A broad retrospective molecular characterization of 348 FFPE platinum-sensitive tumors is required to further refine the definition of molecular subtypes and identify targeted therapies for this patient population. To this end, we have performed a large-scale genomic and transcriptomic retrospective analysis of 348 FFPE tumor samples from a cohort of platinum-sensitive HGSOC patients collected from over 100 clinical sites.

MATERIALS AND METHODS
FFPE tumors and matched PBL specimens were sourced from the MORAB-003-004 clinical trial. Macrodissection of FFPE resected tumor slides was performed to enrich for tumor content. RNA expression was profiled by whole transcriptome RNA-Seq. DNA variants were analyzed by the AmpliSeq® Cancer Hotspot Panel (Thermo Fisher). A subset of tumor and matched germline (PBL) specimens (N=181) were assessed for tumor content. RNA expression was profiled by whole transcriptome RNA-Seq. Genetic and genomic characterization of platinum-sensitive tumors was performed with the OncoScan® FFPE Assay Kit (Affymetrix).

RESULTS
Figure 1. Summary of retrospective molecular characterization of MORAB-003-004. Tumor tissue resected from patients (x-axis) was assessed for tumor content. RNA expression was profiled by whole transcriptome RNA-Seq.

Figure 2. BCR-ABL1 fusion events were identified in 11/146 (7.5%) subjects. A BCR-ABL1 fusion was identified in each of the 11 subjects with available data.

Figure 3. Consensus of aberrations has both f nodal and non-GNAS fusions. The GNAS allele is the most frequent fusion, with 50/146 (34%) subjects found to have a GNAS fusion. The second most frequent fusion was the ABL1 allele, with 25/146 (17%) subjects found to have an ABL1 fusion.

Figure 4. BCR-ABL1 fusions are identified with both high and low tumor content. A BCR-ABL1 fusion was identified in each of the 11 subjects with available data.

Figure 5. Consistent with TCGA and other HGSOC datasets, the CLOVAR nonsynonymous (nES) signature was negatively prognostic (all subjects analyzed independent of treatment). Kaplan-Meier analysis of GCSR score tertiles showed a progressive increase in overall survival for subjects with higher GCSR score tertiles. Higher score tertiles indicated a more favorable outcome for each respective subtype.

CONCLUSIONS
The CLOVAR signature was reproduced in a cohort of FFPE HGSOC tumors with a previously reported association between the mesenchymal subtype and poor prognosis. The spectrum of DNA mutations, CNVs, gene fusions, and transcriptional subtypes affirms the representative nature of this HGSOC cohort. The study further serves as a model for extracting known and novel tumor signatures.