

Highlights of This Issue 4945**SPECIAL FEATURES****CCR Focus**

- 4948 Refining Immunotherapy Approvals**
Susan E. Bates
- 4950 Challenges and Opportunities in Adapting Clinical Trial Design for Immunotherapies**
Lillian L. Siu, S. Percy Ivy, Erica L. Dixon, Amy E. Gravell, Steven A. Reeves, and Gary L. Rosner
- 4959 Immuno-oncology Trial Endpoints: Capturing Clinically Meaningful Activity**
Valsamo Anagnostou, Mark Yarchoan, Aaron R. Hansen, Hao Wang, Franco Verde, Elad Sharon, Deborah Collyar, Laura Q.M. Chow, and Patrick M. Forde
- 4970 The Challenge for Development of Valuable Immuno-oncology Biomarkers**
Janice M. Mehnert, Arta M. Monjazeb, Johanna M.T. Beerthuijzen, Deborah Collyar, Larry Rubinstein, and Lyndsay N. Harris
- 4980 From Famine to Feast: Developing Early-Phase Combination Immunotherapy Trials Wisely**
Daphne Day, Arta M. Monjazeb, Elad Sharon, S. Percy Ivy, Eric H. Rubin, Gary L. Rosner, and Marcus O. Butler
- 4992 Immuno-oncology Clinical Trial Design: Limitations, Challenges, and Opportunities**
Christina S. Baik, Eric H. Rubin, Patrick M. Forde, Janice M. Mehnert, Deborah Collyar, Marcus O. Butler, Erica L. Dixon, and Laura Q.M. Chow

CANCER THERAPY: CLINICAL




- 5003 Genome-wide DNA Methylation Analysis Reveals GABBR2 as a Novel Epigenetic Target for EGFR 19 Deletion Lung Adenocarcinoma with Induction Erlotinib Treatment**
Xiaomin Niu, Fatao Liu, Yi Zhou, Zhen Zhou, Daizhan Zhou, Ting Wang, Ziming Li, Xiangyun Ye, Yongfeng Yu, Xiaoling Weng, Hong Zhang, Junyi Ye, Meilin Liao, Yun Liu, Zhiwei Chen, and Shun Lu

- 5015 A First-in-Human, Phase I, Dose-Escalation Study of TAK-117, a Selective PI3K α Isoform Inhibitor, in Patients with Advanced Solid Malignancies**
Dejan Juric, Johann S. de Bono, Patricia M. LoRusso, John Nemunaitis, Elisabeth I. Heath, Eunice L. Kwak, Teresa Macarulla Mercadé, Elena Geuna, Maria Jose de Miguel-Luken, Chirag Patel, Keisuke Kuida, Serap Sankoh, Eric H. Westin, Fabian Zohren, Yaping Shou, and Josep Tabernero
- 5024 Dynamic Changes in PD-L1 Expression and Immune Infiltrates Early During Treatment Predict Response to PD-1 Blockade in Melanoma**
Ricardo E. Vilain, Alexander M. Menzies, James S. Wilmott, Hojabr Kakavand, Jason Madore, Alexander Guminski, Elizabeth Liniker, Benjamin Y. Kong, Adam J. Cooper, Julie R. Howle, Robyn P.M. Saw, Valerie Jakrot, Serigne Lo, John F. Thompson, Matteo S. Carlino, Richard F. Kefford, Georgina V. Long, and Richard A. Scolyer
- 5034 Immune Correlates of GM-CSF and Melanoma Peptide Vaccination in a Randomized Trial for the Adjuvant Therapy of Resected High-Risk Melanoma (E4697)**
Lisa H. Butterfield, Fengmin Zhao, Sandra Lee, Ahmad A. Tarhini, Kim A. Margolin, Richard L. White, Michael B. Atkins, Gary I. Cohen, Theresa L. Whiteside, John M. Kirkwood, and David H. Lawson
- 5044 Dual Inhibition of HDAC and Tyrosine Kinase Signaling Pathways with CUDC-907 Inhibits Thyroid Cancer Growth and Metastases**
Shweta Kotian, Lisa Zhang, Myriem Boufraqueh, Kelli Gaskins, Sudheer Kumar Gara, Martha Quezada, Naris Nilubol, and Electron Kebebew
- 5055 A Pilot Study of Stereotactic Body Radiation Therapy Combined with Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma**
Anurag K. Singh, Timothy B. Winslow, Mohammad Habiby Kermany, Vincent Goritz, Lilia Heit, Austin Miller, Nicholas C. Hoffend, Leighton C. Stein, Lalith K. Kumaraswamy, Graham W. Warren, Wiam Bshara, Kunle Odunsi, Junko Matsuzaki, Scott I. Abrams, Thomas Schwaab, and Jason B. Muhitch

