

Highlights of This Issue 4525

SPECIAL FEATURES

CCR Drug Updates

4527 Venetoclax in Patients with Previously Treated Chronic Lymphocytic Leukemia

Andrew W. Roberts, Stephan Stilgenbauer, John F. Seymour, and David C.S. Huang

4534 U.S. Food and Drug Administration Approval Summary: Atezolizumab for Metastatic Non–Small Cell Lung Cancer

Chana Weinstock, Sean Khozin, Daniel Suzman, Lijun Zhang, Shenghui Tang, Sakar Wahby, Kirsten B. Goldberg, Geoffrey Kim, and Richard Pazdur

Molecular Pathways

4540 Molecular Pathways: Targeting the Protein Kinase Wee1 in Cancer

Jill J.J. Geenen and Jan H.M. Schellens

SPECIAL REPORT

4545 Clinical Pathways: Recommendations for Putting Patients at the Center of Value-Based Care

Edward Abrahams, Alan Balch, Patricia Goldsmith, Marcia Kean, Amy M. Miller, Gilbert Omenn, Ellen Sonet, John Sprandio, Courtney Tyne, and Kimberly Westrich

CLINICAL TRIAL BRIEF REPORT

4550 Phase I Study of Fenretinide Delivered Intravenously in Patients with Relapsed or Refractory Hematologic Malignancies: A California Cancer Consortium Trial

Ann M. Mohrbacher, Allen S. Yang, Susan Groshen, Shivaani Kummar, Martin E. Gutierrez, Min H. Kang, Denice Tsao-Wei, C. Patrick Reynolds, Edward M. Newman, and Barry J. Maurer

CANCER THERAPY: CLINICAL

4556 Phase I Trial of Intratumoral Injection of *CCL21* Gene–Modified Dendritic Cells in Lung Cancer Elicits Tumor-Specific Immune Responses and CD8⁺ T-cell Infiltration

Jay M. Lee, Mi-Heon Lee, Edward Garon, Jonathan W. Goldman, Ramin Salehi-Rad, Felicity E. Baratelli, Dörthe Schaeue, Gerald Wang, Fran Rosen, Jane Yanagawa, Tonya C. Walsler, Ying Lin, Stacy J. Park, Sharon Adams, Francesco M. Marincola, Paul C. Tumeh, Fereidoun Abtin, Robert Suh, Karen L. Reckamp, Gina Lee, William D. Wallace, Sarah Lee, Gang Zeng, David A. Elashoff, Sherven Sharma, and Steven M. Dubinett

4569 Intra- and Interobserver Reproducibility Assessment of PD-L1 Biomarker in Non–Small Cell Lung Cancer

Wendy A. Cooper, Prudence A. Russell, Maya Cherian, Edwina E. Duhig, David Godbolt, Peter J. Jessup, Christine Khoo, Connall Leslie, Annabelle Mahar, David F. Moffat, Vanathi Sivasubramaniam, Celine Faure, Alena Reznichenko, Amanda Grattan, and Stephen B. Fox

4578 Circulating DNA Demonstrates Convergent Evolution and Common Resistance Mechanisms during Treatment of Colorectal Cancer

Alain R. Thierry, Brice Pastor, Zhi-Qin Jiang, Anastasia D. Katsiampoura, Christine Parseghian, Jonathan M. Loree, Michael J. Overman, Cynthia Sanchez, Safia El Messaoudi, Marc Ychou, and Scott Kopetz

4592 Association of Tissue Abiraterone Levels and *SLCO* Genotype with Intraprostatic Steroids and Pathologic Response in Men with High-Risk Localized Prostate Cancer

Elabe A. Mostaghel, Eunpi Cho, Ailin Zhang, Mohammad Alyamani, Arja Kaipainen, Sean Green, Brett T. Marck, Nima Sharifi, Jonathan L. Wright, Roman Gulati, Lawrence D. True, Massimo Loda, Alvin M. Matsumoto, Daniel Tamae, Trevor N. Penning, Steven P. Balk, Phillip W. Kantoff, Peter S. Nelson, Mary-Ellen Taplin, and R. Bruce Montgomery

4602 *PIK3CA* Mutations Contribute to Acquired Cetuximab Resistance in Patients with Metastatic Colorectal Cancer

Jian-Ming Xu, Yan Wang, You-Liang Wang, Yan Wang, Tao Liu, Ming Ni, Man-Sheng Li, Li Lin, Fei-Jiao Ge, Chun Gong, Jun-Yan Gu, Ru Jia, He-Fei Wang, Yu-Ling Chen, Rong-Rui Liu, Chuan-Hua Zhao, Zhao-Li Tan, Yang Jin, Yun-Ping Zhu, Shuji Ogino, and Zhi-Rong Qian



