Conclusion Pelvic and para-aortic lymphadenectomy in surgical staging of eOC improves DFS for the price of increasing post-operative complications and time to chemotherapy but does not affect OS.

Abstract 28 Figure 1 Kaplan-Meier survival curves for recurrence-freesurvival in the fully triaged MMRd patients

Abstract 29

Introduction Here we aimed to evaluate the prevalence and prognosis of Lynch Syndrome (LS)-associated endometrial cancer (EC) in relation to sporadic mismatch repair deficient EC (MMRd-EC) in the combined PORTEC-1,-2 and -3 trials comprising 1336 ECs.

Methods MMR-status was determined by MMR-immunohistochemistry (MLH1/PMS2/MSH6/MSH2). MMRd-ECs with detected promoter hypermethylation of MLH1 were classified as sporadic (methylated MMRd-EC). For unmethylated MMRd-ECs detected promoter hypermethylation of MLH1 were classified as sporadic MMRd-EC caused by hypermethylation. MMRd-EC seems to have a better overall and recurrence-free survival than sporadic MMRd-EC caused by hypermethylation. Further research into the underlying causes of non-hypermethylated somatic MMRd-EC is ongoing.

Objectives Abnormalities in mismatch repair (MMR) gene may be the result of pathogenic germline (Lynch syndrome) and somatic mutations as well as epigenetic events. We aimed to examine the cause of MMR defects (MMRd) in non-serous/non-mucinous ovarian cancer (OC) through targeted mutational sequencing.

Methods Women with non-serous/mucinous OC (N = 215) were prospectively recruited from three cancer centers in Ontario, Canada. Tumors were assessed for MMR protein expression by immunohistochemistry. Matched MMRd tumor-normal samples were run on a custom NGS panel to identify germline and somatic mutations, copy number variants, rearrangements and promoter methylation in MMR and associated genes.

Results Of 215 women enrolled in our study, 185 (86%) had OC and 30 (14%) had synchronous OC and endometrial cancer. Twenty-eight (13%) cases were MMRd, 11 of which were synchronous. Using the NGS panel, Lynch syndrome (LS) was detected in 39% of MMRd cases (11/28; 7 OC and 4 synchronous): 7 MSH6, 2 MLH1, 1 PMS2, and 1 MSH2. An explanation for the observed MMR phenotype was available for 18/20 deficient cases, including 9/10 MLH1/-PMS2- (7 somatic methylation, 1 bi-allelic somatic deletion, 1 germline mutation), 0/1 PMS2-, 6/7 MSH6- (6 germline mutations) and 2/2 MSH2/-MSH6- (1 germline mutation, 1 bi-allelic somatic mutation). Concordance between clinical and research panel sequencing results was 90%.

Conclusions Use of our custom NGS panel allows for the streamlined assessment of hereditary and somatic causes of MMR deficiency in OC and may be an attractive screening strategy for LS in this population.