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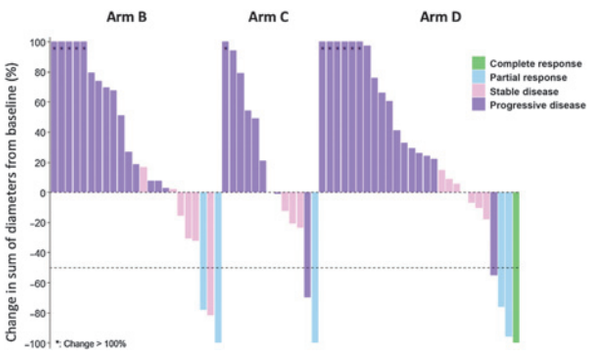
CLINICAL CANCER RESEARCH HIGHLIGHTS

Selected Articles from This Issue

Oral Selinexor in Recurrent Glioblastoma



Lassman *et al.* | Page 452

Glioblastoma is the most common and aggressive primary brain cancer in adults. New therapies are needed. Exportin-1 is a nuclear export protein overexpressed in many solid tumors, including gliomas, which correlates with prognosis. Selinexor is a first-in-class exportin-1 inhibitor with efficacy in various cancers. Lassman and colleagues conducted an international multiarm clinical trial of selinexor in recurrent glioblastoma and demonstrated adequate intratumoral drug penetration and clinically relevant disease control with manageable side effects. Molecular studies identified a signature predictive of response. Ongoing trials evaluate the safety and efficacy of selinexor in combination with other therapies for newly diagnosed and recurrent glioblastoma.

Nivolumab and Lirilumab in Relapsed Resectable SCCHN

Hanna *et al.* | Page 468

Surgery often represents the best chance for disease control in locoregionally recurrent squamous cell carcinoma of the head and neck (SCCHN). Hanna and colleagues investigated dual immune checkpoint inhibition of anti-PD-1, nivolumab and anti-KIR, lirilumab before and after salvage surgery to improve DFS in an open-label, single-arm, nonrandomized, multicenter phase II trial. The authors report substantial rates of pathologic response (43%), excellent safety and tolerability, and overall encouraging survival outcomes in heavily pretreated patients with locoregionally recurrent SCCHN highlighting the promising activity of immune checkpoint blockade in this setting regardless of PD-L1 status. Further investigation of this therapeutic strategy is warranted.

Serial Postoperative ctDNA Monitoring of CRC Recurrence

Henriksen *et al.* | Page 507

Patients with stage III colorectal cancer (CRC) have a high risk of recurrence, indicating a subset with residual disease. Studies have shown postoperative ctDNA detection is associated with recurrence risk. Here, Henriksen and colleagues report the results of a multicenter study exploring the clinical utility of serial ctDNA assessment in a cohort of patients with stage III CRC. Circulating tumor DNA assessments performed postoperative, postadjuvant, and serially during surveillance allowed for recurrence risk stratification, monitoring therapeutic efficacy, and early recurrence detection that could impact treatment decisions and outcomes for CRC patients. ctDNA detected recurrence with a significant lead time compared to CT-imaging and ctDNA growth rates were prognostic of survival. Treatment of ctDNA positive patients with standard adjuvant therapy prevented recurrence in only 20% of patients. ctDNA growth rates may identify patients who could benefit from immediate therapeutic intervention compared to awaiting recurrence. The novel combination of ctDNA detection and growth rate assessment provides unique opportunities for guiding decision-making.

Cotargeting EP4 and PD-1 in Prostate Cancer

Peng *et al.* | Page 552

Cellular heterogeneity underlies the significant clinical heterogeneity and the poor response to immunotherapy in prostate cancer. Peng and colleagues interrogated the transcriptomic profiles of prostate cancer at single-cell resolution and revealed the immunosuppresive property of EP4. A novel EP4 antagonist, YY001, was developed, which strongly restored cytotoxic T-cell function and decreased the infiltration of immunosuppressive MDSCs. Cotargeting EP4 and PD-1 exhibited robust antitumor immune responses in multiple preclinical models, which shows promise to treat advanced prostate cancer and allow for effective combinatorial immunotherapy.

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