Table of Contents

- 5066** Dendritic Cell/Cytokine-Induced Killer Cell Immunotherapy Combined with S-1 in Patients with Advanced Pancreatic Cancer: A Prospective Study
Ni Jiang, Guoliang Qiao, Xiaoli Wang, Michael A. Morse, William R. Gwin, Lei Zhou, Yuguang Song, Yanjie Zhao, Feng Chen, Xinna Zhou, Lefu Huang, Amy Hobeika, Xin Yi, Xuefeng Xia, Yanfang Guan, Jin Song, Jun Ren, and H. Kim Lyerly

PERSONALIZED MEDICINE AND IMAGING

- 5074** Tumor Cell-Free DNA Copy Number Instability Predicts Therapeutic Response to Immunotherapy
 Glen J. Weiss, Julia Beck, Donald P. Braun, Kristen Bornemann-Kolatzki, Heather Barilla, Rhiannon Cubello, Walter Quan Jr, Ashish Sangal, Vivek Khemka, Jordan Waypa, William M. Mitchell, Howard Urnovitz, and Ekkehard Schütz
- 5082** Clinical Utility of Risk Models to Refer Patients with Adnexal Masses to Specialized Oncology Care: Multicenter External Validation Using Decision Curve Analysis
Laure Wynants, Dirk Timmerman, Jan Y. Verbakel, Antonia Testa, Luca Savelli, Daniela Fischerova, Dorella Franchi, Caroline Van Holsbeke, Elisabeth Epstein, Wouter Froyman, Stefano Guerriero, Alberto Rossi, Robert Fruscio, Francesco PG Leone, Tom Bourne, Lil Valentin, and Ben Van Calster
- 5091** Detecting the Presence and Progression of Premalignant Lung Lesions via Airway Gene Expression
Jennifer Beane, Sarah A. Mazzilli, Anna M. Tassinari, Gang Liu, Xiaohui Zhang, Hanqiao Liu, Anne Dy Buncio, Samjot S. Dhillon, Suso J. Platero, Marc E. Lenburg, Mary E. Reid, Stephen Lam, and Avrum E. Spira
- 5101** Utility of Genomic Assessment of Blood-Derived Circulating Tumor DNA (ctDNA) in Patients with Advanced Lung Adenocarcinoma
 Maria C. Schwaederlé, Sandip P. Patel, Hatim Husain, Megumi Ikeda, Richard B. Lanman, Kimberly C. Banks, AmirAli Talasaz, Lyudmila Bazhenova, and Razelle Kurzrock
- 5112** The Novel Association of Circulating Tumor Cells and Circulating Megakaryocytes with Prostate Cancer Prognosis
 Lei Xu, Xueying Mao, Tianyu Guo, Pui Ying Chan, Greg Shaw, John Hines, Elzbieta Stankiewicz, Yuqin Wang, R. Tim D. Oliver, Amar Sabri Ahmad, Daniel Berney, Jonathan Shamash, and Yong-Jie Lu

