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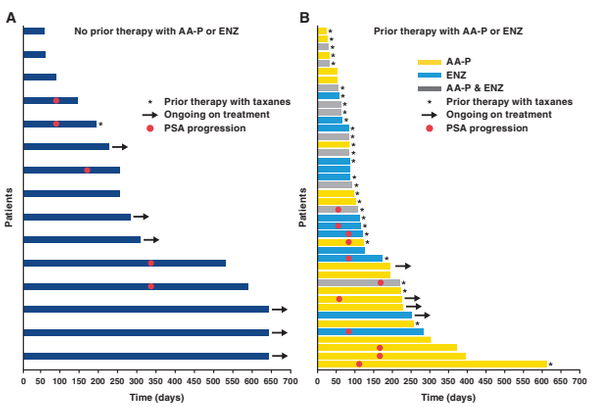
CLINICAL CANCER RESEARCH

HIGHLIGHTS

Selected Articles from This Issue

Apalutamide with Abiraterone Acetate and Prednisone in mCRPC



Posadas *et al.* | Page 3517

Apalutamide, a next-generation androgen receptor (AR) inhibitor, is currently approved for patients with both nonmetastatic and metastatic castration-resistant prostate cancer (mCRPC) receiving androgen deprivation therapy. However, the combination of apalutamide and AR signaling inhibitors, such as abiraterone acetate, in CRPC has not been studied extensively. Posadas and colleagues conducted a phase Ib study to evaluate the pharmacokinetics, safety, and antitumor activity of apalutamide combined with abiraterone acetate and prednisone (AA-P) in patients with mCRPC. No significant pharmacokinetic interaction was observed between apalutamide and abiraterone; however, treatment with apalutamide decreased exposure to prednisone. Treatment with apalutamide plus AA-P was well tolerated, with evidence of antitumor activity in patients with late-stage disease, including those who have disease progression while taking AR signaling inhibitors. These results support further clinical development of this combination in patients with mCRPC.

Glioblastoma-Mediated Immune Dysfunction of Transferred CMV-Specific T Cells

Weathers *et al.* | Page 3565

Cytomegalovirus (CMV) antigens occur in glioblastoma but not in the normal brain, making them potential immunological targets for the treatment of this disease. Weathers and colleagues developed a strategy to expand polyclonal CMV pp65-specific T cells from glioblastoma patients and conducted a phase I trial to assess the safety and efficacy of administering these cells to patients in combination with temozolomide. No dose-limiting toxicities were observed with this regimen. Of 16 patients enrolled, patients showed an objective response, including one complete response. While repeated infusions of CMV-T cells led to increased levels of circulating CMV^{+} $CD8^{+}$ T cells, the effector function of these cells was limited, suggesting that further immunomodulation is necessary for expanding this strategy in further trials.

Therapy Efficacy Post-Venetoclax Failure in R/R CLL

Mato *et al.* | Page 3589

BTK (BTKi) and BCL2 inhibitors (BTKi) are highly effective therapies for CLL in both frontline relapsed/refractory settings. Although the efficacy of venetoclax post-BTKi has been well described, data on BTKi after venetoclax failure is limited. Mato and colleagues assessed the response of patients treated with numerous agents after failing venetoclax therapy. The efficacy of BTKi monotherapy was not dependent on prior venetoclax treatment. BTKi and allogeneic stem cell transplantion were the most effective treatment strategies post-venetoclax. These data support the early use of venetoclax for CLL patients.

Synchronous DCIS and Invasive Ductal Carcinoma

Pareja *et al.* | Page 3682

Ductal carcinoma *in situ* (DCIS) is a nonobligate precursor of invasive breast cancer. To investigate the intralesion genetic heterogeneity and clonality in DCIS, Pareja and colleagues assessed the genomic landscape of synchronously diagnosed ductal carcinoma *in situ* (DCIS) and invasive ductal carcinomas of no special type (IDC-NST), and of pure DCIS *via* whole-exome sequencing. DCIS were revealed to be genetically advanced lesions with high levels of intratumor heterogeneity. The molecular mechanisms underpinning progression to invasive carcinoma were diverse and varied from case to case, and clonal selection was detected in roughly one-third of cases. These findings suggest that progression from DCIS to invasive breast cancer is a multifaceted process.

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