Clinical Cancer Research

Highlights

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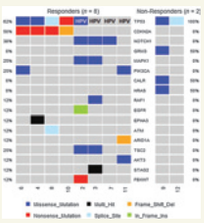
Selected Articles from This Issue

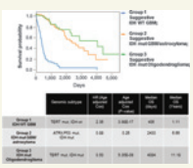
Neoadjuvant AZD1775 Plus Cisplatin/Docetaxel for HNSCC



This is the first published phase I neoadjuvant study of the WEE1 inhibitor, AZD1775, with cisplatin and docetaxel. This novel approach exploits the underlying biology of *TP53*-inactivated tumors, which are incapable of G1 arrest and reliant on the G2/M checkpoint for DNA repair following genotoxic therapy. WEE1's inhibition of CDK2 maintains genomic stability in S-phase, thereby protecting cells against replication stress and subsequent cell death. Treatment was tolerable with encouraging antitumor activity. Pharmacodynamic data demonstrated evidence of replication stress and G2/M override, leading to apoptosis. Given favorable safety, AZD1775 could reduce morbidity of definitive therapy in borderline-resectable, advanced HNSCC. ■

See article by Méndez et al., p. 2740

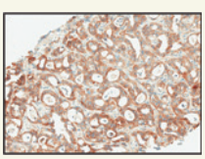
Molecular Diagnosis of Diffuse Gliomas through CSF ctDNA



Diffuse gliomas include different subtypes with diverse prognosis ranging from 1 to 15 years median overall survival. Thus, the subclassification of this type of tumours is crucial for the clinical and surgical managing of patients. The anatomical localization of diffuse gliomas, however, challenges access to tumour specimens for diagnosis. Martínez-Ricarte and colleagues have developed a platform to rapidly genotype seven genes in CSF ctDNA that allow the subclassification of diffuse gliomas. They showed that CSF ctDNA can be used as a liquid biopsy to diagnose diffuse gliomas, avoiding high-risk surgical procedures and facilitating the management of CNS malignancies. ■

See article by Martínez-Ricarte et al., p. 2812

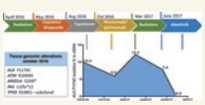
IGF1R/HER3 Blocking Sensitizes Pancreatic Tumors to Therapy



Although IGF-1R is critically involved in pancreatic cancer pathophysiology, IGF-1R inhibitors failed to show clinical benefit. To explore mechanisms of resistance, Camblin and colleagues performed growth factor screening in pancreatic cancer cells and investigated the prevalence of activating growth factors and their receptors in patient samples. The studies reveal that HRG/ErbB3 axis is critical to pancreatic cancer progression and resistance to IGF-1R inhibition. Moreover, they demonstrate that dual IGF-1R and ErbB3 targeting with a novel bispecific antibody increases the activity of standard-of-care chemotherapies. These findings provide mechanistic insight into pancreatic cancer resistance to IGF-1R inhibitors and identify novel therapeutic strategies. ■

See article by Camblin et al., p. 2873

ALK in Small Cell Prostate Cancer



Anaplastic lymphoma kinase (ALK) is an oncogenic kinase implicated in several tumors, including neuroblastoma. Carneiro and colleagues report the first case of small-cell neuroendocrine prostate cancer (NEPC) with *ALK*F1174C activating mutation. The patient responded to second-generation ALK inhibitor alectinib as reflected by declining circulating tumor DNA allele fraction and radiographic stable disease. Alectinib also inhibited the growth of prostate cancer cell lines and organoids expressing *ALK*F1174C. Furthermore, ALK amplification was associated with poor outcome in prostate adenocarcinoma. The findings indicate the involvement of ALK in *de novo* and treatment-emergent NEPC and the therapeutic potential of ALK inhibitors. ■

See article by Carneiro et al., p. 2732

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Clin Cancer Res 2018;24:2711.