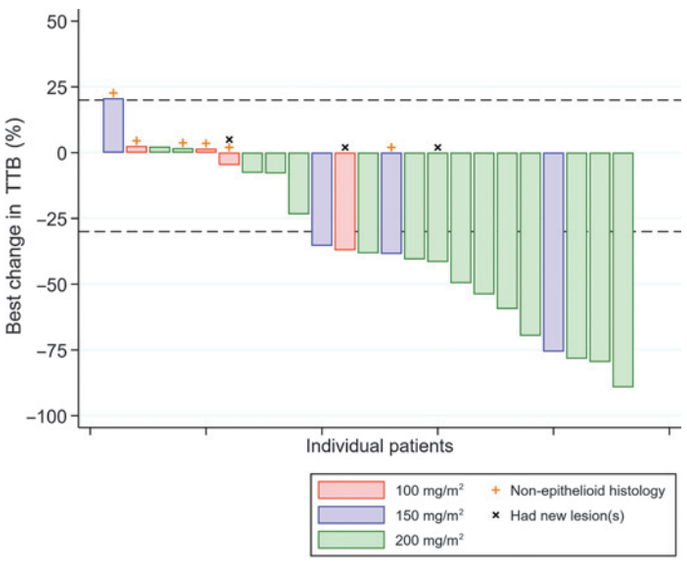
September 15, 2020 | Volume 26 | Number 18

CLINICAL CANCER RESEARCH

HIGHLIGHTS

Selected Articles from This Issue

Ganetespib Plus Chemotherapy in Pleural Mesothelioma



Fennell *et al.* | Page 4748

Malignant pleural mesothelioma (MPM) is an incurable cancer associated with exposure to asbestos, and there remains a critical need for effective front-line therapeutics. Inhibition of heatshock protein 90 (Hsp90) has shown promise in preclinical studies. Fennell and colleagues conducted a dose-escalation study of pemetrexed and cisplatin/carboplatin plus ganetespib, an Hsp90 inhibitor, in patients with chemotherapy-naïve MPM. At the maximum-tolerated dose, 56% showed a partial response, while 83% showed disease control; median progression-free survival was 6.3 months. Patients with tumors harboring epithelioid histology and global loss of heterozygosity benefitted most from this combination. These results support the further development of combination therapies including ganetespib for patients with MPM.

Cabazitaxel in Gastric Cancer

Shah *et al.* | Page 4756

The prognosis of advanced gastric cancer remains dismal, with most patients with advanced disease surviving less than one year. In a multicenter phase II study, Shah and colleagues assessed cabazitaxel, a next generation taxoid, in patients with metastatic gastric cancer. Modest antitumor activity was observed in both taxane-naï;ve and taxane-pretreated patients as 2nd- and 3rd-line therapy. Genomic analyses associated elevated HER2 levels and an M2 tumor-associated macrophage signature with improved survival in patients with metastatic gastric cancer treated with cabazitaxel. Additional study is needed to further elucidate these signatures as prognostic markers for gastric cancer therapy.

Mechanisms of Toxicity in Patients Treated with Axi-cel

Faramand *et al.* | Page 4823

Multiple factors present prior to chimeric antigen receptor T (CAR T) cell infusion influence the development of immune-mediated toxicities. Faramand and colleagues assessed risk factors for severe toxicity or treatment related death in a cohort of 75 patients with large B-cell lymphoma treated with axicabtagene ciloleucel (axi-cel), a standard of care CD19-targeted CAR T therapy. An association was identified between a pro-inflammatory tumor microenvironment—specifically, elevated interleukin 6 levels—and severe cytokine release syndrome (CRS) and neurotoxicity. Furthermore, elevated peak noradrenaline levels were observed in patients developing severe CRS. Analysis of pretreatment patient tumor biopsies revealed an association of myeloid markers with higher toxicity as well. The role of myeloid cells and the tumor microenvironment on mediating toxicities is an evolving concept and warrants further investigation in a clinical trial.

GATA6 Expression and PDAC Subtyping

O'Kane *et al.* | Page 4901

Recent advances in the subtyping of pancreatic adenocarcinoma (PDAC) have revealed two major subtypes of the disease: basal and classical. In an analysis of the COMPASS trial, O'Kane and colleagues assessed the contribution of subtype to response to modified FOLFIRINOX (mFFX) in patients with PDAC. Patients with basal-like tumors showed resistance to mFFX and a shorter median overall survival when compared with patients with classical PDAC. GATA6 and Keratin 5 expression correlated with classifier status: low GATA6 expression and high Keratin 5 expression correlated with the basal subtype. Further analysis of these markers is necessary to assess their utility as surrogate markers for transcriptional subtyping.

Clinical Cancer Research

Selected Articles from This Issue

Clin Cancer Res 2020;26:4713.