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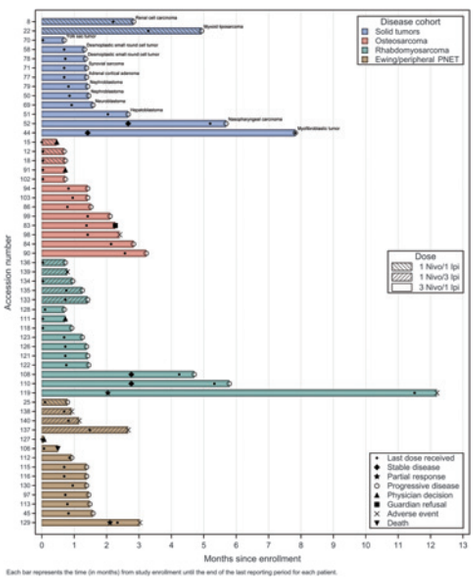
CLINICAL CANCER RESEARCH HIGHLIGHTS

Selected Articles from This Issue

Nivolumab Plus Ipilimumab in Children with Relapsed/Refractory Solid Tumors



Davis *et al.* | Page 5088

Davis and colleagues report the first systematic assessment of the safety and pharmacokinetics of dual immune checkpoint inhibition with ipilimumab and nivolumab in pediatric, adolescent, and young adult patients with relapsed or refractory sarcoma. They establish a recommended phase II dose of nivolumab (3 mg/kg) plus ipilimumab (1 mg/kg) and found the combination to be generally well tolerated. In expanded phase II cohorts, the authors observed two sustained partial responses. They further demonstrate that increased ipilimumab dosing (3 mg/kg) in combination with nivolumab (1 mg/kg) carries higher toxicity without clinical benefit in this population.

Everolimus as Adjuvant Therapy in Advanced HNSCC Patients

Nathan *et al.* | Page 5040

Advanced stage head and neck squamous cell carcinoma (HNSCC) patients are at a high risk of recurrent disease. Due to dismal 5-year survival rates, such patients are in dire need of effective adjuvant therapy. Everolimus, an mTOR inhibitor, has documented activity in HNSCC and is well tolerated with minimal long-term toxicity. In this placebo-controlled phase II trial, Nathan and colleagues are the first to show promising results using everolimus as adjuvant therapy after complete response to definitive treatment in a subset of HPV-negative patients with advanced stage disease. In particular, HPV-negative TP53 mutated tumors appear to yield the best benefit. Thus, subsequent trials using everolimus in this patient population are warranted.

Tilsotolimod Exploits the Tumor Microenvironment in Patients with Solid Tumors

Babiker *et al.* | Page 5079

TLR9 agonists demonstrated efficacy in activation of the innate and adaptive immune system in preclinical models. Babiker and colleagues investigated the activity of tilsotolimod, an investigational synthetic TLR9 agonist, in patients with refractory solid tumors after progression on standard of care therapies. This early phase clinical trial established safety, maximum tolerated dose, and demonstrated early signs of efficacy of tilsotolimod. In addition, translational data revealed activation of the innate and adaptive immune system through the type I interferon (IFN) pathway, IFNγ and IFNα gene upregulation, increase in inflammatory chemokines, activation of myeloid dendritic cells and antigen presentation, and an increase in genes for checkpoint and costimulatory proteins. The translational results suggest further investigation of tilsotolimod in combination with checkpoint inhibitors in solid tumors.

hENT1 Predicts Response to Gemcitabine and Nab-Paclitaxel in Advanced PDAC

Perera *et al.* | Page 5115

Biomarkers are urgently needed to select chemotherapy regimens in pancreatic ductal adenocarcinoma (PDAC). In this study, Perera and colleagues investigated whether mRNA expression levels of hENT1 predict responsiveness to gemcitabinenab-paclitaxel (GnP) in patients with advanced PDAC. The results of this prospective observational clinical trial using tumor-enriched RNA sequencing revealed higher response rates and improved survival in patients receiving GnP, when tumors were considered hENT1high compared to those that were hENT1low. No difference in response or survival were seen in patients receiving modified FOLFIRINOX. An interaction analysis confirmed hENT1 as a predictive biomarker for GnP response. This suggests that hENT1 expression can be used to identify patients who will respond to GnP.

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