Prevalence of Low Anterior Resection Syndrome in Patients with Advanced Stage Epithelial Ovarian Cancer

Introduction/Background
Approximately 50% of high-grade serous ovarian, tubal, or primary peritoneal carcinomas (HGSC) harbor homologous recombination deficiency (HRD). HRD predicts sensitivity for platinum-based chemotherapy and is particularly crucial in selection of patients who could benefit from poly ADP-ribose polymerase inhibitor (PARPi) maintenance treatment after first-line adjuvant chemotherapy. HRD can result from genetic or epigenetic loss of HR genes such as BRCA1/2, however not all genomic alterations leading to HRD are known. We recently developed an optimized HRD test for HGSC (ovaHRDscar) using somatic allelic imbalances; loss of heterozygosity (LOH), large-scale state transitions (LSTs), or telomeric allelic imbalance (TAI). However, the clinical characteristics and real-world significance of HRD remains unknown.

Methodology
We prospectively collected tumor samples from more than 100 patients diagnosed with advanced HGSC or endometrioid ovarian cancer, during primary or interval debulking surgery performed at the Helsinki University Hospital between October 2019 and June 2022. We isolated DNA from fresh-frozen and formalin-fixed paraffin-embedded (FFPE) tumor samples and tested for BRCA1/2 mutations and genomic scarring with ovaHRDscar.

Results
The median age at diagnosis was 67 (range 37–85) years. Of all patients, 33% were diagnosed with Stage III and 67% with Stage IV disease, and 43.5% of patients were treated with neoadjuvant chemotherapy. In 15% of the patients, we found a deleterious BRCA1/2 mutation, two thirds of which were germline mutations. Of the samples, 63.2% were HRD according to ovaHRDscar, including as expected all tumors with BRCA1/2 mutations. Interestingly, 56.3% of the tumors were HRD even in the absence of a BRCA1/2 mutation.

Conclusion
The analysis of the clinical significance of HRDs, including the association with progression-free survival (PFS), platinum-free interval (PFI), and the responses to PARPi are currently ongoing. The results will reveal the real-world clinical outcomes of HRD in advanced ovarian cancer patients.