Abstract EP299/#540 Figure 1 Kaplan-Meier estimates of overall survival

Conclusions Despite differences in patient and treatment characteristics, OS of patients treated in the control arm of OVPH-PREC1 was similar to patients treated outside the trial. This finding does not lend support for the hypothesis that the survival benefit seen in the trial was caused by inferior outcome of patients selected for the trial. These results support the administration of HIPEC in stage III EOC patients undergoing interval CRS in clinical practice.

EP299/#232 GENOMIC INSTABILITY AS A DETERMINANT OF IMMUNE ESCAPE IN OVARIAN CANCER

1Ignacio Vazquez-Garcia*, 2Florian Ulitz, 3Nicholas Ceglia, 4Jamie Lim, 5Michelle Wu, 3Neeman Mohibullah, 7Juliana Nyazov, 8Arvin Eric Ruiz, 9Robert Soslow, Lora Ellenson, 10Nadeem Abu-Rustum, 11Carol Aghajanian, 12Clare Friedman, 13Andrew McPheron, 14Britta Weigelt, 15Dmitry Zamarin, 16Schrib Shah. 1Memorial Sloan Kettering Cancer Center, 2Computational Oncology, Department of Epidemiology and Biostatistics, New York, USA; 3Memorial Sloan Kettering Cancer Center, Department of Surgery, New York, USA; 4Memorial Sloan Kettering Cancer Center, Department of Pathology, New York, USA; 5Memorial Sloan Kettering Cancer Center, 6Integrated Genomics Operation, New York, USA; 7Memorial Sloan Kettering Cancer Center, Cancer Center, Department of Pathology, New York, USA; 8Memorial Sloan Kettering Cancer Center, Department of Medicine, New York, USA

10.1136/ijgc-2022-igcs.390

Objectives Genomic instability is a hallmark of human cancer, with fundamental relevance to cancer etiology and evolution, anti-tumor immunity and therapeutic response. High-grade serous ovarian cancer (HGSOC) is an archetypal cancer of genomic instability defined by distinct mutational processes, intraperitoneal spread and tumor heterogeneity. As immunotherapies have thus far proven ineffective in HGSOC, we sought to establish the determinants of immune evasion in its natural disease history.

Methods We studied the impact of mutational processes and of spatial heterogeneity on cellular phenotypes in the tumor microenvironment (TME), using genome-based stratification of homologous recombination proficient (HRP) and deficient (HRD) disease subtypes, profiling single cell phenotypes from ~1 million cells by single cell RNA sequencing, and site-matched in situ spatial imaging of 160 tumor sites obtained from 42 treatment-naive patients.

Results Mutational processes in HRD-Dup (BRCA1 D1-like) tumors were associated with a high neoantigen burden, cell-intrinsic JAK/STAT signaling and CD8+ T cell dysfunction; HRD-Del (BRCA2 D1-like) tumors presented expanded M2-type macrophage populations; and foldback inversion (FBI, HRP) tumors were associated with cell-intrinsic TGFβ signaling, immune exclusion and predominantly naive T cells. HLA loss of heterozygosity was a common mechanism of immune escape in HRD tumors, connecting evolutionary selection with immune states. Multi-region sampling also revealed substantial spatial variation, highlighting the adnexa as an ‘immune-privileged’ site, and suggesting that organ microenvironments can direct immune pruning in patients with widespread disease.

Conclusions Our findings yield mechanistic insights linking mutational processes in HGSOC to intra- and inter-patient variation in immune resistance, which can be leveraged to optimize future immuno-therapeutic strategies.