Table of Contents

- 4617** Long-Term Efficacy, Survival, and Safety of [¹⁷⁷Lu-DOTA⁰,Tyr³]octreotate in Patients with Gastroenteropancreatic and Bronchial Neuroendocrine Tumors
Tessa Brabander, Wouter A. van der Zwan, Jaap J.M. Teunissen, Boen L.R. Kam, Richard A. Feelders, Wouter W. de Herder, Casper H.J. van Eijck, Gaston J.H. Franssen, Eric P. Krenning, and Dik J. Kwkkeboom
- 4625** Rb Loss and KRAS Mutation Are Predictors of the Response to Platinum-Based Chemotherapy in Pancreatic Neuroendocrine Neoplasm with Grade 3: A Japanese Multicenter Pancreatic NEN-G3 Study
Susumu Hijioaka, Waki Hosoda, Keitaro Matsuo, Makoto Ueno, Masayuki Furukawa, Hideyuki Yoshitomi, Noritoshi Kobayashi, Masafumi Ikeda, Tetsuhide Ito, Shoji Nakamori, Hiroshi Ishii, Yuza Kodama, Chigusa Morizane, Takuji Okusaka, Hiroaki Yanagimoto, Kenji Notohara, Hiroki Taguchi, Masayuki Kitano, Kei Yane, Hiroyuki Maguchi, Yoshiaki Tsuchiya, Izumi Komoto, Hiroki Tanaka, Akihito Tsuji, Syunpei Hashigo, Yoshiaki Kawaguchi, Tetsuya Mine, Atsushi Kanno, Go Murohisa, Katsuyuki Miyabe, Tadayuki Takagi, Nobutaka Matayoshi, Tsukasa Yoshida, Kazuo Hara, Masayuki Imamura, Junji Furuse, Yasushi Yatabe, and Nobumasa Mizuno
- 4633** Phase I and Preliminary Phase II Study of TRC105 in Combination with Sorafenib in Hepatocellular Carcinoma
Austin G. Duffy, Chi Ma, Susanna V. Ulahannan, Osama E. Rahma, Oxana Makarova-Rusher, Liang Cao, Yunkai Yu, David E. Kleiner, Jane Trepel, Min-Jung Lee, Yusuke Tomita, Seth M. Steinberg, Theo Heller, Baris Turkbey, Peter L. Choyke, Cody J. Peer, William D. Figg, Brad J. Wood, and Tim F. Greten
- 4642** A Phase I Study of ABC294640, a First-in-Class Sphingosine Kinase-2 Inhibitor, in Patients with Advanced Solid Tumors
Carolyn D. Britten, Elizabeth Garrett-Mayer, Steven H. Chin, Keisuke Shirai, Besim Ogretmen, Tricia A. Bentz, Alan Brisendine, Kate Anderton, Susan L. Cusack, Lynn W. Maines, Yan Zhuang, Charles D. Smith, and Melanie B. Thomas
- 4651** Perioperative COX-2 and β -Adrenergic Blockade Improves Metastatic Biomarkers in Breast Cancer Patients in a Phase-II Randomized Trial
Lee Shaashua, Maytal Shabat-Simon, Rita Haldar, Pini Matzner, Oded Zmora, Moshe Shabtai, Eran Sharon, Tanir Allweis, Iris Barshack, Lucile Hayman, Jesusa Arevalo, Jeffrey Ma, Maya Horowitz, Steven Cole, and Shamgar Ben-Eliyahu

- 4662** The Longitudinal Transcriptional Response to Neoadjuvant Chemotherapy with and without Bevacizumab in Breast Cancer
Laxmi Silwal-Pandit, Silje Nord, Hedda von der Lippe Gythfeldt, Elen K. Møller, Thomas Fleischer, Einar Rødland, Marit Krohn, Elin Borgen, Øystein Garred, Tone Olsen, Phuong Vu, Helle Skjerven, Anne Fangberget, Marit M. Holmen, Ellen Schlitchting, Elisabeth Wille, Mette Nordberg Stokke, Hans Kristian Moen Vollan, Vessela Kristensen, Anita Langerød, Steinar Lundgren, Erik Wist, Bjørn Naume, Ole Christian Lingjærde, Anne-Lise Børresen-Dale, and Olav Engebraaten

