Highlights of This Issue 4171

SPECIAL FEATURES

CCR Translations

4173 CHK It Out! Blocking WEE Kinase Routs TP53 Mutant Cancer
Julie E. Bauman and Christine H. Chung
See related article, p. 4274

Statistics in Clinical Cancer Research

4176 Historical Controls for Metastatic Pancreatic Cancer: Benchmarks for Planning and Analyzing Single-Arm Phase II Trials
Philip A. Philip, Kari Chansky, Michael LeBlanc, Lawrence Rubinstein, Lesley Seymour, S. Percy Ivy, Steven R. Alberts, Paul J. Catalano, and John Crowley

Molecular Pathways

4186 Molecular Pathways: Targeting NRAS in Melanoma and Acute Myelogenous Leukemia
Douglas B. Johnson, Keiran S.M. Smalley, and Jeffrey A. Sosman

4193 Molecular Pathways: The Basis for Rational Combination Using MEK Inhibitors in KRAS-Mutant Cancers
Shunsuke Okumura and Pasi A. Jänne

Perspectives

4200 Toward a Drug Development Path That Targets Metastatic Progression in Osteosarcoma

Review

4210 Design of Phase I Combination Trials: Recommendations of the Clinical Trial Design Task Force of the NCI Investigational Drug Steering Committee
Channing J. Paller, Penelope A. Bradbury, S. Percy Ivy, Lesley Seymour, Patricia M. LoRusso, Laurence Baker, Larry Rubinstein, Erich Huang, Deborah Collyar, Susan Grosven, Steven Reeves, Lee M. Ellis, Daniel J. Sargent, Gary L. Rosner, Michael L. LeBlanc, and Mark J. Ratain

CANCER THERAPY: CLINICAL

4218 Phase II Study of Single-Agent Orteronel (TAK-700) in Patients with Nonmetastatic Castration-Resistant Prostate Cancer and Rising Prostate-Specific Antigen
Maha Hussain, Paul G. Corn, M. Dror Michaelson, Hans J. Hammers, Joshj J. Alumkal, Charles J. Ryan, Justine Y. Bruce, Susan Moran, Shih-Yuan Lee, H. Mark Lin, and Daniel J. George for the Prostate Cancer Clinical Trials Consortium, a program of the Department of Defense Prostate Cancer Research Program and the Prostate Cancer Foundation

4228 Treatment with Chemotherapy and Dendritic Cells Pulsed with Multiple Wilms’ Tumor 1 (WT1)–Specific MHC Class I/II–Restricted Epitopes for Pancreatic Cancer
Shigeo Koido, Sadamu Homma, Masato Okamoto, Kazuki Takakura, Masako Mori, Shinji Yoshizaki, Shintaro Tsukinaga, Shunichi Odahara, Seita Koyama, Hiroo Imazu, Kan Uchiyama, Mikio Kajihara, Hiroshi Arakawa, Takeyuki Misawa, Yoichi Toyama, Satoru Yanagisawa, Masahiro Ikegami, Shin Kan, Kazumi Hayashi, Hideo Komita, Yuko Kamata, Masaki Itô, Takefumi Ishidao, Sei-ichi Yusa, Shigetaka Shimodaira, Jianlin Gong, Haruo Sugiyama, Toshifumi Okhuse, and Hisao Tajiri

4240 Randomized Phase Ib/II Trial of Rilotumumab or Ganitumab with Panitumumab versus Panitumumab Alone in Patients with Wild-type KRAS Metastatic Colorectal Cancer
Phase I Expansion and Pharmacodynamic Study of the Oral MEK Inhibitor RO4987655 (CH4987655) in Selected Patients with Advanced Cancer with RAS–RAF Mutations

Acquired Resistance to Endocrine Treatments Is Associated with Tumor-Specific Molecular Changes in Patient-Derived Luminal Breast Cancer Xenografts
Paul Cotto, Ivan Bieber, Franck Assayag, Rania El Botty, Sophie Chatseau-Joubert, Aurélie Thuleau, Thomas Bagarre, Benoit Albaud, Audrey Rapinat, David Gentien, Pierre de la Grange, Vonick Sibut, Sophie Vacher, Rana Hatem, Jean-Luc Servely, Jean-Jacques Fontaine, Didier Decaudin, Jean-Yves Pierga, Sergio Roman-Roman, and Elisabetta Marangoni

Multifactorial T-cell Hypofunction That Is Reversible Can Limit the Efficacy of Chimeric Antigen Receptor–Transduced Human T cells in Solid Tumors

