SPECIAL FEATURES

1695 Metformin: A Therapeutic Opportunity in Breast Cancer
Ana M. Gonzalez-Angulo, and Funda Meric-Bernstam

1701 Death Receptor Agonists as a Targeted Therapy for Cancer
Jeffrey Wiezorek, Pamela Holland, and Jonathan Graves

CCR Special Focus

1709 Phase I Clinical Trials: Overcoming Barriers
Susan E. Bates

1710 An Overview of the Optimal Planning, Design, and Conduct of Phase I Studies of New Therapeutics
Patricia M. LoRusso, Scott A. Boerner, and Lesley Seymour

1719 Information Needed to Conduct First-in-Human Oncology Trials in the United States: A View from a Former FDA Medical Reviewer
Adrian M. Senderowicz

1726 Approaches to Phase I Clinical Trial Design Focused on Safety, Efficiency, and Selected Patient Populations: A Report from the Clinical Trial Design Task Force of the National Cancer Institute Investigational Drug Steering Committee
S. Percy Ivy, Lillian L. Siu, Elizabeth Garrett-Mayer, and Larry Rubinstein

1737 Performing Phase I Clinical Trials of Anticancer Agents: Perspectives from within the European Union and Japan
Martin D. Forster, Nagahiro Saijo, Lesley Seymour, and Hilary Calvert

HUMAN CANCER BIOLOGY

1781 Overexpression of Smoothened Activates the Sonic Hedgehog Signaling Pathway in Pancreatic Cancer–Associated Fibroblasts
Kimberly Walter, Noriyuki Omura, Seung-Mo Hong, Margaret Griffith, Audrey Vincent, Michael Borges, and Michael Goggins
Phase II, Randomized Trial to Compare Anastrozole Combined with Gefitinib or Placebo in Postmenopausal Women with Hormone Receptor–Positive Metastatic Breast Cancer
Massimo Cristofanilli, Vicente Valero, Aroop Mangalik, Melanie Royce, Ian Rabinowitz, Francis P. Arena, Joan F. Kroener, Elizabeth Curcio, Claire Watkins, Sarah Bacin, Elsa M. Cora, Elizabeth Anderson, and Patrick J. Magill

A Phase I Pharmacologic Study of Necitumumab (IMC-11F8), a Fully Human IgG1 Monoclonal Antibody Directed Against EGFR in Patients with Advanced Solid Malignancies
Bart Kuenen, Petronella O. Witteveen, Rita Ruijter, Giuseppe Giaccone, Aruna Dontabhaktuni, Floyd Fox, Terry Katz, Hagop Youssoufian, Junming Zhu, Eric K. Rowinsky, and Emile E. Voest

Phase I Pharmacokinetic and Pharmacodynamic Study of the Oral MAPK/ERK Kinase Inhibitor PD-0325901 in Patients with Advanced Cancers
Patricia M. LoRusso, Smitha S. Krishnamurthi, John J. Rinehart, Lisle M. Nabell, Lisa Malburg, Paul B. Chapman, Samuel E. DePrimo, Steven Bentivegna, Keith D. Wilner, Weiwei Tan, and Alejandro D. Ricart

Randomized Phase II Multicenter Trial of Two Schedules of Lapatinib as First- or Second-Line Monotherapy in Patients with Advanced or Metastatic Non–Small Cell Lung Cancer

Mesalazine Reduces Mutations in Transforming Growth Factor β Receptor II and Activin Type II Receptor by Improvement of Replication Fidelity in Mononucleotide Repeats
Christoph Campregher, Clemens Honeder, Heekyung Chung, John M. Carethers, and Christoph Gasche

A High Proportion of DNA Variants of BRCA1 and BRCA2 Is Associated with Aberrant Splicing in Breast/Ovarian Cancer Patients
David J. Sanz, Alberto Acedo, Mar Infante, Mercedes Durán, Lucía Pérez-Cabornero, Eva Esteban-Cardenosa, Ónega Lastra, Franco Pagani, Cristina Miner, and Eladio A. Velasco

Correlation of Segmented Metabolic Tumor Volume with Outcome - Letter

Correlation of Segmented Metabolic Tumor Volume with Outcome - Response
Man Ki Chung, Chung-Hwan Baek, and Joon Young Choi
ABOUT THE COVER

Human pancreatic cancer–associated fibroblasts (CAFs) overexpress the Hedgehog receptor SMO. Here, immunohistochemical labeling highlights overexpression of Smo protein in a human primary pancreatic adenocarcinoma. Strong Smo expression is detected in stromal fibroblasts adjacent to pancreatic cancer cells. For details, see the article by Walter and colleagues on page 1781 of this issue.