CANCER THERAPY: PRECLINICAL

- 5123** HER2 Reactivation through Acquisition of the HER2 L755S Mutation as a Mechanism of Acquired Resistance to HER2-targeted Therapy in HER2⁺ Breast Cancer
Xiaowei Xu, Carmine De Angelis, Kathleen A. Burke, Agostina Nardone, Huizhong Hu, Lanfang Qin, Jamunarani Veeraraghavan, Vidyalakshmi Sethunath, Laura M. Heiser, Nicholas Wang, Charlotte K.Y. Ng, Edward S. Chen, Alexander Renwick, Tao Wang, Sarmistha Nanda, Martin Shea, Tamika Mitchell, Mahitha Rajendran, Ian Waters, Daniel J. Zabransky, Kenneth L. Scott, Carolina Gutierrez, Chandandeep Nagi, Felipe C. Geyer, Gary C. Chamness, Ben H. Park, Chad A. Shaw, Susan G. Hilsenbeck, Mothaffar F. Rimawi, Joe W. Gray, Britta Weigelt, Jorge S. Reis-Filho, C. Kent Osborne, and Rachel Schiff
- 5135** *In Vivo* Hemin Conditioning Targets the Vascular and Immunologic Compartments and Restrains Prostate Tumor Development
Felipe M. Jaworski, Lucas D. Gentilini, Geraldine Gueron, Roberto P. Meiss, Emiliano G. Ortiz, Paula M. Berguer, Asif Ahmed, Nora Navone, Gabriel A. Rabinovich, Daniel Compagno, Diego J. Laderach, and Elba S. Vazquez
- 5149** Trabectedin Overrides Osteosarcoma Differentiative Block and Reprograms the Tumor Immune Environment Enabling Effective Combination with Immune Checkpoint Inhibitors
Chiara Ratti, Laura Botti, Valeria Cancila, Silvia Galvan, Ilaria Torselli, Cecilia Garofalo, Maria Cristina Manara, Lucia Bongiovanni, Cesare F. Valenti, Alessia Burocchi, Mariella Parenza, Barbara Cappetti, Sabina Sangaletti, Claudio Tripodo, Katia Scotlandi, Mario P. Colombo, and Claudia Chiodoni
- 5162** SMAD4 Loss Is Associated with Cetuximab Resistance and Induction of MAPK/JNK Activation in Head and Neck Cancer Cells
Hiroyuki Ozawa, Ruchira S. Ranaweera, Evgeny Izumchenko, Eugene Makarev, Alex Zhavoronkov, Elana J. Fertig, Jason D. Howard, Ana Markovic, Atul Bedi, Rajani Ravi, Jimena Perez, Quynh-Thu Le, Christina S. Kong, Richard C. Jordan, Hao Wang, Hyunseok Kang, Harry Quon, David Sidransky, and Christine H. Chung
- 5176** Expression and Therapeutic Potential of SOX9 in Chordoma
Hua Chen, Cassandra C. Garbutt, Dimitrios Spentzos, Edwin Choy, Francis J. Hornicek, and Zhenfeng Duan

Table of Contents

5187 Entinostat Neutralizes Myeloid-Derived Suppressor Cells and Enhances the Antitumor Effect of PD-1 Inhibition in Murine Models of Lung and Renal Cell Carcinoma

Ashley Orillion, Ayumi Hashimoto, Nur Damayanti, Li Shen, Remi Adelaiye-Ogala, Sreevani Arisa, Sreenivasulu Chintala, Peter Ordentlich, Chingai Kao, Bennett Elzey, Dmitry Gabrilovich, and Roberto Pili

5246 Can Microsatellite Status of Colorectal Cancer Be Reliably Assessed after Neoadjuvant Therapy?

Jennifer B. Goldstein, William Wu, Ester Borras, Gita Masand, Amanda Cuddy, Maureen E. Mork, Sarah A. Bannon, Patrick M. Lynch, Miguel Rodriguez-Bigas, Melissa W. Taggart, Ji Wu, Paul Scheet, Scott Kopetz, Y. Nancy You, and Eduardo Vilar

BIOLOGY OF HUMAN TUMORS

5202 B7-H3 Expression in NSCLC and Its Association with B7-H4, PD-L1 and Tumor-Infiltrating Lymphocytes

Mehmet Altan, Vasiliki Pelekanou, Kurt A. Schalper, Maria Toki, Patricia Gaule, Konstantinos Syrigos, Roy S. Herbst, and David L. Rimm

5210 Relationship of the Breast Ductal Carcinoma *In Situ* Immune Microenvironment with Clinicopathological and Genetic Features