Sonic Hedgehog Paracrine Signaling Activates Stromal Cells to Promote Perineural Invasion in Pancreatic Cancer
Xuqi Li, Zheng Wang, Qingyong Ma, QinHong Xu, Han Liu, Wanxing Duan, Jianjun Lei, Jiguang Ma, Xiu Wang, Shifang Lv, Liang Han, Wei Li, Jian Guo, Kun Guo, Dong Zhang, Exri Wu, and Keping Xie

Functional Kinomics Identifies Candidate Therapeutic Targets in Head and Neck Cancer
Russell Moser, Chang Xu, Michael Kao, James Annis, Luisa Angelica Lerma, Christopher M. Schaupp, Kay E. Gurley, In Sock Jang, Asel Biktasova, Wendell G. Yarbrough, Adam A. Margolin, Carla Grandori, Christopher J. Kemp, and Eduardo Méndez

See related commentary, p. 4173

Intraperitoneal Oxidative Stress in Rabbits with Papillomavirus-Associated Head and Neck Cancer Induces Tumoricidal Immune Response That Is Adoptively Transferable
Annette Rossmann, Robert Mandic, Jochen Heinis, Helmut Hoffken, Oliver Kissner, Ralf Künscher, Eberhard Weihe, and Michael Bette

Kidney Cancer Is Characterized by Aberrant Methylation of Tissue-Specific Enhancers That Are Prognostic for Overall Survival
Caroline Y. Hu, Davoud Mohtat, Yiting Yu, Yi-An Ko, Niraj Shenoy, Sanchari Bhattacharya, Maria C. Izquierdo, Ae Seo Deok Park, Orsolya Gircz, Nishanth Vallumsela, Krishna Gundabolu, Kristin Ware, Tushar D. Bhaqat, Masako Suzuki, James Pullman, X. Shirley Liu, John M. Greally, Katalin Susztak, and Amit Verma

Targeting Cancer Cells via the Reactive Oxygen Species-Mediated Unfolded Protein Response with a Novel Synthetic Polyphenol Conjugate
Soon Young Shin, Jong Min Lee, Mi So Lee, Dongsoo Koh, Hyeryoung Jung, Yoongho Lim, and Young Han Lee

Molecular Testing for Lymph Node Metastases as a Determinant of Colon Cancer Recurrence: Results from a Retrospective Multicenter Study
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>4370</td>
<td>A Novel KLF4/LDHA Signaling Pathway Regulates Aerobic Glycolysis in and Progression of Pancreatic Cancer</td>
<td>Min Shi, Jiujie Cui, Jiawei Du, Daoyan Wei, Zhiliang Jia, Jun Zhang, Zhenggang Zhu, Yong Gao, and Keping Xie</td>
</tr>
<tr>
<td>4390</td>
<td>Circulating CD4⁺ T Cells That Produce IL4 or IL17 When Stimulated by Melan-A but Not by NY-ESO-1 Have Negative Impacts on Survival of Patients with Stage IV Melanoma</td>
<td>Henning Zelba, Benjamin Weide, Alexander Martens, Evelyna Derhovanessian, Jithendra Kini Bailur, Christina Kyzirakos, Annette Pflugfelder, Thomas K. Eigentler, Anna Maria Di Giacomo, Michele Maio, Erik H.J.G. Aarntzen, Jolanda de Vries, Antje Sucker, Dirk Schadendorf, Petra Büttner, Claus Garbe, and Graham Pawelec</td>
</tr>
<tr>
<td>4400</td>
<td>PBX1 Is a Favorable Prognostic Biomarker as It Modulates 13-cis Retinoic Acid–Mediated Differentiation in Neuroblastoma</td>
<td>Nilay Shah, Jianjun Wang, Julia Selich-Anderson, Garrett Graham, Hasan Siddiqui, Xin Li, Javed Khan, and Jeffrey Toretsky</td>
</tr>
</tbody>
</table>

**CORRECTIONS**

- Correction: Interleukin-7 Mediates Selective Expansion of Tumor-Redirected Cytotoxic T Lymphocytes (CTLs) without Enhancement of Regulatory T-Cell Inhibition
- Correction: A Phase I Trial of LY2510924, a CXCR4 Peptide Antagonist, in Patients with Advanced Cancer
- Correction: Bim Polymorphisms: Influence on Function and Response to Treatment in Children with Acute Lymphoblastic Leukemia

**ABOUT THE COVER**

Integrative analysis of clear cell renal cell carcinoma shows predominant hypermethylation. A circos plot shows alterations in DNA methylation (hypermethylation in blue, outer ring), copy number variations (amplifications in red and deletions in green, middle ring), and expression (underexpressed in green, overexpressed in orange; innermost ring) in renal cell carcinoma when compared. For details, see the article by Hu and colleagues on page 4349 of this issue.