

June 15, 2015 • Volume 21 • Number 12

**Highlights of This Issue 2655****SPECIAL FEATURES****CCR 20<sup>th</sup> Anniversary Commentary**

- 2657** CCR 20<sup>th</sup> Anniversary Commentary: From Regulatory T Cells to Checkpoint Monoclonal Antibodies—Immuno-oncology Advances Clinical Cancer Research  
Dominik Wolf and Anna Maria Wolf

**CCR Translations**

- 2660** CD38-Targeted Immunochemotherapy in Refractory Multiple Myeloma: A New Horizon  
Jacob P. Laubach and Paul G. Richardson  
*See related article, p. 2802*
- 2663** "Vertical" Inhibition of HER2 Yields Horizontal Gains in the Clinic  
George W. Sledge and Mark D. Pegram  
*See related article, p. 2737*


**CCR Perspectives in Drug Approval**

- 2666** FDA Approval: Belinostat for the Treatment of Patients with Relapsed or Refractory Peripheral T-cell Lymphoma  
Hyon-Zu Lee, Virginia E. Kwitkowski, Pedro L. Del Valle, M. Stacey Ricci, Haleh Saber, Bahru A. Habtemariam, Julie Bullock, Erik Bloomquist, Yuan Li Shen, Xiao-Hong Chen, Janice Brown, Nitin Mehrotra, Sarah Dorff, Rosane Charlab, Robert C. Kane, Edvardas Kaminskas, Robert Justice, Ann T. Farrell, and Richard Pazdur

**Molecular Pathways**

- 2671** Molecular Pathways: Leveraging the BCL-2 Interactome to Kill Cancer Cells—Mitochondrial Outer Membrane Permeabilization and Beyond  
Hetal Brahmabhatt, Sina Oppermann, Elizabeth J. Osterlund, Brian Leber, and David W. Andrews

**Reviews**

- 2677** Management of Cutaneous and Extracutaneous Side Effects of Smoothed Inhibitor Therapy for Advanced Basal Cell Carcinoma  
Shalini V. Mohan and Anne Lynn S. Chang
- 2684** Targeting FGFR Signaling in Cancer  
 Mehdi Touat, Ecaterina Ileana, Sophie Postel-Vinay, Fabrice André, and Jean-Charles Soria


**CANCER THERAPY: CLINICAL**

- 2695** A Phase I First-in-Human Study of Enoticumab (REGN421), a Fully Human Delta-like Ligand 4 (Dl14) Monoclonal Antibody in Patients with Advanced Solid Tumors  
Elena Gabriela Chiorean, Patricia LoRusso, Robert Matthew Strother, Jennifer R. Diamond, Anne Younger, Wells A. Messersmith, Lieve Adriaens, Liming Liu, Richard J. Kao, Albert Thomas DiCioccio, Ana Kostic, Russell Leek, Adrian Harris, and Antonio Jimeno
- 2704** A Phase I/II Study of the mTOR Inhibitor Everolimus in Combination with HyperCVAD Chemotherapy in Patients with Relapsed/Refractory Acute Lymphoblastic Leukemia  
Naval Daver, Yanis Boumber, Hagop Kantarjian, Farhad Ravandi, Jorge Cortes, Michael E. Rytting, Jitesh D. Kawedia, Jordan Basnett, Kirk S. Culotta, Zhihong Zeng, Hongbo Lu, Mary Ann Richie, Rebecca Garris, Lianchun Xiao, Wenbin Liu, Keith A. Baggerly, Elias Jabbour, Susan O'Brien, Jan Burger, Linda J. Bendall, Deborah Thomas, and Marina Konopleva
- 2715** Phase I Study of Vorinostat as a Radiation Sensitizer with <sup>131</sup>I-Metaiodobenzylguanidine (<sup>131</sup>I-MIBG) for Patients with Relapsed or Refractory Neuroblastoma  
Steven G. DuBois, Susan Groshen, Julie R. Park, Daphne A. Haas-Kogan, Xiaodong Yang, Ethan Geier, Eugene Chen, Kathy Giacomini, Brian Weiss, Susan L. Cohn, M. Meaghan Granger, Gregory A. Yanik, Randall Hawkins, Jesse Courtier, Hollie Jackson, Fariba Goodarzi, Hiroyuki Shimada, Scarlett Czamecki, Denice Tsao-Wei, Judith G. Villablanca, Araz Marachelian, and Katherine K. Matthey

# Table of Contents

**2722** TBCRC 019: A Phase II Trial of Nanoparticle Albumin-Bound Paclitaxel with or without the Anti-Death Receptor 5 Monoclonal Antibody Tigatuzumab in Patients with Triple-Negative Breast Cancer

