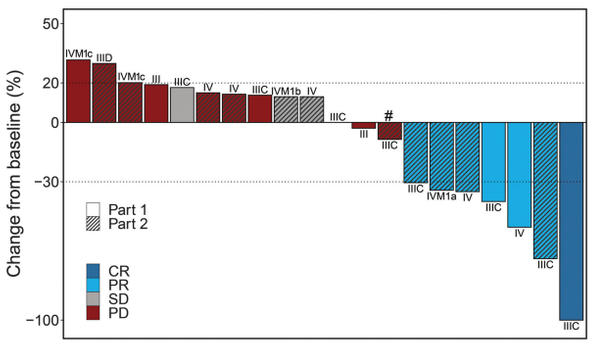
January 1, 2023 | Volume 29 | Number 1

CLINICAL CANCER RESEARCH
HIGHLIGHTS

Selected Articles from This Issue

ONCOS-102 Plus Pembrolizumab in Anti-PD-1 Resistant Melanoma



Shoushtari *et al.* | Page 100

Shoushtari and colleagues report a pilot trial of ONCOS-102, a novel oncolytic adenovirus encoding GM-CSF, administered intratumorally either sequentially or in combination with pembrolizumab in patients with melanoma resistant to prior PD-1 blockade. Treatment was well tolerated. Objective responses were seen in 7 of 20 patients, and size reductions in noninjected lesions suggested local delivery of ONCOS-102 can drive a systemic anti-tumor effect. Serial biopsies of injected tumors at baseline, Week 3 (following ONCOS-102 and prior to pembrolizumab), and Week 9 (following ONCOS-102 and pembrolizumab) indicated that while most tumors experience $CD8^+$ and $CD4^+$ infiltration after ONCOS-102 injection, sustained infiltration at Week 9 was associated with clinical benefit. Future trials of ONCOS-102 and checkpoint inhibition are warranted in anti-PD-1-resistant melanoma. These findings suggest trials using viral agents in anti-PD-1-resistant disease should not solely rely on early onset of cytotoxicity to predict clinical response.

Preclinical and Clinical Results Using Talazoparib and Low-Dose Chemotherapy

Wainberg *et al.* | Page 40

Wainberg and colleagues report on the combination of very low doses of chemotherapy (10% of the usual dose) with a full dose of talazoparib (TAL). The study design reports preferentially increasing the dose of TAL before increasing the chemotherapy to improve the hematologic profile as well as exploring efficacy signals among non-BRCA patients. This phase I study demonstrates that TAL with low-dose temozolomide or irinotecan shows an improved hematologic toxicity profile than most prior chemo/PARP inhibitor combinations and has signals of clinical activity in small cell lung cancer and ovarian cancer. The results of this phase I study are supportive of ongoing trials with this combination.

Molecular and Immune Associations of Obesity in Melanoma

Hahn *et al.* | Page 154

Obesity has been unexpectedly associated with improved outcomes with immune checkpoint inhibitors and BRAF-targeted therapies in metastatic melanoma; however, the biology underlying this observation is unknown. Hahn and colleagues examined associations between body mass index (BMI) and molecular, immune, and metabolic features of melanoma tumors as well as host microbiome in 782 patient specimens. Host BMI was associated with altered tumor metabolism, with downregulation of oxidative phosphorylation (OXPHOS) and other metabolic pathways in tumors from high BMI patients. OXPHOS has been associated with resistance to targeted and immune therapies, suggesting a potential mechanism underlying the "obesity paradox" in metastatic melanoma.

Circulating Tumor DNA in Follicular Lymphoma

Fernández-Miranda *et al.* | Page 209

Circulating tumor DNA (ctDNA) levels are associated with tumor volume and minimal residual disease in lymphoid malignancies. Fernández-Miranda and colleagues suggest that pre-treatment ctDNA levels in follicular lymphoma patients could be useful to predict response to treatment and early progression as an independent predictive biomarker or in combination with clinical variables. Circulating tumor DNA levels and cell-free DNA genotyping at mid-treatment and end-of-treatment are associated with treatment response and early progression follicular lymphoma. Circulating tumor DNA measurement at diagnosis and follow-up is a valuable tool that might feasibly be used in clinical trials and, eventually, in daily clinical practice.

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doi: 10.1158/1078-0432.CCR-29-1-HI