Association between angiogenesis-related genes and the response to multimodal therapy in high grade serous advanced ovarian carcinoma (AOC)

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Aim: Cytoreductive surgery plus chemotherapy is the standard of care in high grade serous AOC. To date, the outcome prediction after multimodal therapy remains one of the most important challenges for patients (pts) stratification according to effective treatments. Angiogenesis has maintained its prominent role in the ovarian cancer research field for years, being one of the most studied processes for the identification of alternative therapies in AOC. Previous studies identified several genes involved in angiogenesis as prognostic markers in this tumour.

Methods: We included 39 pts with stages III or IV high grade serous ovarian cancer. These pts underwent surgical cytoreduction and received a carboplatin plus paclitaxel chemotherapy regimen. RNAs were collected from formalin-fixed paraffin embedded samples. Expression levels of 82 angiogenesis-related genes were measured using quantitative real-time polymerase chain reaction (qRT-PCR).

Results: 74% of pts (29 out of 39) achieved a complete response after surgical and chemotherapy treatments. The only clinical factor associated to treatment complete response was the remaining tumour after debulking surgery (HR 18.9, 95% CI (2.0 - 2458.5)). Regarding the genetic variables analyzed, we found that the expression of ANGPT1, ARNT, CD34, EGF and MMP3 genes were related to response in the univariate analysis. We tried also to generate a genetic model for response prediction, being the most interesting one composed of the combined expression of 7 genes (AGT, CD34, EGF, EPO-R, IL8, MMP3 and MMP7). After leave one out cross validation (LOOCV), we obtained an AUC of 0.67 and the accuracy assigned was 0.74. The only factor that remains statistically significant in the multivariate analysis (including clinical and genetic factors) was the residual tumour after surgery.

Conclusions: Remaining tumour after debulking surgery remains the most important factor to date to successfully achieve a complete response after the multimodal treatment in high-grade serous AOC pts. The specific roles of genes identified in this study will need to be further studied.

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