Background Clinical cancer management with precision therapeutics is generally optimized with predictive molecular and phenotypic profiling. However, in ovarian cancer (OC) there has been limited clinical benefit demonstrated. Vigil (Gradalis, Dallas, TX) is a novel plasmid engineered autologous tumor cell immunotherapy designed to achieve a trifecta of immune anticancer activity using a unique bi-shRNA DNA based technology. The trifecta of systemic activity involves knock down of TGFβ1 and TGFβ2 which function as tumor suppressor cytokines, increased GMCSF expression to enhance local immune function and presentation of personal clonal neoantigen epitopes via use of autologous cancer tissue. Phase 2b randomized double blind controlled study (VITAL) of Vigil involving newly diagnosed stage IIIB/IV OC patients undergoing frontline maintenance therapy revealed significant improvement in relapse free and overall survival (RFS/OS) in BRCA1/2 wt, HRP patient subgroups. We explored molecular biomarker relationship to clinical benefit with NanoString assessment and comparison to RFS and OS.

Methods All patients enrolled on the VITAL study had RNA isolated from tumor tissue at time of procurement and submitted for NanoString PanCancer Immuno-Oncology 360™ CodeSet using the nCounter® SPRINT platform. All 750 genes underwent a predefined statistical NanoString algorithm (NSA) to assess correlation with RFS and OS. First, a univariate Cox model was used to determine the gene Z-score for RFS and OS in Vigil treated patients at 1% significance. Next, a Cox proportional hazards model with interaction term was utilized to identify genes predictive of Vigil response in both Vigil and placebo treated patients. Patients were then dichotomized into high and low expression based on median gene expression and Kaplan Meier curves were generated. Finally, the my.stepwise.coxph function was used to select genes associated with RFS and OS in Vigil treated patients.

Results Using NSA, high expression of ENTPD1/CD39 (the rate limiting enzyme in the adenosine pathway) was identified as a predictor of RFS (n=23 vs n=23; median not achieved vs 8.1 months, p=0.00007) and OS (n=23 vs n=23; median not achieved vs 41.4 months, p=0.013) benefit to Vigil irrespective of HRP status. Results further suggested additional benefit in HRP subset but were limited by small number of patients.

Conclusions NSA was successfully implemented and identified ENTPD1/CD39 high expression correlated with RFS and OS benefit in OC treatment population to Vigil. Further consideration of NSA utilization to identify populations that would benefit from investigational targeted therapies is warranted. ENTPD1 high may predict a more sensitive OC population to Vigil.

Trial Registration NCT02346747