Multimodal analysis of plasma ctdna is an independent prognostic marker of survival in ovarian cancer: the mito 16a/mango ov2 clinical trial experience.

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Abstract

Background: Epithelial Ovarian Cancer (EOC) is frequently diagnosed at an advanced stage, and although patients initially respond to platinum-based chemotherapy, most experience relapse. Traditional biomarkers, such as CA-125, have limited predictive accuracy. Circulating tumor DNA (ctDNA), obtained via liquid biopsy, has emerged as a promising tool for monitoring cancer progression, capturing molecular heterogeneity, and detecting minimal residual disease. This study, conducted within the MITO-16a/MaNGO-OV2a clinical trial, evaluates the prognostic utility of two independent ctDNA-derived metrics: plasma tumor fraction (TF) and the proportion of mononucleosome fragmentomic (PF) ratio in predicting outcomes in ovarian cancer patients.

Objective: To assess the potential of combining TF and PF for enhanced prognostic accuracy in terms of overall survival (OS) and progression-free survival (PFS) in EOC.

Methods: A total of 403 plasma samples were collected from 174 patients within the MITO-16a/MaNGO-OV2a clinical trial. Samples were obtained post-surgery, pre-chemotherapy (B1, 167 samples), post-chemotherapy (B2, 116 samples), and at the end of bevacizumab maintenance (B3, 120 samples). TF was measured using shallow whole-genome sequencing (sWGS), and PF was assessed through fragment length analysis. Kaplan-Meier survival curves and Cox regression models were used to evaluate the associations between TF, fragmentomics, and survival outcomes.

Results: At B1, patients with TF levels above the 15.08% cutoff exhibited significantly shorter PFS (15.9 months) compared to those with lower TF levels (22.7 months). Multivariate analysis confirmed TF as an independent prognostic marker for survival (PFS: HR=1.03, p=0.006; OS: HR=1.03, p=0.02). PF was also an independent prognostic marker for PFS and OS (PFS: p=0.01; OS: p=0.005). Combining TF and PF further enhanced prognostic accuracy, with patients showing high TF and PF levels experiencing significantly shorter PFS (HR=3.58, p<0.001) and OS (HR=4.06, p<0.001).

Conclusion: in the post-surgery setting, before chemotherapy, multimodal ctDNA-based approach provides valuable prognostic insights in advanced EOC, potentially informing treatment decisions and disease monitoring. The integration of fragmentomics with TF analysis enhances prognostic predictions, underscoring the clinical utility of liquid biopsy in EOC management.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.