Andres Forero-Torres, Katherine E. Varley, Vandana G. Abramson, Yufeng Li, Christos Vakilav, Nancy U. Lin, Minetta C. Liu, Hope S. Rugo, Rita Nanda, Anna M. Storniolo, Tiffany A. Traina, Sujata Patil, Catherine H. Van Poznak, Julie R. Nangia, William J. Irvin Jr, Helen Krontiras, Jennifer F. De Los Santos, Paul Haluska, William Grizzle, Richard M. Myers, and Antonio C. Wolff on behalf of the Translational Breast Cancer Research Consortium (TBCRC)  
*See related article, p. 2771*

**2730**  A Phase I Dose-Escalation Study of Antibody BI-505 in Relapsed/Refractory Multiple Myeloma

Markus Hansson, Peter Gimsing, Ashraf Badros, Titti Martinsson Niskanen, Hareth Nahi, Fritz Offner, Morten Salomo, Elisabeth Sonesson, Morten Mau-Sorensen, Yvonne Stenberg, Annika Sundberg, Ingrid Teige, Jan Van Droogenbroeck, Stina Wichert, Maurizio Zangari, Björn Frendeus, Magnus Korsgren, Martine Poelman, and Guido Tricot

**2737** Phase I Study to Assess the Combination of Afatinib with Trastuzumab in Patients with Advanced or Metastatic HER2-Positive Breast Cancer

Alistair Ring, Duncan Wheatley, Helen Hatcher, Robert Laing, Ruth Plummer, Martina Uttenreuther-Fischer, Graham Temple, Katy Pelling, and David Schnell  
*See related commentary, p. 2663*

**2745** Progression-Free and Overall Survival in ALK-Positive NSCLC Patients Treated with Sequential Crizotinib and Ceritinib

Justin F. Gainor, Daniel S.W. Tan, Tomasso De Pas, Benjamin J. Solomon, Aziah Ahmad, Chiara Lazzari, Filippo de Marinis, Gianluca Spitaleri, Katherine Schultz, Luc Friboulet, Beow Y. Yeap, Jeffrey A. Engelman, and Alice T. Shaw

## PERSONALIZED MEDICINE AND IMAGING

**2753**  CD44 Isoform Status Predicts Response to Treatment with Anti-CD44 Antibody in Cancer Patients

Fabian Birzele, Edgar Voss, Adam Nopora, Konrad Honold, Florian Heil, Sabine Lohmann, Henk Verheul, Christophe Le Tourneau, Jean-Pierre Delord, Carla van Herpen, Devalingam Mahalingam, Andrew L. Coveler, Valerie Meresse, Stefan Weigand, Valeria Runza, and Michael Cannarile

**2763** Estrogen Receptor Expression in 21-Gene Recurrence Score Predicts Increased Late Recurrence for Estrogen-Positive/HER2-Negative Breast Cancer

Mitch Dowsett, Ivana Sestak, Richard Buus, Elena Lopez-Knowles, Elizabeth Mallon, Anthony Howell, John F. Forbes, Aman Buzdar, and Jack Cuzick

**2771** Significance of Circulating Tumor Cells in Metastatic Triple-Negative Breast Cancer Patients within a Randomized, Phase II Trial: TBCRC 019

Costanza Paoletti, Yufeng Li, Maria C. Muñiz, Kelley M. Kidwell, Kimberly Aung, Dafydd G. Thomas, Martha E. Brown, Vandana G. Abramson, William J. Irvin Jr, Nancy U. Lin, Minetta C. Liu, Rita Nanda, Julie R. Nangia, Anna M. Storniolo, Tiffany A. Traina, Christos Vakilav, Catherine H. Van Poznak, Antonio C. Wolff, Andres Forero-Torres, and Daniel F. Hayes on behalf of the Translational Breast Cancer Research Consortium (TBCRC)  
*See related article, p. 2722*

## CANCER THERAPY: PRECLINICAL


**2780** Methionine Deprivation Induces a Targetable Vulnerability in Triple-Negative Breast Cancer Cells by Enhancing TRAIL Receptor-2 Expression  
Elena Strelakova, Dmitry Malin, David M. Good, and Vincent L. Cryns

**2792** Radiation Enhancement of Head and Neck Squamous Cell Carcinoma by the Dual PI3K/mTOR Inhibitor PF-05212384

Andrew J. Leiker, William DeGraff, Rajani Choudhuri, Anastasia L. Sowers, Angela Thetford, John A. Cook, Carter Van Waes, and James B. Mitchell

**2802** Preclinical Evidence for the Therapeutic Potential of CD38-Targeted Immuno-Chemotherapy in Multiple Myeloma Patients Refractory to Lenalidomide and Bortezomib

