



## PI3K Inhibitor Buparlisib with MEK Inhibitor Trametinib

Bedard *et al.* Page 730

This phase Ib study provides information on a potential new treatment with MEK and PI3K inhibitors for epithelial low-grade ovarian cancer. The combination of oral pan-PI3K inhibitor buparlisib and MEK1/2 inhibitor trametinib has a MTD of buparlisib 70 mg and trametinib 1.5 mg daily and a RP2D of buparlisib 60 mg and trametinib 1.5 mg daily in patients with mutant BRAF/RAS solid tumors. Predominant toxicities of the combination were gastrointestinal and dermatological, requiring frequent dose interruption and/or dose modification. This oral combination demonstrated promising antitumor efficacy (29% confirmed ORR) in KRAS mutant low-grade ovarian cancer.

## BRCA1-like Profile Predicts High-Dose Alkylating Chemotherapy

Schouten *et al.* Page 763

Preclinical evidence suggests the benefit of double-strand break-inducing chemotherapy in BRCA1 deficient cancer cells. BRCA1-like classification was tested to predict for benefit of tandem ifosfamide, epirubicin, and carboplatin in high-risk breast cancer patients. Patients with a BRCA1-like tumor had a five-fold reduction in recurrences or death. Patients with a defect in DNA repair through BRCA1 inactivation, identified by BRCA1-like classification, benefit from the investigated regimen. This can be further investigated using the same biomarker-treatment combination, which is available right now, or exchanging for an alternative biomarker or treatment that would improve, respectively, identification or treatment of relevant patients.

## Real-time NIR Image-Guided Surgery for Optimal Tumor Resection

Neuman *et al.* Page 771

Positive Surgical Margin (PSM) is a major concern of radical prostatectomy. If the cancer can be visualized in real time during surgery, PSM can be minimized or eliminated. Neuman and colleagues designed and fabricated an optimized light source/camera combination for use with a small molecule that fluoresce in the near-infrared range. They demonstrate reduction of PSM in a mouse model and the utility of this combination in a large animal laparoscopic surgical model. This system has the potential to be implemented in contemporary prostate cancer surgery without affecting the common surgical pathway, help detect residual disease, and minimize or eliminate PSM.

## CD70 Is Regulated by pVHL and Enhances CD27 Release in ccRCC

Ruf *et al.* Page 889

CD70 is strongly expressed in clear cell renal cell carcinoma (ccRCC). Ruf and colleagues performed comprehensive *in situ* and functional *in vitro* assays to elucidate the mechanism of CD70's upregulation in ccRCC. They demonstrated that CD70 expression is driven by HIF as a consequence of pVHL loss of function. Furthermore, CD70-expressing ccRCC and the presence of CD27<sup>+</sup> T cells in tumor infiltrating lymphocytes correlated with worse patient outcome. CD70-mediated release of sCD27 *in vitro* may explain the increased sCD27 concentrations in sera of patients with CD70-expressing tumors and suggest sCD27 as a putative serum marker for CD70-positive ccRCC patients.