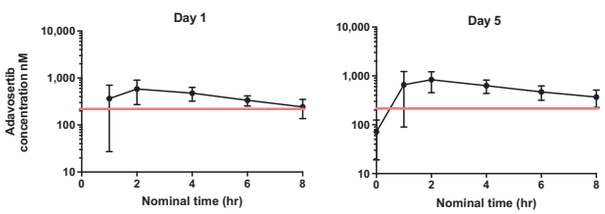
March 15, 2020 | Volume 26 | Number 6

CLINICAL CANCER RESEARCH

HIGHLIGHTS

Selected Articles from This Issue

Pediatric Phase I Trial of Adavosertib/AZD1775 and Irinotecan



Cole *et al.* | Page 1213

Adavosertib (AZD1775) is a first-in-class Wee1 inhibitor that has shown promise in several adult solid tumors, and work in preclinical models has suggested efficacy in pediatric tumors. Cole and colleagues performed a phase I trial of adavosertib in combination with irinotecan in pediatric cancer patients. The combination treatment was tolerable. Moreover, preliminary evidence of clinical activity was observed in this heavily pretreated relapsed and recurrent cohort. The adavosertib/irinotecan combination is currently being assessed in a phase II expansion trial in patients with relapsed and refractory neuroblastoma, medulloblastoma, and CNS embryonal tumors or rhabdomyosarcoma.

Tisotumab Vedotin in Recurrent or Metastatic Cervical Cancer

Hong *et al.* | Page 1220

Cervical cancer carries a high risk of relapse, but there is currently no second-line standard of care for this disease. Tissue factor (TF) is frequently highly expressed in cervical cancer and is associated with poor prognosis, making it a potential therapeutic target. Hong and colleagues assessed tisotumab vedotin, an antibody-drug conjugate targeting TF, in patients with cervical cancer (N=55) as part of the innovaTV 201 study. Tisotumab vedotin was well tolerated in this cohort. Responses to tisotumab vedotin were observed regardless of histological subtype and prior treatment. This work supports the continued clinical assessment of tisotumab vedotin in patients with cervical cancer.

TP53-Specific T Cells from Peripheral Blood Lymphocytes

Malekzadeh *et al.* | Page 1267

TP53 is the most commonly mutated gene in cancer, but efforts to target mutant *TP53* have been unsuccessful. Malekzadeh and colleagues assessed antigen-experienced T cells in peripheral blood lymphocytes (PBL) from patients with p53-mutant cancer. In five patients with intra-tumoral TIL responses to mutated *TP53*, PBL T-cell responses were similar in reactivity to the intratumoral responses. CD4+ and CD8+ T cells specific for neoantigens from the R175H, Y220C and R248W mutations in *TP53* were detected. Moreover, *TP53* mutation-specific T cells also recognized cell lines bearing the appropriate human leukocyte antigen restriction element and *TP53* mutation, indicating that these T cells can detect p53 neoantigens. This suggests that targeting mutant *TP53* may be possible through cell-therapy approaches.

4-1BB Agonism Licenses PD-1 Blockade in Glioblastoma

Woroniecka *et al.* | Page 1349

Although immune checkpoint blockade has shown promise in many cancer subtypes, this strategy has not been successful in glioblastoma and intracranial tumors. Woroniecka and colleagues assessed 4-1BB levels on tumor-infiltrating lymphocytes (TIL) from human and murine gliomas. Nonexhausted CD8+ TILs expressed 4-1BB. 4-1BB agonist treatment stimulated these TIL, both *in vitro* and in mouse models, and prevented exhaustion. The combination of PD-1 blockade and 4-1BB agonism in mice promoted survival of mice bearing gliomas. These findings suggest that 4-1BB agonism may prevent resistance to immune checkpoint inhibition.