Clinical Cancer Research
Highlights
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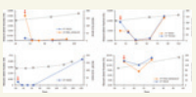
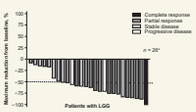
Rapid Alternation of TKIs in GIST



Mutations in *KIT* often arise and provide resistance to imatinib in gastrointestinal stromal tumors (GIST). Serrano and colleagues assessed alternating treatments of the KIT inhibitors sunitinib and regorafenib in patients with GIST whose disease is resistant to tyrosine kinase inhibitors. Of 13 evaluable patients, the best-observed response was stable disease in four patients. While dose-limiting toxicities were identified, recommended phase 2 doses were established for this combination. Secondary mutations in *KIT* were identified in the plasma of patients, further establishing a role for these mutations in resistance. This study confirms that surveillance of ctDNA may help to guide treatment in patients with GIST. ■

See article by Serrano et al., p. 7287

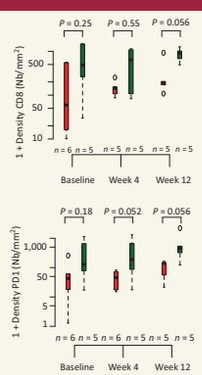
Phase I/IIa Study of Dabrafenib in Pediatric Low-Grade Glioma



Low-grade glioma (LGG) is the most prevalent pediatric brain tumor. Although many patients are able to undergo surgery, most require additional treatment regimens that confer significant morbidities. Hargrave and colleagues conducted a phase I/IIa clinical trial assessing oral dabrafenib in *BRAF* V600-mutant pediatric LGG. This treatment was tolerable in the 32 patients assessed. The objective response rate was 44%, and the one-year progression-free survival was 85%. These promising results support further study of dabrafenib in *BRAF* V600-mutant pediatric cancer patients. ■

See article by Hargrave et al., p. 7303

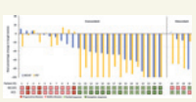
Epigenetic Immunocombination in Advanced Melanoma Patients



Preclinical evidence has suggested that epigenetic modulation can enhance the efficacy of immunotherapy. In a phase Ib clinical trial, Di Giacomo and colleagues assessed the combination of the DNA demethylating agent guadecitabine and ipilimumab. Dose-limiting toxicities were not observed. Overall methylation levels decreased in patients receiving this combination, and immune-related pathways were upregulated. HLA class I expression on melanoma cells was elevated, and changes in the immune infiltrate were observed, including elevated CD8+ T cells, PD-1+ T cells, and CD20+ B cells. The immune-related overall response was 26%, with two confirmed complete responses and three confirmed partial responses observed. Overall, this combination warrants further study. ■

See article by Di Giacomo et al., p. 7351

PET Imaging for Expanding Eligibility and Treatment Response



Some patients with advanced cancer never develop RECIST-measurable disease, as RECIST has limited utility for measuring some tumors, notably bone lesions. Ulaner and colleagues report the efficacy of using PET Response Criteria (PRC) to supplement RECIST in the identification of eligible patients for a multicenter phase II basket trial of neratinib for rare HER2-mutant cancers (SUMMIT). Of the 29 patients assessed by both RECIST and PRC, measured responses were concordant for 25 (86%). Overall, trial enrollment increased by 22% due to the inclusion of patients with PRC-measurable disease. A 64% response rate was observed in these patients, including one complete and four partial responses. This work supports the use of PRC as a supplement to RECIST in future trials. ■

See article by Ulaner et al., p. 7381

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