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CLINICAL CANCER RESEARCH
HIGHLIGHTS
Selected Articles from This Issue

Cabozantinib in Hormone-Naïve Metastatic Prostate Cancer

Corn et al. | Page 990

Metastatic prostate cancer remains an incurable disease. Treatment with cabozantinib, an oral small-molecule inhibitor of c-Met/VEGFR2 signaling, leads to bone scan responses and significant pain relief but not overall survival improvement in patients with metastatic castration-resistant prostate cancer. To explore the hypothesis that cabozantinib could delay the onset of castration resistance, Corn and colleagues combined cabozantinib with androgen deprivation in patients with hormone-naïve metastatic prostate cancer. Responses in bone scan and measurable disease were observed in 81% of and 90% of evaluable patients, respectively. Elevated plasma concentrations of lumican, CXCL5, CD25, and CD30 and high expression of tumoral pFGFR1 were associated with shorter progression-free survival after treatment. These data suggest that therapy combinations involving cabozantinib are worth further study in metastatic prostate cancer.

Dose Escalation Study of Cemiplimab in Advanced Tumors

Papadopoulos et al. | Page 1025

Although blockade of the programmed cell death receptor-1 (PD-1)/programmed cell death-ligand 1 (PD-L1) pathway has demonstrated clinical benefit in multiple cancers, some cancer subtypes are resistant to checkpoint blockade. Papadopoulos and colleagues assessed cemiplimab, a high-affinity monoclonal antibody against PD-1, as monotherapy or in combination with hypofractionated radiotherapy (hfRT) and/or cyclophosphamide (CPA) in patients with advanced solid tumors. There were no dose-limiting toxicities associated with cemiplimab treatment. Encouraging signs of efficacy, including two complete responses and seven partial responses, were observed. Cemiplimab can be safely administered with hfRT and/or CPA as well. Cemiplimab has recently been approved in the United States for the treatment of patients with cutaneous squamous cell carcinoma.

Pembrolizumab and Vorinostat in Head and Neck Cancer

Glumac et al. | Page 1054

Aggressive variant prostate cancer (AVPC) is not driven by androgen receptor and lacks expression of prostate-specific membrane antigen (PSMA), usually used for imaging metastatic prostate cancer. Thus, there remains an unmet need to identify novel antigens and targeted imaging agents for the detection and monitoring of this lethal form of prostate cancer. Glumac and colleagues identified CD133 as a targetable antigen that is overexpressed on the surface of non-AR driven, PSMA-negative prostate cancer cells. As an antibody against CD133, HA10 IgG was labeled for near-infrared and positron emission tomography imaging. [89Zr]Zr-HA10 IgG was validated in imaging studies and shown to be highly selective for CD133-expressing prostate cancer cells, suggesting its potential for noninvasive immunoPET imaging of this subset of patients with AVPC.

Proteomics of Pancreatic Ductal Adenocarcinoma Metastases

Law et al. | Page 1065

Pancreatic ductal adenocarcinoma (PDAC) is a deadly disease that metastasizes at early stages. Through quantitative mass spectrometry analysis of liver metastases obtained at rapid autopsy, Law and colleagues identified four unique metastatic PDAC microenvironment subtypes: inflammatory, progenitor-like, metabolic, and proliferative. Patients treated with FOLFIRINOX showed improved survival if their metastases were categorized as metabolic or progenitor-like. The classification system and the protein expression signatures described here provide a basis to facilitate the design and implementation of subtype-specific PDAC treatment strategies.