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Research Article

## Genome-wide copy number alterations in circulating tumor DNA as a novel biomarker in high grade serous ovarian cancer patients

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### Abstract

**Purpose:** High-Grade Serous Epithelial Ovarian Cancer (HGS-EOC), is defined by high levels of somatic copy number alterations (SCNA) with marked spatial and temporal tumor heterogeneity. Biomarkers serving to monitor drug response and detect disease recurrence are lacking, a fact which reflects an unmet clinical need. **Experimental Design:** 185 plasma samples and 109 matched tumor biopsies were collected from 46 HGS-EOC patients, and analyzed by shallow whole genome sequencing (sWGS). The percentage of tumor fraction (TF) in the plasma was used to study the biological features of the disease at the time of diagnosis (T0) and correlated with patients' survival. Longitudinal analysis of TF was correlated with CA-125 levels and radiological images to monitor disease recurrence. **Results:** Gain in the clonal regions 3q26.2 and 8q24.3 was observed in the 87.8% and 78.05% of plasma samples, suggesting that plasma sWGS mirrors solid biopsies. At T0, multivariate analysis revealed that plasma TF levels are an independent prognostic marker of relapse ( $p < 0.022$ ). After Pt-based treatment, ctDNA analysis showed a change in the heterogeneous pattern of genomic amplification, including an increased frequency of amplification compared to before platinum-based treatment in the 19p31.11 and 19q13.42 regions. TF in serially collected ctDNA samples outperformed CA-125 in anticipating clinical and radiological progression by 240 days (range: 37-491). **Conclusions:** Our results support the notion that sWGS is an inexpensive and useful tool for the genomic analysis of ctDNA in HGS-EOC patients to monitor disease evolution and to anticipate relapse better than serum CA-125, the used routine clinical biomarker.

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