## Highlights of This Issue

### 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 Bhattacharya

- **4942**
  - Cancer Stem Cells and Chemosensitivity
  - Marcello Maugeri-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 Dunibier, 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, Daoudie Tie, Rudi H. Brakenhoff, 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, Hirotsama Yamamoto, Yasutomo Nasu, Takekis Kishimoto, Harvey L. Pass, Hideki Matsui, Nam-ho Huh, and Shinichiro Miyoshi

- **4968**
  - Interleukin-7 Inhibits Tumor-Induced CD27—CD28 Suppressor T Cells: Implications for Cancer Immunotherapy
  - Yue Zhang, Lukas W. Pfannenstiel, Elzbietta Bolesta, Carolina L. Monte, Xiaooyu 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 Lao, Qin 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 Argiris, 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. Frederick, David Raben, and Lynn E. Heasley

Mitoxantrone Inhibits HIF-1α Expression in a Topoisomerase II–Independent Pathway
Ying-Min Toh and Tsai-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 Camphausen, James Mitchell, and Deborah E. Citrin

The Efficacy of IGF-I Receptor Monoclonal Antibody against Human Gastrointestinal Carcinomas is Independent of k-ras Mutation Status
Hiroyuki Yamamoto, Hirokazu Ohashi, Hiroaki Taniguchi, Yoshiaki Ariyura, David P. Carbone, Kohzoh Imai, and Yasuhiisa Shinomura

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 Shafer-Weaver, Amir Gandjakhche, 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. Rachmann, Bent Brockmeyer, Kathleen DePreter, André Oberthür, Sandra Ackermann, Yvonne Kahler, Kristian Pajtler, Jessica Theissen, Frank Westermann, Jo Vandesompele, Frank Speleman, 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, Edgar G. Rizzatti, Patricia Perez-Galan, Delong Liu, Quyuan Wang, Peter J. Munson, Nalini Raghavachari, Therese White, Megan M. Tew, Kieron Dunleavy, Yi-Hong Ye, Wyndham H. Wilson, and Adrian Wiestner

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, Ashish 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
Shivangi Kummar, Mark Raffeld, Lamin Juwara, Yvonne Hornmeyer, 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, Weinling 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, Annabell 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

EGFRvIII Affect Outcome of Patients with Squamous Cell Carcinoma of the Head and Neck Receiving Cetuximab–Docetaxel Treatment
Ingeborg Tinhofer, 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
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.