcinoma Receiving Gefitinib or Standard Chemotherapy as First-Line Therapy
Young Joo Lee, Kyong-Ah Yoon, Ji-Youn Han, Heung Tae Kim, Tak Yun, Geon Kook Lee, Hyae Young Kim, and Jin Soo Lee

Baseline Circulating Tumor Cell Counts Significantly Enhance a Prognostic Score for Patients Participating in Phase I Oncology Trials

Expression of Amphiregulin and EGFRvIII Affect Outcome of Patients with Squamous Cell Carcinoma of the Head and Neck Receiving Cetuximab–Docetaxel Treatment
Ingeborg Tinholfer, Konrad Klinghammer, Wilko Weichert, Maren Knödler, Albrecht Stenzinger, Thomas Gauler, Volker Budach, and Ulrich Keilholz

Class III β-Tubulin in Advanced NSCLC of Adenocarcinoma Subtype Predicts Superior Outcome in a Randomized Trial
Adam Christian Vilmar, Eric Santoni-Rugiu, and Jens Benn Sørensen

PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE

EGF61 Polymorphism Predicts Complete Pathologic Response to Cetuximab-Based Chemoradiation Independent of KRAS Status in Locally Advanced Rectal Cancer Patients
ABOUT THE COVER

Three-dimensional structure of the trastuzumab/pertuzumab/HER2 ternary complex. Yellow, orange, and magenta are trastuzumab, pertuzumab, and HER2, respectively. Trastuzumab and pertuzumab bind to HER2 without competing with each other. For further details, please see Yamashita-Kashima and coworkers on page 5060 in this issue.