Shona Hendry, Jia-Min B. Pang, David J. Byrne, Sunil R. Lakhani, Margaret C. Cummings, Ian G. Campbell, G. Bruce Mann, Kylie L. Gorringe, and Stephen B. Fox

5218 MONARCH 1, A Phase II Study of Abemaciclib, a CDK4 and CDK6 Inhibitor, as a Single Agent, in Patients with Refractory HR⁺/HER2⁻ Metastatic Breast Cancer

Maura N. Dickler, Sara M. Tolaney, Hope S. Rugo, Javier Cortés, Véronique Diéras, Debra Patt, Hans Wildiers, Clifford A. Hudis, Joyce O'Shaughnessy, Esther Zamora, Denise A. Yardley, Martin Frenzel, Andrew Koustenis, and José Baselga

5225 Ribonucleotide Reductase Catalytic Subunit M1 (RRM1) as a Novel Therapeutic Target in Multiple Myeloma

Morihiko Sagawa, Hiroto Ohguchi, Takeshi Harada, Mehmet K. Samur, Yu-Tzu Tai, Nikhil C. Munshi, Masahiro Kizaki, Teru Hideshima, and Kenneth C. Anderson

5238 Gene Expression Profiling in BRAF-Mutated Melanoma Reveals Patient Subgroups with Poor Outcomes to Vemurafenib That May Be Overcome by Cobimetinib Plus Vemurafenib

Matthew J. Wongchenko, Grant A. McArthur, Brigitte Dréno, James Larkin, Paolo A. Ascierto, Jeffrey Sosman, Luc Andries, Mark Kocck, Stephen D. Hurst, Ivor Caro, Isabelle Rooney, Priti S. Hegde, Luciana Molinero, Huibin Yue, Ilsung Chang, Lukas Amler, Yibing Yan, and Antoni Ribas

5255 miR-196b-5p Regulates Colorectal Cancer Cell Migration and Metastases through Interaction with HOXB7 and GALNT5

Verena Stiegelbauer, Petra Vychytilova-Faltejskova, Michael Karbiener, Anna-Maria Pehserl, Andreas Reicher, Margit Resel, Ellen Heitzer, Cristina Ivan, Marc Bullock, Hui Ling, Alexander Deutsch, Annika Wulf-Goldenberg, Jan Basri Adiprasito, Herbert Stoeger, Johannes Haybaeck, Marek Svoboda, Michael Stotz, Gerald Hoefler, Ondrej Slaby, George Adrian Calin, Armin Gerger, and Martin Pichler

5267 Targeting the Wnt Pathway and Cancer Stem Cells with Anti-progastrin Humanized Antibodies as a Potential Treatment for



K-RAS-Mutated Colorectal Cancer

Alexandre Prieur, Monica Cappellini, Guillaume Habif, Marie-Paule Lefranc, Thibault Mazard, Eric Morency, Jean-Marc Pascussi, Maud Flacelière, Nathalie Cahuzac, Bérengère Vire, Benjamin Dubuc, Amandine Durochat, Pierre Liaud, Jérémy Ollier, Caroline Pfeiffer, Sophie Poupeau, Véronique Saywell, Chris Planque, Eric Assenat, Frédéric Bibeau, Jean-François Bourgaux, Pascal Pujol, Alain Sézeur, Marc Ychou, and Dominique Joubert

5281 miR-193a-3p is a Key Tumor Suppressor in Ulcerative Colitis-Associated Colon Cancer and Promotes Carcinogenesis through Upregulation of IL17RD

Joel Pekow, Katherine Meckel, Urszula Dougherty, Yong Huang, Xindi Chen, Anas Almoghrabi, Reba Mustafi, Fatma Ayaloglu-Butun, Zifeng Deng, Haider I. Haider, John Hart, David T. Rubin, John H. Kwon, and Marc Bissonnette

5292 Chronic Lymphocytic Leukemia with Mutated IGHV4-34 Receptors: Shared and Distinct Immunogenetic Features and Clinical Outcomes

