Poster 23: Identifying Non-Responders Early: Blood-Based Markers of Resistance in Endometrial Cancer to Atezolizumab and Bevacizumab

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Topic
Endometrial

Objectives
The treatment paradigm for advanced and recurrent endometrial cancer (EC) is evolving with immune checkpoint inhibitors (ICI) as standard of care for dMMR tumors and increasingly used in pMMR disease. However, many patients do not derive durable benefit and this highlights the need for early biomarkers of response. In a Phase 2 clinical trial, we evaluated atezolizumab plus bevacizumab (atezo/bev) in recurrent EC without prior ICI and aimed to identify early blood-based correlates of response. We hypothesized that peripheral immune profiling during treatment would reveal immune programs associated with non-response.

Methods
Peripheral blood was collected at baseline and after two cycles from patients in a multicenter, single-arm phase II trial (NCT03526432) of atezolizumab (1200mg) plus bevacizumab (15mg/kg) in advanced or recurrent EC without prior ICI. High-dimensional immune profiling with 42 markers was performed using cytometry by time of flight. Patients were categorized as responders (complete response, partial response, stable disease) or non-responders (progressive disease) and longitudinal immune profiles were compared.

Results
Non-responders showed expansion of suppressive myeloid populations, including non-classical monocytes and reduced CD45+ leukocyte frequencies. An immunosuppressive T cell profile was observed, with higher Treg frequencies, enrichment of ICOS+ Tregs, and an elevated Treg/Teff ratio. CD8+ T cells demonstrated dysfunction, with persistent Fas+CD27+ populations but diminished cytotoxic potential, reflected by reduced granzyme B expressing TCRγδ T cells and decreased differentiated CD8+CD56-CD57+ effector cells.

Conclusions
We identified blood-based immune markers detectable early in treatment of patients who did not respond to atezo/bev. There was an association of an early, systemic immune-angiogenic escape program characterized by coordinated myeloid expansion, regulatory T cell enrichment, and impaired effector T cell maturation. These findings suggest limited response can be seen early after two treatment cycles and reflects active immune suppression rather than exhaustion. Early peripheral immune profiling may enable prediction of non-response and inform combination strategies to restore effective antitumor immunity in EC.