PERSONALIZED MEDICINE AND IMAGING


- 4671** Immune-Related Tumor Response Dynamics in Melanoma Patients Treated with Pembrolizumab: Identifying Markers for Clinical Outcome and Treatment Decisions
Mizuki Nishino, Anita Giobbie-Hurder, Michael P. Manos, Nancy Bailey, Elizabeth I. Buchbinder, Patrick A. Ott, Nikhil H. Ramaiya, and F. Stephen Hodi
- 4680** Feasibility of Ultra-High-Throughput Functional Screening of Melanoma Biopsies for Discovery of Novel Cancer Drug Combinations
Adam A. Friedman, Yun Xia, Lorenzo Trippa, Long Phi Le, Vivien Igras, Dennie T. Frederick, Jennifer A. Wargo, Kenneth K. Tanabe, Donald P. Lawrence, Donna S. Neuberg, Keith T. Flaherty, and David E. Fisher
- 4693** Analytic, Preanalytic, and Clinical Validation of p53 IHC for Detection of TP53 Missense Mutation in Prostate Cancer
Liana B. Guedes, Fawaz Almutairi, Michael C. Haffner, Gaurav Rajoria, Zach Liu, Szczepan Klimek, Roberto Zoino, Kasra Yousefi, Rajni Sharma, Angelo M. De Marzo, George J. Netto, William B. Isaacs, Ashley E. Ross, Edward M. Schaeffer, and Tamara L. Lotan
- 4704** Androgen Receptor Variant AR-V9 Is Coexpressed with AR-V7 in Prostate Cancer Metastases and Predicts Abiraterone Resistance 
Manish Kohli, Yeung Ho, David W. Hillman, Jamie L. Van Etten, Christine HENZLER, Rendong Yang, Jamie M. Sperger, Yingming Li, Elizabeth Tseng, Ting Hon, Tyson Clark, Winston Tan, Rachel E. Carlson, Ligu Wang, Hugues Sicotte, Ho Thai, Rafael Jimenez, Haojie Huang, Peter T. Vedell, Bruce W. Eckloff, Jorge F. Quevedo, Henry C. Pitot, Brian A. Costello, Jin Jen, Eric D. Wieben, Kevin A.T. Silverstein, Joshua M. Lang, Liewei Wang, and Scott M. Dehm

Table of Contents

- 4716** **Monitoring Daily Dynamics of Early Tumor Response to Targeted Therapy by Detecting Circulating Tumor DNA in Urine**
Hatim Husain, Vladislava O. Melnikova, Karena Kosco, Brian Woodward, Soham More, Sandeep C. Pingle, Elizabeth Weihe, Ben Ho Park, Muneesh Tewari, Mark G. Erlander, Ezra Cohen, Scott M. Lippman, and Razelle Kurzrock
- 4724** ***In Vivo* Detection of EGFRvIII in Glioblastoma via Perfusion Magnetic Resonance Imaging Signature Consistent with Deep Peritumoral Infiltration: The ϕ -Index**
Spyridon Bakas, Hamed Akbari, Jared Pisapia, Maria Martinez-Lage, Martin Rozycki, Saima Rathore, Nadia Dahmane, Donald M. O'Rourke, and Christos Davatzikos
- 4735** **Low Tumor Mitochondrial DNA Content Is Associated with Better Outcome in Breast Cancer Patients Receiving Anthracycline-Based Chemotherapy**
Marjolein J.A. Weerts, Antoinette Hollestelle, Anieta M. Sieuwerts, John A. Foekens, Stefan Sleijfer, and John W.M. Martens
- 4744** **Sensitivity and Specificity of Cetuximab-IRDye800CW to Identify Regional Metastatic Disease in Head and Neck Cancer**
Eben L. Rosenthal, Lindsay S. Moore, Kiranya Tipirmeni, Esther de Boer, Todd M. Stevens, Yolanda E. Hartman, William R. Carroll, Kurt R. Zinn, and Jason M. Warram
- 4753** **Clinical Features and Outcomes of Patients with Colorectal Cancers Harboring NRAS Mutations**
Andrea Cercek, Maria Inez Braghiroli, Joanne F. Chou, Jaclyn F. Hechtman, Nancy Kemeny, Leonard Saltz, Marinela Capanu, and Rona Yaeger
- 4761** **A Gene Signature for Selecting Benefit from Hypoxia Modification of Radiotherapy for High-Risk Bladder Cancer Patients**
Lingjian Yang, Janet Taylor, Amanda Eustace, Joely J. Irlam, Helen Denley, Peter J. Hoskin, Jan Alsner, Francesca M. Buffa, Adrian L. Harris, Ananya Choudhury, and Catharine M.L. West

