Clinical Cancer Research **Highlights**

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Selected Articles from This Issue

## Combination Therapy with Enzalutamide and Cancer Vaccine

**Ardiani *et al.*** **Page 6205**

Most patients on androgen deprivation therapy eventually develop castration-resistant prostate cancer (CRPC). Here, the recently approved androgen antagonist enzalutamide was evaluated in combination with immunotherapy in a mouse transgenic prostate cancer model. This article described a novel immunogenic modulation property of enzalutamide, where treatment of enzalutamide improves tumor cells' sensitivity to T-cell mediated attack. *In vivo*, enzalutamide reduced genitourinary tissue weight, enlarged thymus, and increased levels of T-cell excision circles. The combination of enzalutamide and immunotherapy significantly improved overall survival of transgenic mice with advanced disease. These data support the combination of enzalutamide and immunotherapy as a promising treatment for CRPC.

## HERV-K Immunogenicity and Poor Prognosis of Prostate Cancer

**Reis *et al.*** **Page 6112**

The role of human endogenous retroviruses (HERV) in cancer is uncertain. To explore the expression and immunogenicity of a recently described GAG protein encoded by HERV-K, Reis and colleagues analyzed cancer patient tissues and sera for reactivity to GAG-HERV-K. GAG-HERV-K was highly expressed in prostate cancer tissues and regulated both by promoter demethylation and androgen stimulation. A subset of prostate cancer patients had serum antibodies to GAG-HERV-K, which correlated with advanced disease stages and worse survival. This work characterizes one of the first human tumor antigens of retroviral origin, with potential as a biomarker for progression of prostate cancer.

## CP-870,893 Plus Gemcitabine in Pancreatic Carcinoma

**Beatty *et al.*** **Page 6286**

CD40, a member of the TNF receptor superfamily, is a major determinant of antitumor immunity. In this phase I study, Beatty and colleagues investigated the tolerability and clinical impact of an agonist CD40 monoclonal antibody (CP-870,893) when administered in combination with gemcitabine for the treatment of patients with chemotherapy-naive advanced pancreatic carcinoma. Treatment was well-tolerated and associated with preliminary evidence of efficacy. Using novel analyses of metabolic imaging, treatment response heterogeneity was observed between primary and metastatic lesions. Findings from this study highlight the biologic heterogeneity of pancreatic carcinoma and demonstrate a role for metabolic imaging in understanding treatment responses.

## Proteomic Markers of BMN 673 Response in SCLC

**Cardnell *et al.*** **Page 6322**

Building on their recent findings that PARP1 is a potential therapeutic target in small cell lung cancer (SCLC), Cardnell and colleagues evaluated the activity of a novel PARP inhibitor and identified biomarkers of response. SCLC xenograft models exhibited exquisite sensitivity to the PARP inhibitor, BMN 673. Further, the authors identified a group of DNA repair proteins that are potential predictive biomarkers and discovered a role for cotargeting the PI3K pathway to enhance sensitivity to PARP inhibition. The biomarkers identified here show great promise as predictors of response and have potential to impact ongoing trials of BMN 673 and other PARP inhibitors in SCLC.

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