Once-Daily Adavosertib in Solid Tumors

Takebe et al. | Page 3834

Adavosertib (AZD1775) is a Wee1 kinase inhibitor that abrogates G1/S and G2/M cell cycle arrest, leading to replication stress and, ultimately, tumor cell death. Takebe and colleagues performed a clinical trial of once-daily adavosertib in patients with solid tumors. Adavosertib was well tolerated, and plasma exposures were similar to a twice-daily regimen. Six patients (14%) showed a partial response. Elevated tumor CCNE1 mRNA expression was identified as a potential biomarker for response, particularly in ovarian and endometrial cancers. These results suggest adavosertib monotherapy may hold promise in patients with advanced solid tumors when combined with biomarker selection using CCNE1 expression as a precision medicine approach to induce synthetic lethality.

PD-L1 and Inflammatory Gene Expression in Gastric Cancer

Lei et al. | Page 3926

Checkpoint inhibitors demonstrated clinically meaningful antitumor activity and a manageable safety profile in chemotherapy-refractory gastroesophageal cancer (GEC). Lei and colleagues performed an exploratory analysis of the CheckMate 032 GEC cohort comparing the clinical utility of PD-L1, assessed using percentage of tumor cell (%TC) versus combined positive score (CPS), to predict nivolumab ± ipilimumab treatment efficacy. The analysis demonstrated that increased objective response and overall survival were observed with CPS compared with %TCs at higher cut-offs. Additionally, the study showed that multiple inflammatory gene expression signatures, including the four-gene signature of CD274, CD8A, LAG3, and STAT1, were associated with response, warranting further investigation.

PR-HMRG Fluorescent Probe for Glioblastoma

Kitagawa et al. | Page 3936

Maximal safe resection is an important first step to the successful management of glioma patients. Intraoperative fluorescent labeling is effective in maximizing the extent of tumor resection while minimizing the risk of excessive resection of the non-tumorous surrounding brain; however, the currently used probe lacks sufficient sensitivity and is not able to be readministered. Kitagawa and colleagues established a novel fluorescent labeling system for rapid intraoperative detection of glioblastoma using a topical, proline-arginine hydroxymethyl rhodamine green-based probe (PR-HMRG). This probe successfully distinguished tumor from peritumoral tissues in animal studies due to Calpain-1 protease activity. Further work will be needed to determine this probe’s clinical applicability.

Heterogeneity of IFN Response and Immunity in Cervical SCC

Chen et al. | Page 3990

Combining immune checkpoint blockade (ICB) with radiation therapy is considered a promising strategy, but only a subset of patients responds to treatment. Chen and colleagues assessed changes in immune infiltration after chemoradiotherapy (CCRT) in patients with cervical cancer. CCRT led to increased CD8⁺ T-cell infiltration and interferon induction, but only in a subset of patients. This heterogeneity in antitumor immunity and interferon response validates the observation that combination CCRT and ICB will only be of clinical benefit to certain patients. Additional studies are needed to identify biomarkers for patients who will benefit from CCRT.