Tumor-informed ctDNA detection as a predictive marker for postoperative residual disease in epithelial ovarian cancer: A feasibility study

C. Grimm1, V. Paspalj2, L. Postl2, L. Saal3, C. Brueffer3, N. Segui Gracia3, M. Alcaide3, S. Polterauer2, L. Oton3, Y. Chen3, G. Hofstetter4, L. Müllauer4

1 Gynecology and Gynecologic Oncology, MedUni Wien-Medical University of Vienna, Vienna, Austria, 2 General Gynecology and Gynecologic Oncology, MedUni Wien-Medical University of Vienna, Vienna, Austria, 3 SAGA Diagnostics AB, SAGA Diagnostics AB, Lund, Sweden 4 Department of Pathology, MedUni Wien-Medical University of Vienna, Vienna, Austria

Background

Complete tumor resection is the most relevant prognostic factor for overall survival in high grade serous ovarian cancer (HGSOC) patients. The current standard for classification of postoperative residual disease (RD) is surgeon’s subjective evaluation at the end of surgery. Thus, a reliable objective predictive marker is currently missing.

Methods

In this prospective single-center feasibility study, patients with HGSOC, who underwent surgery between July 2021 to December 2022, were included. Tumor tissue was assessed intraoperatively and blood samples were performed preoperatively, at day 2 and 10 postoperatively and subsequently at cycle 1, 3 and 6 of chemotherapy. Low-coverage whole genome sequencing (WGS) was used to identify structural variants (SV), single nucleotide variants (SNVs) and indels in tumor tissue in order to develop personalized digital PCR (dPCR) fingerprint assays.

Results

So far, 33 patients are included in the present analysis, with a median follow up time of 7 (IQR 2-10) months. In all tumor samples, dPCR assays were successfully developed and validated, with a median of 5 biomarkers (SVs and SNVs) per patient. For each patient, an individual SV profile could be established, which remained largely constant throughout multiple tumor localizations of each patient. 32/33 (97%) patients had circulating tumor DNA (ctDNA) detected at baseline at levels ranging from 0.0005 - 31% VAF. Three (10%) patients have been lost to follow without postoperative ctDNA samples. ctDNA was persistently detected in all patients with macroscopic tumor residuals. A significant decrease in ctDNA was observed in all patients with stage I-IIIB disease who had macroscopic complete resection (8 patients). In 8/22 (36%) patients with complete resection, ctDNA decreased below the detection limit. Clinical follow up is ongoing, and analysis of longitudinal samples will be presented at the congress.

Conclusions

In this feasibility study, tumor-informed ctDNA was preoperatively detectable in 97% participants. In patients with multiple tumor biopsies, the fingerprint could be used for monitoring of each location. A decrease in ctDNA detection correlated with complete tumor resection.

Legal entity responsible for the study

Medical University of Vienna.

Funding

SAGA Diagnostics.

Disclosure

or part-time Employment: SAGA Diagnostics. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology