Poster 53: Actionable Biomarker Co-Expression in Advanced Ovarian Cancer: Folate Receptor alpha Expression and Related Markers

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Topic
Ovarian

Objectives
Folate receptor-α is an established therapeutic target in ovarian cancer and identifies candidates for treatment with the antibody–drug conjugate mirvetuximab soravtansine. However, patterns of co-expression between folate receptor-α and other actionable biomarkers, and their implications for treatment selection and outcomes, remain incompletely characterized; we aimed to characterize biomarker co-expression patterns.

Methods
We conducted a single-institution cohort study of 110 patients with platinum-resistant ovarian cancer treated with mirvetuximab soravtansine (2019-2025). Tumor biomarkers were assessed using immunohistochemistry, fluorescence in situ hybridization, and next-generation sequencing. Co-expression patterns among ten biomarkers including folate receptor-α, estrogen receptor, progesterone receptor, human epidermal growth factor receptor-2, BRCA, homologous recombination, loss of heterozygosity, programmed death-ligand 1, claudin-6, and tumor mutational burden were evaluated using Jaccard similarity indices, Cohen's kappa statistics, and correlation analyses. Exploratory survival analyses examined progression-free survival and overall survival by folate receptor-α expression and estrogen receptor-defined subgroups.

Results
Folate receptor-α expression was high in 80% of tumors and intermediate/low in 20%. Co-expression analyses demonstrated largely independent biomarker patterns, reflecting significant biological heterogeneity. A hormone receptor–associated cluster emerged, including strong co-expression between folate and estrogen receptor (Jaccard=0.76), and moderate overlap between estrogen receptor and claudin-6 (0.62), programmed death-ligand-1 and estrogen receptor (0.56), and programmed death-ligand-1 and folate receptor (0.50). Survival outcomes were comparable between folate receptor-α-high and folate receptor-α-intermediate/low tumors. Among folate receptor-α-high tumors, estrogen receptor expression (≥10%) did not meaningfully stratify progression free or overall survival outcomes.

Conclusions
These findings support evaluating folate receptor-α expression along a graded continuum, challenging the current binary classification for mirvetuximab soravtansine monotherapy eligibility. Biomarker co-expression in advanced ovarian cancer is heterogeneous, with emerging patterns supporting biomarker-informed combination and sequencing strategies, with preclinical works signifying the role of estrogen receptor modulation potentiating treatment efficacy. Prospective validation is needed to refine multi-marker frameworks and guide biologically driven treatment decisions.

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