Objectives
- Debubbling surgery followed by adjuvant platinum-based therapy is the standard of care for patients diagnosed with ovarian cancer.
- While most patients derive significant clinical benefit from this treatment approach, a subset progresses rapidly.
- No known biomarkers are able to accurately identify which patients will fail standard-of-care therapy.
- A test that could identify patients unlikely to benefit from standard of care (SOC) approaches could inform treatment strategy.
- The aim of this study was to develop a test able to provide useful prognostic information for patients with ovarian cancer undergoing surgery and adjuvant chemotherapy.

Methods
- Serum samples were taken at the time of surgery were available for 138 patients with primary ovarian cancer.
- Matrix-assisted laser desorption/ionization (MALDI) mass spectra were generated from the tumor tissue using the Deep MALDI method. This approach allows investigators to probe the serum proteome over four orders of magnitude in abundance.
- Spectra were processed to render them comparable and features (peaks) were defined. The integrated areas under the spectra for these features were used to generate feature values.
- Patient clinical data were input into a test development platform optimized for the design of molecular diagnostic tests and able to produce reliable results from development set data. This platform utilizes machine learning methods to design a binary classifier using a semi-supervised approach that iteratively refines classifier and training class simultaneously.
- A hierarchical classification schema was designed to stratify patients into three groups with better (positive), worse (negative) and intermediate outcomes.
- The cohort was split into good and poor outcome groups and then the poor outcome groups was again split into better and worse outcome groups to identify the patients with the poorest outcomes.
- Classifiers were trained on clinically distinct subgroups and only samples that classified into the good prognosis group across all classifiers were assigned a positive prediction.
- Performance of the test was assessed using sample classifications only from data when the sample was not used in training (out-of-bag estimator).
- Test performance was evaluated using Kaplan-Meier plots of time-to-event outcomes. Differences in survival between groups were assessed with hazard ratios (HRs) and log-rank p values.
- The test was also assessed as a binary classification by combining the intermediate and positive outcome groups to define a new negative group which could be compared with the positive group.
- The performance of the test was also assessed in the subgroup of patients with confirmed FIGO stage III or IV disease.

Results

Entire Cohort
- The test classified 28 (20%) and 49 (36%) patients in the poorest and best prognosis groups, respectively.
- In the entire cohort (Figure 1), DFS in the negative (N) group was significantly shorter than in the intermediate (I) and positive (P) groups (N vs. I: HR = 0.28 (95% CI 0.16-0.46), p < 0.001; N vs. P: HR = 0.14 (95% CI 0.07-0.29), p < 0.001; the same was true for OS (N vs. I: HR = 0.28 (95% CI 0.15-0.52), p < 0.001; N vs. P: HR = 0.14 (95% CI 0.05-0.37), p < 0.001) (Figure 2).
- Only 52% of patients in the N group were disease free at 6 months vs. 95% in the P group (Table 3).
- Only 41% of patients in the N group were alive at 12 months vs. 95% in the P group (Table 3).
- The binary test classified 20 patients in the N group and 59 patients (20% and 39%, respectively) in the intermediate (I) and positive (P) groups (95% CI 0.85-0.95).

Conclusions
- The developed test stratifies patients into groups with significantly different outcome.
- The test can identify patients who are likely to progress rapidly, with SOC treatment approaches and are unlikely to be optimally debulked.
- Validation of the findings of this study is necessary in independent cohorts and further development of the test is ongoing.

References