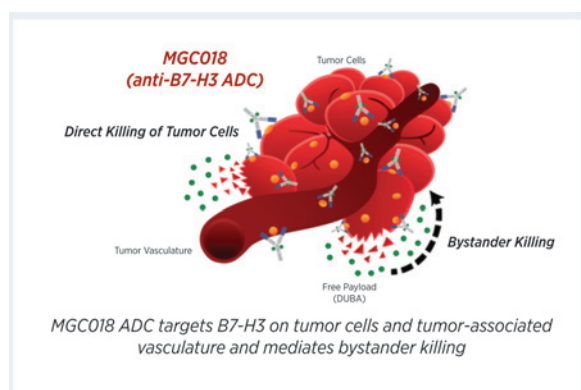


MOLECULAR CANCER THERAPEUTICS

HIGHLIGHTS

Selected Articles from This Issue

MGC018, a Duocarmycin-based ADC Targeting B7-H3 for Cancer

Scribner *et al.* | Page 2235

B7-H3, a member of the B7 family of immune regulators, is often overexpressed in cancers. In this manuscript, Scribner and colleagues disclose MGC018, an antibody-drug conjugate (ADC) targeting B7-H3. MGC018 carries a duocarmycin payload linked to the humanized IgG1/kappa monoclonal antibody. Their ADC showed antitumor activity in a range of patient-derived xenografts, including triple-negative breast cancer, prostate cancer, and head and neck squamous cell carcinoma. Preclinical results in this First Disclosure support the clinical development of MGC018 in solid cancers.

Synergistic MEK and mTORC1/2 Inhibition in Melanoma

Wei *et al.* | Page 2308

There are many clinical and pathological similarities between human and canine mucosal melanomas. Two axes common to both species are the Ras/MAPK and PI3K/Akt/mTOR pathways. Wei and colleagues investigated the use of an MEK inhibitor (trametinib) previously investigated in canine models combined with the PI3K/mTOR inhibitor sapanisertib. The combined therapy reduced pS6/pERK, modified Bim/Bcl-xL expression, and limited tumor metastasis. Optimizing the dosage strategy required daily dose of trametinib and staggering the dose of sapanisertib. Taken together, the data indicates careful dose refinement is required for this combined approach and shows cytotoxicity in mucosal melanoma.

Therapeutic Mechanisms of CD73-mAb and CD73-ADC in Lung Cancer

Jin *et al.* | Page 2340

Resistance to tyrosine kinase inhibitors and immunotherapy continues to be a concern for lung cancer patients. In this manuscript, Jin and colleagues exploit and observed overexpression in CD73 using a humanized anti-CD73 monoclonal antibody and antibody-drug conjugate (ADC). Treatment with the MMAE-bearing CD73-ADC generated anti-tumor responses against CD73-high tumors and led to accumulation of pro-inflammatory macrophages and dendritic cells. Their results underline the potential for the clinical development of CD73-ADC for CD73-dysregulated lung cancer patients.

Circulating Tumor Cells in Cervical Cancer

Tewari *et al.* | Page 2363

There is still a high need for solutions to recurrent, persistent, or metastatic cervical cancer. Anti-angiogenic therapies have shown promise, and continued translation requires predictive biomarkers of response. One cost-efficient biomarker that is well-suited to guide second-line therapy after anti-VEG therapy are circulating tumor cells (CTCs). Therefore, Tewari and colleagues investigated their association with survival and ability to predict anti-VEGF therapy. Patients above and below the median CTCs were stratified as those with and without bevacizumab. Bevacizumab therapy reduced the hazard of death and progression for patients with high pre-treatment CTCs. Therefore, CTCs may have prognostic significance in cervical cancer.