Ribociclib, Everolimus, and Exemestane in HR⁺, HER2⁻ Advanced Breast Cancer

Bardia et al. | Page 6417

The combination of endocrine therapy and CDK4/6 inhibitors has become common for patients with HR⁺, HER2⁻ advanced breast cancer (ABC); however, endocrine resistance often occurs, leading to recurrence. Preclinical and clinical data suggest that targeting the PI3K signaling pathway may delay the development of this resistance mechanism. Bardia and colleagues performed a dose escalation/expansion phase Ib trial of triplet therapy with ribociclib, everolimus, and exemestane in women with ABC. This triplet regimen showed a safety profile consistent with the known profiles of the individual agents and was generally well tolerated. Preliminary evidence of antitumor activity of this combination was observed. Elevated ESR1 expression correlated with improved response to this regimen, while elevated MAPK genes correlated with poor response. Investigation in a larger cohort is warranted to further understand this combination treatment.

Immunoradiotherapy Response in Advanced Solid Malignancies

Onderdonk et al. | Page 6437

Multisite stereotactic body radiotherapy followed by pembrolizumab (SBRT+P) has been deemed safe in advanced solid tumors (AST). However, the effect of this combination on overall survival (OS) remains unclear. Luke and Onderdonk and colleagues performed a phase I clinical trial in patients with AST to address this question. ORR, PFS, and OS did not differ between patients receiving pembrolizumab with complete- or partial-Rx SBRT to multiple sites. The primary effect of combination treatment was observed in irradiated metastases with no evidence of an abscopal effect. Elevated post-SBRT expression of DNASE1 correlated with evidence of increased cytolytic T-cell function and tumor response. A larger, randomized trial is necessary for further assessment of this treatment approach.

CT Volume and Modeling to Detect Cancer Treatment Effects

Maitland et al. | Page 6464

Response evaluation criteria in solid tumors (RECIST) has many detractors. To improve on RECIST-based clinical trials, new strategies like digital measurement of tumor volume, and computational modeling of linear lesion measurements over time have separately been proposed but not widely adopted. Maitland and colleagues directly measured tumor volume from CT images of patients with colorectal cancer in 2 phase III trials and used these measurements for tumor growth inhibition modeling. The observed improvements in statistical power suggest that if both methods were applied together, trials to show one treatment strategy is superior to another would require many fewer patients.

Concomitant Neurotoxicities of Cisplatin

Trendowski et al. | Page 6550

Millions of cancer patients each year receive cisplatin-based chemotherapy. Hearing loss, tinnitus, and peripheral neuropathy are neurotoxic side effects of cisplatin that have been studied independently; however, a subset of patients remains at risk for multiple neurotoxicities. Trendowski and colleagues determined that patients who were older, received larger cumulative cisplatin doses, had higher residual serum platinum levels, used tobacco, or had hypertension were at greater risk for multiple severe toxicities. Recommended survivorship care plans should include monitoring of blood pressure, encouragement of smoking cessation, and avoidance of additional ototoxic insults, such as noise exposure.
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