Presurgery ctdna clearance predicts response to neoadjuvant chemo-immunotherapy in advanced serous ovarian cancer

Abstract Submitter: Paul Van Der Leest, Netherlands*

Co-Authors: Lot Aronson, Bram Thijssen, Mirthe Lanfermeijer, Dorothé Linders, Kalpana Ramkisoensing, Lodewyk Wessels, Hugo Horlings, Willemien van Driel, Daan van den Broek, Gabe Sonke

*The Netherlands Cancer Institute

Abstract

Background

While immune checkpoint inhibitors (ICIs) have revolutionized cancer care, their efficacy in ovarian cancer remains limited. The phase 2 Neo-Pembro trial suggested improved survival to neoadjuvant chemo-immunotherapy for a subset of high-grade serous ovarian cancer (HGSOC) patients. However, biomarkers to predict response to treatment are lacking.

Objective

Here, we monitored circulating tumor DNA (ctDNA) dynamics of HGSOC patients treated with neoadjuvant chemo-immunotherapy in the Neo-Pembro trial to predict treatment efficacy.

Methods

33 previously untreated patients with stage IV HGSOC underwent six cycles of carboplatin-paclitaxel, complemented with pembrolizumab after two cycles and interval cytoreductive surgery after three cycles, followed by adjuvant maintenance ICI treatment for one year. Whole exome sequencing of tumor tissue DNA and targeted sequencing on plasma-derived circulating cell-free DNA were performed to develop personalized droplet digital PCR (ddPCR) assays for 29 patients. Longitudinal ctDNA levels were plotted against progression-free survival (PFS), overall survival (OS) and pathological response.

Results

Baseline ctDNA abundance and early ctDNA dynamics were not related to treatment response and survival. Patients that display ctDNA clearance presurgery had a significantly improved PFS (HR=0.19) and OS (HR=0.15). All patients with a major pathological response presented ctDNA clearance presurgery and remained negative at end of adjuvant maintenance ICI treatment (EOT), of which six did not experience disease recurrence. In all patients with detectable ctDNA at EOT, disease progression eventually occurred. Patients that were ctDNA negative at EOT had prolonged PFS (HR=0.16) and OS (HR=0.12).

Conclusion

Clearance of ctDNA by neo-adjuvant treatment was related to treatment response and associated with prolonged PFS and OS. Detectable ctDNA postsurgery or at EOT was indicative for disease progression, while ctDNA negativity suggested a survival benefit. These data imply that ctDNA monitoring during neoadjuvant chemo-immunotherapy can assist in response prediction and possibly personalized precision therapy. Prospective studies should pursue to evaluate the clinical benefit ctDNA-guided treatment management in advanced HGSOC.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.