Aliki Xochelli, Panagiotis Baliakas, Ioannis Kavakiotis, Andreas Agathangelidis, Lesley-Ann Sutton, Eva Minga, Stavroula Ntoufa, Eugen Tausch, Xiao-Jie Yan, Tait Shanafelt, Karla Plevova, Myriam Boudjogra, Davide Rossi, Zadié Davis, Alba Navarro, Yorick Sandberg, Fie Juhl Vojdeman, Lydia Scarfo, Niki Stavroyianni, Andrey Sudarikov, Silvio Veronese, Tatiana Tzenou, Teodora Karan-Djurasevic,

Table of Contents

Mark Catherwood, Dirk Kienle, Maria Chatzouli, Monica Facco, Jasmin Bahlo, Christiane Pott, Lone Bredo Pedersen, Larry Mansouri, Karin E. Smedby, Charles C. Chu, Véronique Giudicelli, Marie-Paule Lefranc, Panagiotis Panagiotidis, Gunnar Juliusson, Achilles Anagnostopoulos, Ioannis Vlahavas, Darko Antic, Livio Trentin, Marco Montillo, Carsten Niemann, Hartmut Döhner, Anton W. Langerak, Sarka Pospisilova, Michael Hallek, Elias Campo, Nicholas Chiorazzi, Nikos Maglaveras, David Oscier, Gianluca Gaidano, Diane F. Jelinek, Stephan Stilgenbauer, Ioanna Chouvarda, Nikos Darzentas, Chrysoula Belessi, Frederic Davi, Anastasia Hadzidimitriou, Richard Rosenquist, Paolo Ghia, and Kostas Stamatopoulos

5302 Unique and Novel Urinary Metabolomic Features in Malignant versus Benign Adrenal Neoplasms

Dhaval Patel, Matthew D. Thompson, Soumen K. Manna, Kristopher W. Krausz, Lisa Zhang, Naris Nilubol, Frank J. Gonzalez, and Electron Kebebew

5311 Evaluation of Tumor-Derived Exosomal miRNA as Potential Diagnostic Biomarkers for Early-Stage Non-Small Cell Lung Cancer Using Next-Generation Sequencing

Xiance Jin, Yanfan Chen, Hanbin Chen, Shaoran Fei, Didi Chen, Xiaona Cai, Linger Liu, Baochai Lin, Huafang Su, Lihao Zhao, Meng Su, Huanle Pan, Lanxiao Shen, Deyao Xie, and Congying Xie

LETTER TO THE EDITOR

5320 mTOR Pathway Mutations and Response to Rapalogs in RCC—Letter

Juan M. Roldan-Romero, Juan F. Rodríguez-Moreno, Jesus García-Donás, and Cristina Rodríguez-Antona

RETRACTION

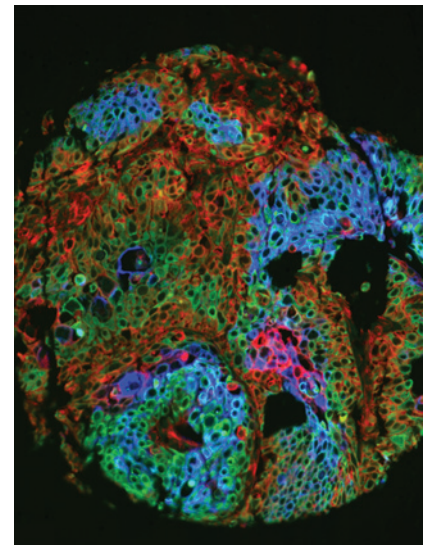
5321 Retraction: Polymorphisms of the *CYP1B1* Gene as Risk Factors for Human Renal Cell Cancer

 AC icon indicates AuthorChoice

For more information please visit www.aacrjournals.org

ABOUT THE COVER

The cover shows a section of non-small cell lung cancer histospot. Immunohistochemistry stain shows simultaneous detection of B7-H3 (red channel), B7-H4 (blue channel), and cytokeratin (green channel). Visually, in this histospot, B7-H3 and B7-H4 proteins do not show colocalization. For details, see the article by Altan and colleagues on page 5202 of this issue



Clinical Cancer Research

23 (17)

Clin Cancer Res 2017;23:4945-5322.

Updated version Access the most recent version of this article at:
<http://clincancerres.aacrjournals.org/content/23/17>

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/23/17>.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.