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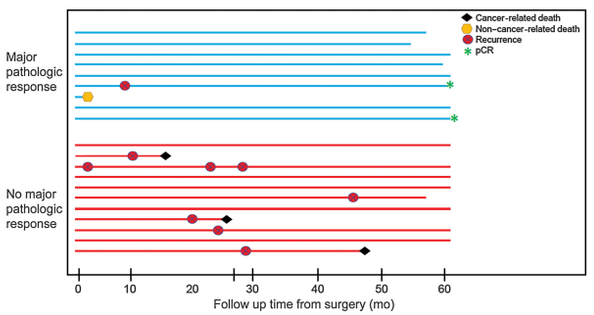
CLINICAL CANCER RESEARCH HIGHLIGHTS

Selected Articles from This Issue

Five-Year Clinical Outcomes after Neoadjuvant Nivolumab in Resectable NSCLC



Rosner *et al.* | Page 705

Neoadjuvant immune checkpoint blockade increasingly is incorporated into the perioperative treatment setting for solid tumor malignancies, including resectable non-small cell lung cancer (NSCLC). However, long-term outcomes, specifically survival, after treatment with these agents are still maturing. In this article, Rosner and colleagues present the five-year clinical outcomes after neoadjuvant nivolumab for resectable NSCLC, representing the longest follow up data available after neoadjuvant anti-PD-1 therapy in any cancer type. In addition to the durable clinical benefit of neoadjuvant nivolumab highlighted in this report, the examination of key subgroups and biomarkers may help clinicians and investigators as they look to navigate this rapidly evolving treatment landscape. Several questions remain on how to further optimize perioperative outcomes for patients with resectable NSCLC, making long-term follow up data, as reported here, particularly valuable.

Molibresib for the Treatment of Relapsed/Refractory Hematologic Malignancies

Dawson *et al.* | Page 711

Molibresib is a selective, small molecule inhibitor of the bromodomain and extra terminal (BET) protein family. Dawson and colleagues present the results of this open-label, two-part, phase I/II study in 111 patients with hematological malignancies, which demonstrated that treatment with molibresib was tolerable, though its use was limited by gastrointestinal and thrombocytopenia toxicities. The most common adverse events were diarrhea ($n = 55$ [50%]), nausea ($n = 51$ [46%]), and thrombocytopenia ($n = 44$ [40%]). Across the whole study, six patients achieved a complete response, and seven patients achieved a partial response (objective response rate: 13% [95% CI: 6.9–20.6]). This modest anti-tumor activity with molibresib monotherapy is consistent with emerging evidence that some (but not all) epigenetic therapies may need to be used as part of combination therapy to achieve maximal clinical benefit in relapsed/refractory myeloid disease and leukemia. As such, investigations into combinatorial approaches that use BET inhibition and other targeted therapies may be warranted.

A Clinical Trial of Nivolumab and Temozolomide for Neuroendocrine Neoplasms

Owen *et al.* | Page 731

In a phase II trial of combination nivolumab and temozolomide in patients with advanced neuroendocrine tumors (NET) and carcinomas (NEC), Owen and colleagues report a response rate of 32% including a 64% response rate in patients with lung neuroendocrine neoplasms. Responses were observed in patients with both NET and NEC but confirmed responses only occurred in patients with lung and pancreatic tumors. Exploratory immune cell profiling revealed an increase in circulating $CD8^+$ T cells and decrease in $CD4^+$ T cells during treatment. LAG-3 expressing total T cells were lower in patients experiencing a partial response. The results indicated that the combination nivolumab and temozolomide demonstrated promising activity in NEN.

Memory Enriched CD19CAR in Adults with Relapsed/Refractory ALL

Aldoss *et al.* | Page 742

Aldoss and colleagues report memory-enriched CD19-directed chimeric antigen receptor (CD19-CAR) T-cell therapy demonstrated favorable safety profile and yielded an excellent response rate in adults with relapsed/refractory (r/r) B-cell acute lymphoblastic leukemia (ALL). Their study cohort included high-risk patients with r/r ALL who had limited available salvage options, such as patients who had failed prior novel therapies and allogeneic hematopoietic cell transplant (alloHCT), older adults, ALL with Philadelphia-like genotype and patients with extramedullary relapse. The incidence of severe cytokine release syndrome (CRS) and neurotoxicity were relatively low following therapy with CD19-CAR T cells, with no grade ≥4 CRS. Long-term outcomes for patients who responded to CD19-CAR T cells and underwent subsequent consolidation with alloHCT were outstanding. The intriguing safety and response data from this study support further development of this promising therapy in high-risk adults with ALL in early stages of the disease to improve long term outcomes.

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