**HIGHLIGHTS**

**Immune Activation after Ipilimumab in Cervical Cancer**

*Da Silva et al.* | Page 5621

Immune biomarkers remain lacking to predict response to immunotherapy in ovarian cancer. Da Silva and colleagues performed a phase I clinical trial (GOG-9929) assessing adjuvant immune modulation therapy with the checkpoint inhibitor ipilimumab (anti-CTLA4) following chemoradiation therapy (CRT) in women with newly diagnosed node-positive human papillomavirus-related cervical cancer. In these patients, CRT alone stimulated T-cell activation. Addition of ipilimumab sustained and, in the CD4+ T-cell population, enhanced T-cell activation. Expansion of the CD4+ICOS and CD4+PD-1+ populations post-CRT were associated with lower risk of progression while increases in inflammatory cytokines TNFa, IL-6, and IL-8 post-CRT were associated with higher risk of tumor progression. These data suggest that ipilimumab after CRT may strengthen the antitumor response to cervical cancer. This combination may promote favorable immune changes in high risk patients.

**Vorinostat and Sirolimus or Everolimus in Hodgkin Lymphoma**

*Janku et al.* | Page 5579

Activation of the PI3K/AKT/mTOR pathway contributes to cancer progression and therapeutic resistance. Preclinical and early clinical data have suggested that dual targeting of HDAC and mTOR may have synergistic activity in treatment-refractory Hodgkin lymphoma. To explore this hypothesis, Janku and colleagues designed a phase I study combining vorinostat, an HDAC inhibitor, with sirolimus or everolimus, mTOR inhibitors, in patients with relapsed/refractory Hodgkin lymphoma. These combinations showed promising clinical efficacy, with an objective response rate of 55% and 33% in patients treated with vorinostat plus sirolimus and vorinostat plus everolimus, respectively. These results provide rationale for future investigation in Hodgkin lymphoma.

**Integrative Analysis of Pleomorphic Dermal Sarcomas**

*Klein et al.* | Page 5638

Pleomorphic dermal sarcoma (PDS) is a rare malignant cutaneous tumor with an unknown cell of origin. Klein and colleagues performed whole exome sequencing, transcriptomic analysis, as well as quantitative image analysis on a collection of PDS tumors. PDS exhibited a universally high mutational load (42.7 mutations per mega base) with an inflamed, immunogenic tumor microenvironment. Three cases of PDS showed response to immune checkpoint blockade. Local mutation rate variation together with mRNA expression data demonstrated that PDS formed a distinct entity of fibroblastic differentiation, with PDGFRB as a lineage marker that may qualify as diagnostic biomarker. Further study will further elucidate the clinical utility of these data.

**Immunologic Changes with Chemotherapy in TNBC**

*Axelrod et al.* | Page 5668

Anti-PD-L1 immunotherapy was recently approved for metastatic triple negative breast cancer (TNBC) in combination with nab-paclitaxel. However, the effects of chemotherapy on local and systemic immune responses in women with breast cancer require further assessment. Axelrod and colleagues show that, specifically in patients with TNBC, increases in immune-related genes over the course of chemotherapy treatment correlated with improved outcome. However, increased evidence of cytotoxic T cells in the peripheral blood was associated with persistent disease following chemotherapy and disease recurrence following surgery. Such immune-related signatures may identify patients likely to respond to similar treatment regimens.
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