Clinical Cancer Research

Highlights

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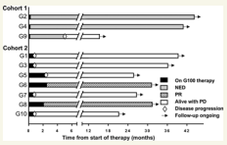
Selected Articles from This Issue

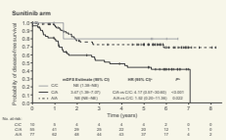
Intratumoral G100 for Merkel Cell Carcinoma



Cancers with an immunosuppressive tumor microenvironment (TME) are less likely to respond to immunotherapy. In this study, Bhatia and colleagues treated ten Merkel cell carcinoma patients with intratumoral G100, a TLR4 agonist. G100 treatment led to an immunologically active TME with increased infiltration and activation of $CD8^+$ and $CD4^+$ T cells. Two out of three patients with locoregional disease showed sustained responses greater than 41 months. Of seven patients with metastatic disease, two showed partial responses lasting at least 33 months. Treatment was well-tolerated with mild local inflammation and no systemic toxicity. Intratumoral G100 warrants additional investigation, both as a monotherapy and in combination with other agents. ■

See article by Bhatia et al., p. 1185

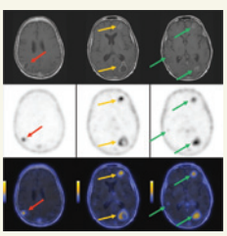
Pharmacogenomic Analysis of S-TRAC Trial



Identifying patients who are most likely to respond to adjuvant therapy remains a major challenge in the treatment of many cancers, including renal cell carcinoma (RCC). George and colleagues investigated correlations between improved disease-free survival (DFS) and single nucleotide polymorphisms (SNPs) in angiogenesis- and hypoxia-related genes. SNPs in *VEGFR1*, *VEGFR2*, and *eNOS* were associated with improved DFS in patients with high-risk RCC who received adjuvant sunitinib, a VEGF inhibitor. This study identified SNPs that should be further tested for their potential to help identify the patients most likely to benefit from adjuvant sunitinib treatment, while reducing unnecessary toxicity risk in others. ■

See article by George et al., p. 1165

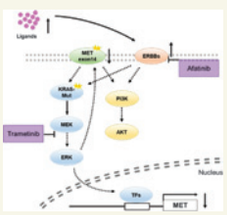
[^{18}F]$\alpha_v\beta_6$-BP in Mice and Humans



The effective detection of metastatic lesions is often not feasible until a cancer has become advanced. Hausner and colleagues describe a novel approach to detect metastases using PET imaging. An integrin $\alpha_v\beta_6$ binding peptide was radiolabeled with 4-[^{18}F]fluorobenzoic acid ([^{18}F]$\alpha_v\beta_6$-BP); this peptide was found to bind specifically to integrin $\alpha_v\beta_6$, which is uniquely expressed on cancer cells, in *in vitro* and *in vivo* models. The authors extended their study to several patients, concluding that [^{18}F]$\alpha_v\beta_6$ -BP was effective in revealing primary tumors and metastases smaller than 1 cm in several organs (including brain, bone, liver, and lung) using PET imaging. This molecule has the potential to vastly improve the early detection of metastatic disease. ■

See article by Hausner et al., p. 1206

KRAS Mutation in *MET* exon14 NSCLC



Despite harboring actionable mutations, many cancers ultimately develop resistance to targeted therapy. Suzawa and colleagues examined clinical and genomic data from 113 lung cancer patients harboring *MET*ex14 alterations to identify mechanisms through which resistance to MET tyrosine kinase inhibitors occur. Patients were more likely to harbor concurrent activating *KRAS* mutations in *MET*ex14 cancers than in cancers dependent on other driver alterations. *KRAS* mutation or amplification was found to cause resistance to MET inhibition through constitutive activation of the RAS/ERK pathway. Combining MET inhibition with EGFR/ERBB2 inhibition successfully reduced the growth of dual-mutant cells both *in vitro* and *in vivo*, providing a potential therapeutic combination to combat resistance to MET inhibitors in lung cancer patients. ■

See article by Suzawa et al., p. 1248