CANCER THERAPY: PRECLINICAL



- 4769** **A Zebrafish Model Discovers a Novel Mechanism of Stromal Fibroblast-Mediated Cancer Metastasis**
Caifeng Liu, Yunjian Zhang, Sharon Lim, Kayoko Hosaka, Yunlong Yang, Tatiana Pavlova, Twana Alkasalias, Johan Hartman, Lasse Jensen, Xiaoming Xing, Xincheng Wang, Yongtian Lu, Guohui Nie, and Yihai Cao
- 4780** **Histone Deacetylase Inhibitor Enhances the Efficacy of MEK Inhibitor through NOXA-Mediated MCL1 Degradation in Triple-Negative and Inflammatory Breast Cancer**
Angie M. Torres-Adorno, Jangsoon Lee, Takahiro Kogawa, Peter Ordentlich, Debu Tripathy, Bora Lim, and Naoto T. Ueno
- 4793** **Elacestrant (RAD1901), a Selective Estrogen Receptor Degradar (SERD), Has Antitumor Activity in Multiple ER⁺ Breast Cancer Patient-derived Xenograft Models**
Teeru Bihani, Hitisha K. Patel, Heike Arlt, Nianjun Tao, Hai Jiang, Jeffrey L. Brown, Dinesh M. Purandare, Gary Hattersley, and Fiona Garner
- 4805** **Mitochondrial BAX Determines the Predisposition to Apoptosis in Human AML**
Frank Reichenbach, Cornelius Wiedenmann, Enrico Schalk, Diana Becker, Kathrin Funk, Peter Scholz-Kreisel, Franziska Todt, Denise Wolleschak, Konstanze Döhner, Jens U. Marquardt, Florian Heidel, and Frank Edlich
- 4817** **Dual Inhibition of EZH2 and EZH1 Sensitizes PRC2-Dependent Tumors to Proteasome Inhibition**
Ola Rizq, Naoya Mimura, Motohiko Oshima, Atsunori Saraya, Shuhei Koide, Yuko Kato, Kazumasa Aoyama, Yaeko Nakajima-Takagi, Changshan Wang, Tetsuhiro Chiba, Anqi Ma, Jian Jin, Tohru Iseki, Chiaki Nakaseko, and Atsushi Iwama

BIOLOGY OF HUMAN TUMORS

- 4831** **Epigenetic Regulation of KPC1 Ubiquitin Ligase Affects the NF- κ B Pathway in Melanoma**
Yuuki Iida, Aaron Ciechanover, Diego M. Marzese, Keisuke Hata, Matias Bustos, Shigeshi Ono, Jinhua Wang, Matthew P. Salomon, Kevin Tran, Stella Lam, Sandy Hsu, Nellie Nelson, Yelena Kravtsova-Ivantsiv, Gordon B. Mills, Michael A. Davies, and Dave S.B. Hoon



