Clinical Cancer Research **Highlights**

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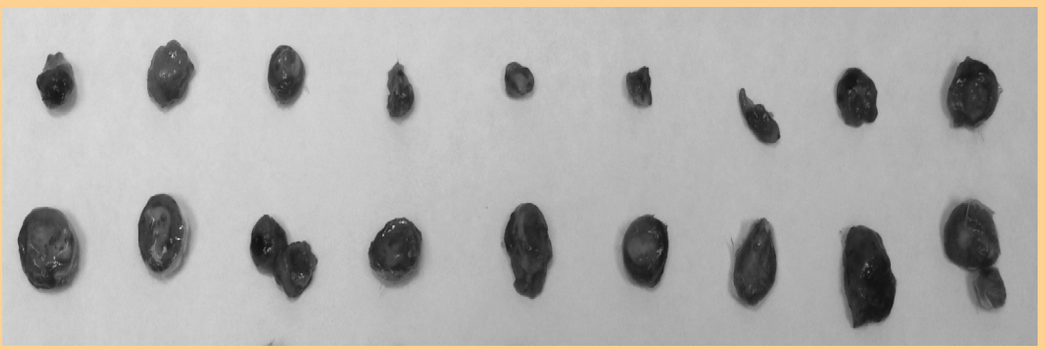
Selected Articles from This Issue



Dual Inhibition of SET and Activated Kinases in Leukemia

Agarwal *et al.* **Page 2092**

The SET oncoprotein, an inhibitor of the protein phosphatase 2A (PP2A) tumor suppressor, is overexpressed in leukemia. To evaluate the efficacy of SET antagonism in chronic myeloid leukemia (CML) and acute myeloid leukemia (AML), Agarwal and colleagues utilized OP449, a specific, cell-penetrating peptide that antagonizes SET's inhibition of PP2A. OP449 inhibited the growth of CML and AML cells harboring a broad range of oncogenic lesions, and this activity was further enhanced when used in combination with small-molecule inhibitors of activated kinases. This synergistic approach combining targeting of SET and phosphatase activation with relevant oncogenic kinase pathway inhibition may offer a novel therapeutic paradigm for treatment-refractory malignancies.

Tertiary Lymphoid Tissue in Colorectal Cancer

Di Caro *et al.* **Page 2147**

Di Caro and colleagues defined the cellular and structural organization of tertiary lymphoid tissue (TLT) rich in B and T cells and quantitatively evaluated its accumulation at the tumor invasive margin. In a retrospective cohort study involving 351 stage II-III colorectal cancer (CRC) patients, they provided phenomenologic evidence that the antitumor algorithm represented by TLT and TILs densities coordinates in predicting better prognosis. Thus, by collecting TILs and improving the antitumor immune response, TLT represents a novel prognostic biomarker for human CRC, which the authors recommend as a critical target in the design of tailored immune-based therapeutic approaches.

Prognostic Value of *GABRE∼miR-452∼miR-224* Methylation in Prostate Cancer

Kristensen *et al.* **Page 2169**

A new study by Kristensen and colleagues revealed frequent downregulation and aberrant promoter hypermethylation of the genomic *GABRE∼miR-452∼miR-224* locus in prostate cancer (PC). PC patients with high promoter methylation were at significantly higher risk of biochemical recurrence after radical prostatectomy than patients with low methylation, as demonstrated in two large independent PC patient cohorts. Results further suggested that a simple test for *GABRE∼miR-452∼miR-224* methylation may add significant independent prognostic value to routine clinicopathologic predictors of PC outcome. Finally, the study showed tumor-suppressive functions of miR-224 and miR-452 in PC cell lines, nominating the *GABRE∼miR-452∼miR-224* locus as a candidate therapeutic target.

First-In-Human Phase I Study of Lurbinectedin (PM01183)

Elez *et al.* **Page 2205**

Lurbinectedin (PM01183) is a novel anticancer agent. In this first-in-human study, using an accelerated titration design, its dose was escalated over 200 times to the recommended dose (RD) of 4.0 mg/m2 as 1-hour infusion every three weeks. The RD was expanded using an equivalent 7.0 mg flat dose. PK analysis showed linearity across dose ranges. Myelosuppression was correlated with AUC. At the RD, transient nonfebrile neutropenia was observed. Other toxicities (fatigue, nausea, vomiting) were mild. Observed efficacy comprised one confirmed partial response in advanced pancreatic cancer, and tumor shrinkage in synovial sarcomas (2) and melanoma. Lurbinectedin is continuing clinical development.

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