Ceralasertib + Paclitaxel in Advanced Cancers

Kim et al. | Page 4700

ATR is an essential component of the DNA damage cascade, and inhibition of ATR has led to cancer cell cytotoxicity in preclinical models. In this phase I trial, Kim and colleagues assessed the combination of the ATR inhibitor ceralasertib and paclitaxel in patients with advanced solid tumors. This combination was well tolerated. In the full cohort, an ORR of 22.6% was observed. However, in patients with melanoma who developed resistance to checkpoint inhibition, the ORR was 33.3%. Furthermore, patients with elevated LDH were shown to respond. Further clinical study of this combination is warranted.

Analysis of Rituximab/Lenalidomide for Indolent Non-Hodgkin Lymphoma

Tuscano et al. | Page 4726

The combination of rituximab and lenalidomide was previously determined to be effective for indolent non-Hodgkin lymphoma. To expand on the understanding of this treatment strategy, Tuscano and colleagues examined data from two phase 2 trials of this combination to assess long-term survival and identify predictive biomarkers. An ORR of 82% was observed for patients with both previously untreated and relapsed/refractory disease. Durable remissions were observed, some lasting longer than 10 years. GranB+ CD8+ T cells were correlated with long-term complete responses, as was elevated plasma IFNγ. In pre-treatment samples, low IDO2 expression was correlated with long-term complete response. These results, while encouraging, should be further validated in additional clinical trials.

The NIBIT-M2 Phase III, Multicenter, Randomized Clinical Trial

Di Giacomo et al. | Page 4737

The long-term efficacy of checkpoint inhibitors in asymptomatic melanoma brain metastases is presently unknown. In this clinical setting, the phase III study NIBIT-M2, by Di Giacomo and colleagues, with combined treatment of ipilimumab plus nivolumab, led to a remarkable 5-year survival of 41%. Early and delayed treatment-related toxicity was limited. Survival was higher in patients with BRAF-mutant brain metastases compared to patients with BRAF-wild type brain metastases. The durability of response indicates that ipilimumab, combined with nivolumab, is presently the most effective long-lasting systemic treatment for melanoma patients with asymptomatic brain metastases and should be carefully evaluated against surgery or radiotherapy.

Immunogenic Prostate Cancer and Loss of Key Tumor Suppressors

Calagua et al. | Page 4836

Prostate cancer is generally considered poorly immunogenic, with rare infiltration of lymphocytes and low tumor expression of programmed death-ligand 1 (PD-L1). However, Calagua and colleagues examined high-risk localized prostate cancers and found that approximately one-quarter expressed PD-L1 and were T-lymphocyte-infiltrated. T-cell subsets included exhausted progenitors and differentiated effectors. Surprisingly, overall T-cell density and T-cell subsets were similar to those in kidney cancers. Immunogenic cases were characterized by losses of key tumor suppressors, BRCA2, RB1, and CHD1. Together, these findings identify an immunogenic subset of prostate cancer that may be more effectively targeted by immunotherapies.

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