Clinical Cancer Research
Highlights
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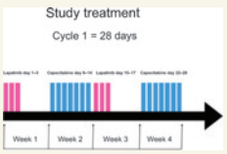
Selected Articles from This Issue

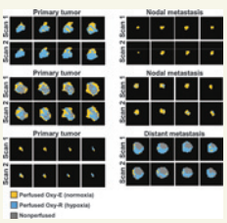
High-Dose Lapatinib with Capecitabine for CNS Metastasis



Treatment options are limited for breast cancer patients with central nervous system (CNS) metastasis. The combination of capecitabine and lapatinib, at conventional doses, has activity against HER2-positive breast cancer brain metastases; however, few patients respond, especially long-term. In this study, Morikawa and colleagues evaluated the safety and toxicities associated with intermittent high dose lapatinib alternating with intermittent fixed dose capecitabine in HER2-positive breast cancer patients with CNS metastasis. This regimen resulted in manageable toxicity and promising efficacy and will inform future phase II/III trials. ■

See article by Morikawa et al., p. 3784

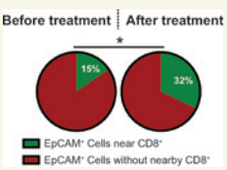
OE-MRI Detects Radiotherapy-Induced Hypoxia Modification



Hypoxia is a negative prognostic feature in nearly all cancer types and predicts treatment failure. Validated, widely available tests are lacking for clinical use. Salem and colleagues provide the first-in-human evidence that oxygen-enhanced MRI (OE-MRI) can track changes in hypoxia that are induced by radiotherapy. OE-MRI was well-tolerated in patients with non-small cell lung cancer, and radiotherapy-induced hypoxia modification was detected. OE-MRI has potential to select patients for hypoxia-modification, track therapeutic efficacy, and identify tumors that may fail immunotherapy. ■

See article by Salem et al., p. 3818

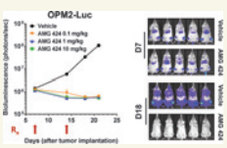
CXCR4 and PD-1 Blockade in Human Pancreatic Cancer



Immunotherapy has been ineffective for patients with pancreatic ductal adenocarcinoma (PDA). In this study, Seo and colleagues demonstrate that $CD8^+$ T cells are often present in PDA, but are localized to the stroma, rather than immediately adjacent to cancer cells. Using slice culture live microscopy from primary PDA tumors, the authors demonstrate that inhibition of the CXCR4 chemokine receptor led to the migration of clonally expanded $CD8^+$ T cells to the cancer cell-rich regions of the tumors. Subsequent PD-1 blockade activated effective cancer cell killing. These results provide a new basis for the rational selection of combination immunotherapy for PDA, a disease with limited treatment options. ■

See article by Seo et al., p. 3934

Anti-CD38/CD3 T-cell–Recruiting Antibody for Myeloma Therapy



Relapse remains a major issue for patients with multiple myeloma due to the presence of minimal residual disease (MRD) posttherapy. Bispecific T cell-engager antibody therapy has been effective in the elimination of MRD in other hematological malignancies. Zuch de Zafra and colleagues describe AMG 424, a novel bispecific T-cell–recruiting antibody targeted at CD3 and CD38, the multiple myeloma surface cell marker. AMG 424 effectively killed CD38-positive cells *in vitro* and showed antitumor activity in mouse and nonhuman primate models. AMG 424 is a promising candidate for multiple myeloma patients and is currently in clinical development. ■

See article by Zuch de Zafra et al., p. 3921