Table of Contents

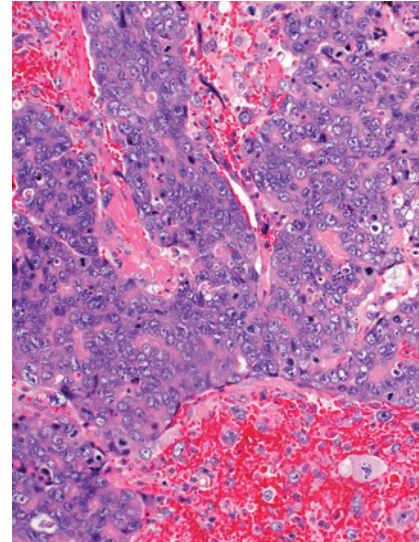
- 4843** **Suppression of Lymphocyte Functions by Plasma Exosomes Correlates with Disease Activity in Patients with Head and Neck Cancer**
Sonja Ludwig, Theofanis Floros,
Marie-Nicole Theodoraki, Chang-Sook Hong,
Edwin K. Jackson, Stephan Lang, and Theresa L. Whiteside
- 4855** **Genomic Analysis of Thymic Epithelial Tumors Identifies Novel Subtypes Associated with Distinct Clinical Features**
 Hyun-Sung Lee, Hee-Jin Jang, Rohan Shah, David Yoon,
Masatsugu Hamaji, Ori Wald, Ju-Seog Lee,
David J. Sugarbaker, and Bryan M. Burt
- 4865** **Global Protease Activity Profiling Provides Differential Diagnosis of Pancreatic Cysts**
Sam L. Ivry, Jeremy M. Sharib, Dana A. Dominguez,
Nilotpal Roy, Stacy E. Hatcher, Michele T. Yip-Schneider,
C. Max Schmidt, Randall E. Brand, Walter G. Park,
Matthias Hebrok, Grace E. Kim, Anthony J. O'Donoghue,
Kimberly S. Kirkwood, and Charles S. Craik
- 4875** **Whole-Exome Sequencing of Metaplastic Breast Carcinoma Indicates Monoclonality with Associated Ductal Carcinoma Component**
Bracha Erlanger Avigdor, Katie Beierl,
Christopher D. Gocke, Daniel J. Zabransky,
Karen Cravero, Kelly Kyker-Snowman, Berry Button,
David Chu, Sarah Croessmann, Rory L. Cochran,
Roisin M. Connolly, Ben H. Park, Sarah J. Wheelan, and
Ashley Cimino-Mathews
- 4885** **RET Signaling in Prostate Cancer**
Kechen Ban, Shu Feng, Longjiang Shao, and
Michael Ittmann
- 4897** **Characterization of the T-Cell Receptor Repertoire and Immune Microenvironment in Patients with Locoregionally Advanced Squamous Cell Carcinoma of the Head and Neck**
 Vassiliki Saloura, Aiman Fatima, Makda Zewde,
Kazuma Kiyotani, Ryan Brisson, Jae-Hyun Park,
Yuji Ikeda, Theodore Vougiouklakis, Riyue Bao,
Arun Khattri, Tanguy Seiwert, Nicole Cipriani,
Mark Linggen, Everett Vokes, and Yusuke Nakamura
- 4908** **Overexpressed Fatty Acid Synthase in Gastrointestinal Stromal Tumors: Targeting a Progression-Associated Metabolic Driver Enhances the Antitumor Effect of Imatinib**
Chien-Feng Li, Fu-Min Fang, Yen-Yang Chen,
Ting-Ting Liu, Ti-Chun Chan, Shih-Chen Yu,
Li-Tzong Chen, and Hsuan-Ying Huang
- 4919** **Enrichment of PI3K-AKT-mTOR Pathway Activation in Hepatic Metastases from Breast Cancer**
Mariaelena Pierobon, Corinne Ramos, Shukmei Wong,
K. Alex Hodge, Jessica Aldrich, Sara Byron,
Stephen P. Anthony, Nicholas J. Robert,
Donald W. Northfelt, Mohammad Jahanzeb,
Linda Vocila, Julia Wulfkuhle, Guido Gambarà,
Rosa I. Gallagher, Bryant Dunetz, Nicholas Hoke,
Ting Dong, David W. Craig, Massimo Cristofanilli,
Brian Leyland-Jones, Lance A. Liotta,
Joyce A. O'Shaughnessy, John D. Carpten, and
Emanuel F. Petricoin
- 4929** **Acquired MET Y1248H and D1246N Mutations Mediate Resistance to MET Inhibitors in Non-Small Cell Lung Cancer**
Anna Li, Jin-ji Yang, Xu-chao Zhang, Zhou Zhang, Jian Su,
Lan-ying Gou, Yu Bai, Qing Zhou, Zhenfan Yang,
Han Han-Zhang, Wen-Zhao Zhong, Shannon Chuai,
Qi Zhang, Zhi Xie, Hongfei Gao, Huajun Chen,
Zhen Wang, Zheng Wang, Xue-ning Yang, Bin-chao Wang,
Bin Gan, Zhi-hong Chen, Ben-yuan Jiang, Si-pei Wu,
Si-yang Liu, Chong-rui Xu, and Yi-long Wu
- 4938** **PD-L1 Expression in Melanoma: A Quantitative Immunohistochemical Antibody Comparison**
Joel C. Sunshine, Peter L. Nguyen, Genevieve J. Kaunitz,
Tricia R. Cottrell, Sneha Berry, Jessica Esandrio,
Haiying Xu, Aleksandra Ogurtsova, Karen B. Bleich,
Toby C. Cornish, Evan J. Lipson, Robert A. Anders, and
Janis M. Taube

 **AC icon indicates AuthorChoice**
For more information please visit www.aacrjournals.org

Table of Contents

ABOUT THE COVER

The cover shows a section of a mastectomy from a patient with a primary metaplastic breast carcinoma. This hematoxylin and eosin-stained section shows a component of the tumor with high-grade ductal differentiation. For details, see the article by Avigdor and colleagues on page 4875 of this issue.



Clinical Cancer Research

23 (16)

Clin Cancer Res 2017;23:4525-4944.

Updated version Access the most recent version of this article at:
<http://clincancerres.aacrjournals.org/content/23/16>

E-mail alerts [Sign up to receive free email-alerts](#) related to this article or journal.

Reprints and Subscriptions To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions To request permission to re-use all or part of this article, use this link <http://clincancerres.aacrjournals.org/content/23/16>.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.