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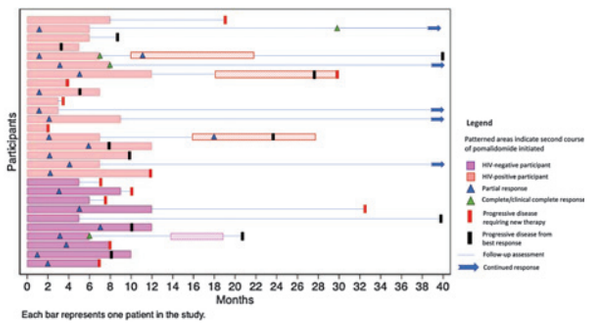
CLINICAL CANCER RESEARCH HIGHLIGHTS

Selected Articles from This Issue



Pomalidomide in Kaposi Sarcoma

Ramaswami *et al.* | Page 840

Kaposi sarcoma (KS) arises after Kaposi sarcoma herpesvirus infection and frequently develops in HIV-positive individuals. Ramaswami and colleagues conducted a clinical trial of pomalidomide, an oral immunomodulating thalidomide derivative, in patients with KS with or without HIV. The overall response rate was 71%, with 67% of HIV-positive patients and 80% of HIV-negative participants showing a response. Baseline IL-6 levels were higher in nonresponders compared with responders, although further assessment of IL-6 as a biomarker is warranted. Based on these results, the United Stated Food and Drug Administration granted accelerated approval to pomalidomide for the treatment KS.

Phase 1a/b Open-Label Trial of Etigilimab in Solid Tumors

Mettu *et al.* | Page 882

TIGIT is a novel target in the field of cancer immunotherapy. To explore the potential of anti-TIGIT immunotherapy, Mettu and colleagues conducted a phase 1a/b study to evaluate the safety, tolerability, and preliminary efficacy of the novel anti-TIGIT antibody etigilimab alone (phase 1a) and in combination with the anti-PD-1 nivolumab (phase 1b) in patients with refractory solid tumors. This first-in-human study showed etigilimab was well tolerated. Signs of anti-tumor activity were observed, with eight patients showing stable disease and one patient showing a partial response. Biomarker analyses demonstrated evidence of clear dose-dependent target engagement by etigilimab. These findings lay a foundation for future clinical trials targeting TIGIT.

Neuroendocrine Prostate Cancer Detection Using cfDNA

Berchuck *et al.* | Page 928

Detecting neuroendocrine prostate cancer (NEPC) in men with metastatic castration-resistant prostate cancer (mCRPC) has important prognostic and therapeutic implications but is challenging in clinical practice. To address this unmet need, Berchuck and colleagues developed a noninvasive biomarker, termed NEPC Risk Score, based on tissue-informed cell-free DNA (cfDNA) methylation analysis. Applying the NEPC Risk Score to cfDNA from two independent mCRPC cohorts discriminated between men with versus without NEPC with high accuracy. These data support the further clinical development of this cfDNA methylation-based biomarker to noninvasively identify men with NEPC who should be considered for platinum-based chemotherapy or clinical trials of NEPC-directed therapies.

Hyperprogression in Sarcoma after PD-1 Blockade

Klemen *et al.* | Page 939

PD-1 blockade has provided benefit for some patients with advanced sarcomas. However, predicting response is not feasible currently. Furthermore, the relevance of hyperprogressive disease (HPD) is unclear. Klemen and colleagues performed a pooled analysis of prospective trials evaluating checkpoint inhibition in patients with sarcoma. In total, 134 patients were assessed, of which 16% had a complete or partial response, 36% had stable disease, 34% had progressive disease without HPD, and 11% with HPD. Patients with HPD and non-HPD progressive disease showed similarities in terms of disease subtype, clinical features, and genomic alterations. Interestingly, patients developing HPD had smaller tumors at baseline than patients who progressed without HPD. Additional clinical studies will be required to further understand HPD in patients with sarcoma.

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