2025 ASCO® ANNUAL MEETING

Topic Category: Gynecologic Cancer > Ovarian Cancer

Authors: Rachel Culp-Hill, Charles Nichols, Brendan Giles, Robert A. Law, Enkhtuya Radnaa, Kian Behbakht, Benjamin G Bitler, Emma Crosbie, Vuna Fa, Violeta Guthrie, James Robert White, Abigail McElhinny

A multi-omics approach using lipids and proteins for early detection in individuals with signs and symptoms of ovarian cancer

Background:
Late-stage ovarian cancer (OC) is diagnosed in 80% of patients, leading to a five-year survival rate below 30% and ranking OC as the fifth leading cause of cancer-related deaths in women. Non-specific abdominal symptoms overlap with benign disorders, delaying diagnosis. Testing symptomatic individuals can detect low disease burden, enabling high complete cytoreduction rates. However, current diagnostic tools lack sensitivity and specificity for early-stage OC, underscoring the critical need for novel biomarkers and approaches.

Methods:
We conducted a multi-omics analysis of serum from two independent, clinically annotated cohorts. Specimens were analyzed using UHPLC-MS untargeted lipidomics and a protein biomarker panel. Cohort #1 (N=544) from the University of Colorado Gynecologic Tissue and Fluid Bank and commercial vendors included patients diagnosed with OC (N=219: 80 early-stage I/II, 139 late-stage III/IV), and non-cancerous controls (N=325) for biomarker discovery. Cohort #2 (N=423) from Manchester University NHS Foundation Trust and commercial vendors included prospectively enrolled individuals with signs and symptoms of OC. Samples included patients diagnosed with OC (N=109 total: 52 stage I/II, 57 stage III/IV), and non-cancerous controls (N=314). Cohorts were processed independently.

Results:
Over 1000 features were identified in both cohorts. There was a significant overlap in common features confirming importance in indication for use population. The top features confirmed in both cohorts enabled machine learning-based modeling. Biomarker classes were modeled separately (lipids only, proteins only) and in combination (lipids and proteins), employing 20-fold cross validation. Models containing multi-omic features consistently exhibit the highest AUC compared to individual biomarker classes. AUC for the top-performing model applied to both cohorts was 95% (CI 94-96) for all controls vs. all OC, and 92% (CI 89-95) for all controls vs. early-stage OC. When compared with normal individuals, the AUC vs all OC across stages and sub-types was 97% (CI 96-98).

Conclusions:
Our top-performing models contain >50 multi-omic features common across two independent cohorts, comprised of 967 unique individuals. Combining LC-MS-based lipidomic profiling of serum with proteins represents a promising new approach as a clinical diagnostic for detecting OC in this complex patient

population. Early detection in women with signs and symptoms of OC and faster triage to specialty care may lead to improved patient outcomes.