**CONTENTS**

**Highlights of This Issue** 6367

**SPECIAL FEATURES**

**CCR Translations**

6369  **Therapeutic Oligonucleotides: The Road Not Taken**
Cy A. Stein and Sanjay Goel
See commentary p. 6582

**Molecular Pathways**

6373  **The Role of Erythropoietin and Erythropoiesis-Stimulating Agents in Tumor Progression**
Benjamin D. Hedley, Alison L. Allan, and Anargyros Xenocostas

6381  **TLX1-Induced T-cell Acute Lymphoblastic Leukemia**
Kim De Keersmaecker and Adolfo A. Ferrando

**CCR Focus**

6388  **Antibody Conjugates: The Future Is Now**
Susan E. Bates

6389  **Antibody Conjugate Therapeutics: Challenges and Potential**
Beverly A. Teicher and Ravi V.J. Chari

6398  **Antibody Fusion Proteins: Anti-CD22 Recombinant Immunotoxin Moxetumomab Pasudotox**
Robert J. Kreitman and Ira Pastan

6406  **Antibody-Radiouclide Conjugates for Cancer Therapy: Historical Considerations and New Trends**
Martina Steiner and Dario Neri

6417  **Antibody-Drug Conjugates of Calicheamicin Derivative: Gemtuzumab Ozogamicin and Inotuzumab Ozogamicin**
Alejandro D. Ricart

6428  **Brentuximab Vedotin (SGN-35)**
Jessica Katz, John E. Janik, and Anas Younes

**CANCER THERAPY: PRECLINICAL**

6437  **Trastuzumab Emtansine: A Unique Antibody-Drug Conjugate in Development for Human Epidermal Growth Factor Receptor 2–Positive Cancer**
Patricia M. LoRusso, Denise Weiss, Ellie Guardino, Sandhya Girish, and Mark X. Slwkowski

6448  **SAR3419: An Anti-CD19-Maytansinoid Immunoconjugate for the Treatment of B-Cell Malignancies**
Veronique Blanc, Anne Bousseau, Anne Caron, Chantal Carrez, Robert J. Lutz, and John M. Lambert

6459  **Polo-like Kinase 1 Inhibitors and Their Potential Role in Anticancer Therapy, with a Focus on NSCLC**
René H. Medema, Chia-Chi Lin, and James Chih-Hsin Yang

6467  **Tumor-Derived Autophagosome Vaccine: Induction of Cross-Protective Immune Responses against Short-lived Proteins through a p62-Dependent Mechanism**
Christopher G. Twitty, Shawn M. Jensen, Hong-Ming Hu, and Bernard A. Fox

6482  **Synergistic Action of a RAF Inhibitor and a Dual PI3K/mTOR Inhibitor in Thyroid Cancer**
Ning Jin, Tianyin Jiang, David M. Rosen, Barry D. Nelkin, and Douglas W. Ball

6490  **The Novel Chemical Entity YTR107 Inhibits Recruitment of Nucleophosmin to Sites of DNA Damage, Suppressing Repair of DNA Double-Strand Breaks and Enhancing Radiosensitization**
Significant Biological Role of Sp1 Transactivation in Multiple Myeloma

Dicer-Mediated Upregulation of BCRP Confers Tamoxifen Resistance in Human Breast Cancer Cells

EGFR- and VEGF(R)-Targeted Small Molecules Show Synergistic Activity in Colorectal Cancer Models Refractory to Combinations of Monoclonal Antibodies
Virginie Poindessous, Djamilia Ouaret, Karima El Ouadrani, Aude Battistella, Virginie F. Mégalophonos, Nyam Kamsu-Kom, Amélie Petitprez, Alexandre E. Escargueil, Pascaline Boudou, Sylvie Dumont, Pascale Cervera, Jean-François Félou, Thierry André, Christophe Tournigand, Benoist Chibaudel, Aimery de Gramont, and Annette K. Larsen

Toll-like Receptor 9 Agonist IMO Cooperates with Cetuximab in KRas Mutant Colorectal and Pancreatic Cancers
Roberta Rosa, Davide Melisi, Vincenzo Damiano, Roberto Bianco, Sonia Garofalo, Teresa Gelardi, Sudhir Agrawal, Federica Di Nicolantonio, Aldo Scarpa, Alberto Bardelli, and Giampaolo Tortora

High XRCC1 Protein Expression Is Associated with Poorer Survival in Patients with Head and Neck Squamous Cell Carcinoma

Discriminant Analysis of 18F-Fluorothymidine Kinetic Parameters to Predict Survival in Patients with Recurrent High-Grade Glioma
Mirwais Wardak, Christiana Schiepers, Magnus Dahlbom, Timothy Cloughesey, Wei Chen, Nagiehettar Satyamurthy, Johannes Czernin, Michael E. Phelps, and Sung-Cheng Huang

PTEN Protein Loss by Immunostaining: Analytic Validation and Prognostic Indicator for a High Risk Surgical Cohort of Prostate Cancer Patients
Tamara L. Lotan, Bora Gurel, Siobhan Sutcliffe, David Esopi, Wennwan Liu, Junfeng Xu, Jessica L. Hicks, Ben R. Park, Elizabeth Humphreys, Alan W. Partin, Misop Han, George J. Netto, William B. Isaacs, and Angelo M. De Marzo

Aflibercept (VEGF Trap) in Inoperable Stage III or Stage IV Melanoma of Cutaneous or Uveal Origin
Ahmad A. Tarhini, Paul Frankel, Kim A. Margolin, Scott Christensen, Christopher Ruel, Janice Shippe-Spotloe, David R. Gandara, Alice Chen, and John M. Kirkwood

A Phase 1 Dose Escalation, Pharmacokinetic, and Pharmacodynamic Evaluation of eIF-4E Antisense Oligonucleotide LY2275796 in Patients with Advanced Cancer

See article p. 6369

Comparison of Continuous versus Categorical Tumor Measurement–Based Metrics to Predict Overall Survival in Cancer Treatment Trials
Ming-Wen An, Sumithra J. Mandrekar, Megan E. Branda, Shauna L. Hillman, Alex A. Adjei, Henry C. Pitot, Richard M. Goldberg, and Daniel J. Sargent
LETTERS TO THE EDITOR

KRAS rs61764370 in Epithelial Ovarian Cancer–Letter
Joanne B. Weidhaas and Frank J. Slack

KRAS rs61764370 in Epithelial Ovarian Cancer–Response
Harvey A. Risch, Andrew Berchuck, and Paul D.P. Pharoah; for the Ovarian Cancer Association Consortium

ABOUT THE COVER

The work by Poindessous and colleagues shows that inhibition of EGFR- and VEGF(R)-signaling by combinations of two small molecule tyrosine kinase inhibitors (TKI), afatinib and vargatef, has synergistic activity in colorectal cancer models that are refractory to combinations of the monoclonal antibodies cetuximab and bevacizumab. Importantly, only the TKIs were able to attenuate the phosphorylation of intracellular EGFR- and VEGFR-receptors which was accompanied by the induction of apoptotic cell death as indicated by TUNEL staining (nuclear DNA in blue, apoptotic nuclei in white). This work provides a rationale for clinical trials of the afatinib and vargatef combination, even in patients with mutant KRAS. For details, see the article by Poindessous and colleagues on page 6522 of this issue.