Inger S. Nijhof, Richard W.J. Groen, Willy A. Noort, Berris van Kessel, Regina de Jong-Korlaar, Joost Bakker, Jeroen J.L. van Bueren, Paul W.H.I. Parren, Henk M. Lokhorst, Niels W.C.J. van de Donk, Anton C.M. Martens, and Tuna Mutis  
*See related commentary, p. 2660*

**2811**  The MET Inhibitor AZD6094 (Savolitinib, HMPL-504) Induces Regression in Papillary Renal Cell Carcinoma Patient-Derived Xenograft Models

Alwin G. Schuller, Evan R. Barry, Rhys D.O. Jones, Ryan E. Henry, Melanie M. Frigault, Garry Beran, David Linsenmayer, Maureen Hattersley, Aaron Smith, Joanne Wilson, Stefano Cairo, Olivier Déas, Delphine Nicolle, Ammar Adam, Michael Zinda, Corinne Reimer, Stephen E. Fawell, Edwin A. Clark, and Celina M. D'Cruz

# Table of Contents

## BIOLOGY OF HUMAN TUMORS

- 2820** The Use of Transcriptional Profiling to Improve Personalized Diagnosis and Management of Cutaneous T-cell Lymphoma (CTCL)  
Ivan V. Litvinov, Elena Netchiporouk, Brendan Cordeiro, Marc-André Doré, Linda Moreau, Kevin Pehr, Martin Gilbert, Youwen Zhou, Denis Sasseville, and Thomas S. Kupper
- 2830** Prognostic Significance of Tryptophan Catabolism in Adult T-cell Leukemia/Lymphoma  
Ayako Masaki, Takashi Ishida, Yasuhiro Maeda, Susumu Suzuki, Asahi Ito, Hisashi Takino, Hiroka Ogura, Haruhito Totani, Takashi Yoshida, Shiori Kinoshita, Tomoko Narita, Masaki Ri, Shigeru Kusumoto, Atsushi Inagaki, Hirokazu Komatsu, Akio Niimi, Ryuzo Ueda, Atae Utsunomiya, Hiroshi Inagaki, and Shinsuke Iida
- 2840** The Ovarian Cancer Chemokine Landscape Is Conducive to Homing of Vaccine-Primed and CD3/CD28–Costimulated T Cells Prepared for Adoptive Therapy  
Emese Zsiros, Priyanka Duttagupta, Denarda Dangaj, Hongzhe Li, Renee Frank, Thomas Garrabrant, Ian S. Hagemann, Bruce L. Levine, Carl H. June, Lin Zhang, Ena Wang, Francesco M. Marincola, Davide Bedognetti, Daniel J. Powell Jr, Janos Tanyi, Michael D. Feldman, Lana E. Kandalaft, and George Coukos
- 2851** Immunohistochemical Loss of LKB1 Is a Biomarker for More Aggressive Biology in *KRAS*-Mutant Lung Adenocarcinoma  
Antonio Calles, Lynette M. Sholl, Scott J. Rodig, Ashley K. Pelton, Jason L. Hornick, Mohit Butaney, Christine Lydon, Suzanne E. Dahlberg, Geoffrey R. Oxnard, David M. Jackman, and Pasi A. Jänne
- 2861** HPV Serum Antibodies as Predictors of Survival and Disease Progression in Patients with HPV-Positive Squamous Cell Carcinoma of the Oropharynx  
Kristina R. Dahlstrom, Karen S. Anderson, Julia N. Cheng, Diego Chowell, Guojun Li, Marshall Posner, and Erich M. Sturgis
- 2870** SIRT1/PGC1 $\alpha$ -Dependent Increase in Oxidative Phosphorylation Supports Chemotherapy Resistance of Colon Cancer  
Thomas T. Vellinga, Tijana Borovski, Vincent C.J. de Boer, Szabolcs Fatrai, Susanne van Schelven, Kari Trumpi, Andre Verheem, Nikol Snoeren, Benjamin L. Emmink, Jan Koster, Inne H.M. Borel Rinkes, and Onno Kranenburg

 AC icon indicates Author Choice

 CME icon indicates that this article is available for continuing medical education credit at <http://cme.aacrjournals.org>

For more information please visit [www.aacrjournals.org](http://www.aacrjournals.org)

## ABOUT THE COVER

The cover shows head and neck squamous cell carcinoma (UMSCC1) xenograft tissue sections harvested after treatment with the dual PI3k/mTOR inhibitor PF-05212384. Immunohistochemical staining demonstrates a significant reduction in phospho-S6 fluorescence (green) with intravenous PF-05212384 treatment. For details, see the article by Leiker and colleagues on page 2792 of this issue.

