Clinical Cancer Research
Highlights
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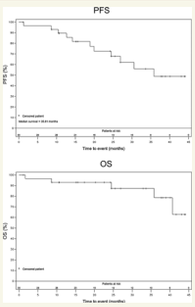
Selected Articles from This Issue

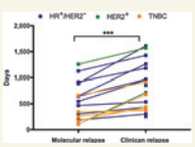
KMP in eNDMM



Bortezomib combined with melphalan and prednisone (MPV) has been a standard of care for elderly patients with newly-diagnosed, transplant-ineligible multiple myeloma (eNDMM). Carfilzomib is a next-generation proteasome inhibitor with a more favorable safety profile than bortezomib. In this phase I trial, Leleu and colleagues assess weekly treatment of carfilzomib in conjunction with melphalan and prednisone (KMP) in eNDMM patients. The maximum tolerated dose of carfilzomib was determined to be 70 mg/m^2. Overall, the KMP regimen resulted in a 93.3% overall response rate, with 46.6% of patients achieving complete response. Further study of the KMP treatment regimen is warranted in eNDMM patients. ■

See article by Leleu et al., p. 4224

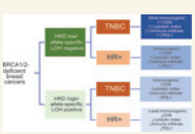
Personalized ctDNA Detection of Breast Cancer Recurrence



Up to 30% of breast cancer patients ultimately experience relapse of their disease, despite the elimination of detectable disease following treatment. Coombes and colleagues describe a liquid biopsy approach whereby breast cancer patients were monitored semi-annually after adjuvant chemotherapy completion. Monitoring was accomplished in a patient-specific manner using information derived from whole-exome sequencing of each patient's primary tumor. Out of 49 patients assessed, 18 experienced recurrence. ctDNA was detected in 16 of these women up to 2 years ahead of clinical evidence of disease relapse. Therefore, patient-specific ctDNA can be used for breast cancer surveillance, providing an opportunity for early intervention of relapsed disease. ■

See article by Coombes et al., p. 4255

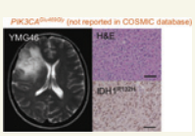
Immunogenic Signatures of *BRCA1/2*-Mutant Breast Cancer



Breast cancers with *BRCA1/2* mutations have elevated genomic instability, rendering them, in theory, more susceptible to checkpoint inhibitors; however, only 20% of patients with *BRCA1/2* alterations respond to PD-1/PD-L1 inhibition. Kraya and colleagues demonstrate that *BRCA1/2*-mutant breast cancers maintaining homologous recombination show a more immunogenic profile than those with homologous recombination deficiency. Hormone receptor status also contributed to the overall immunogenicity of tumors. The combination of *BRCA1/2* status, homologous recombination deficiency, and hormone receptor status may more effectively predict breast cancer patients who will respond to checkpoint inhibitors. ■

See article by Kraya et al., p. 4363

PI3K Pathway Activation in Progression of Oligodendroglioma



Although oligodendroglial tumors are rather indolent, most patients will ultimately develop aggressive disease. Effective analysis of the molecular mechanisms of this tumor type has been hampered by a lack of model systems relevant to the disease. Tateishi and colleagues describe the generation of six novel patient-derived xenograft models of anaplastic oligodendroglioma. All successfully engrafted tumors harbored genetic activation of the PI3K/AKT/mTOR pathway; in contrast, tumors that did not form xenografts lacked detectable activation of this pathway. PI3K/AKT/mTOR-mutant xenografts were vulnerable to alkylating agents and PI3K/AKT/mTOR pathway inhibitors. This work implicates PI3K/AKT/mTOR signaling in the progression of oligodendroglial tumors and supports PI3K/AKT/mTOR inhibitors as potential treatment options for advanced disease. ■

See article by Tateishi et al., p. 4375

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