Immune Related Gene Expression Profiling after Neoadjuvant Chemotherapy (NACT) of Ovarian High Grade Serous Carcinoma

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BACKGROUND

- In patients with stage III or IV HGSOC who are not suitable for primary surgery (PDS), 3 cycles of platinum based NACT followed by interval surgery (IDS) and adjuvant chemotherapy is an accepted treatment approach.
- NACT enhances host immune response by increasing levels of PD1, CTLA4 and PDL1[1]. Gene expression profiling of tumors has identified prognostic signatures for patient selection with immunotherapy[2].
- The purpose of this study is to assess the effect of neoadjuvant chemotherapy (NACT) on immune activation in stage IIIC/IV tubo-ovarian high-grade serous carcinoma (HGSOC).

OBJECTIVES AND METHODS

- Pre- and post-treatment omental biopsies were obtained from a total of 45 patients with advanced ovarian cancer undergoing platinum-based noadjuvant chemotherapy.
- FFPE tissue was assessed for availability of material for RNA purification. Hematoxylin and eosin stained slides were reviewed by an expert pathologist and tumor samples containing at least 50% of tumor cells were selected for RNA extraction.
- T-cell density and phenotype, immune activation, and markers of cancer-related inflammation were measured.
- Nanostring platform, PanCancer Immune Profiling Panel (IO 360 Panel) was used to perform multiplex gene expression analysis of 770 genes from 24 different immune cell types, common checkpoint inhibitors, CT antigens, and genes covering both the adaptive and innate immune response.

ACKNOWLEDGEMENTS

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REFERENCES

1. Böhm S et al. Clin Cancer Res 2016.
2. Ribas A et al. J Clin Oncol 2015.

RESULTS

- An **increase of inflammatory signature** was found in surgical samples in comparison to their paired biopsy samples *(fig 2A)*.
- In concordance with the differential gene expression, we found **an increase in neutrophils and mast cell** population in samples after de NACT treatment *(fig 2B)*.
- With respect to **TILs**, we also found an **increase in TILs** when comparing biopsy samples with tumour samples after NACT.
- There were a significant decrease in the ratio Th1 cells vs TILs (A), Treg vs TILs (B) and NK cells vs TILs (C) after NACT *(fig 3)*.
- The CD8 cell population in tumors sections by IHC in tumors and stroma areas increase in the surgical samples after NACT, mainly due to an **increase in CD8 T cells in the tumour area** *(fig 4)*.
- We did not find any significant differences in PD-L1, but **PD-1 shows a clear significantly increased expression after NACT** *(fig 5)*.

Figure 1. Study design

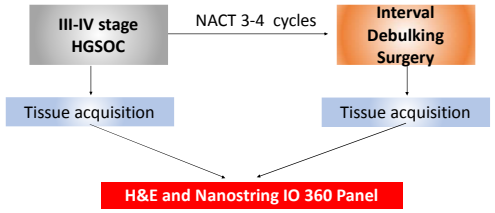


Figure 2. Differential mRNA expression between biopsies and surgical samples

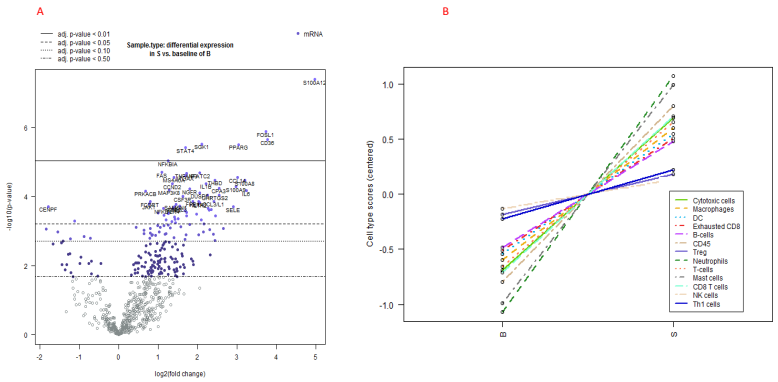


Figure 3. Individual boxplots of the 3 lowest cell type scores in surgical samples

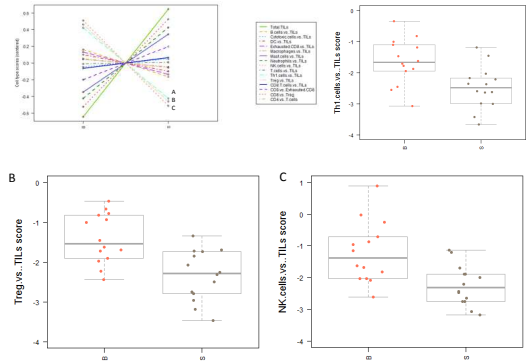


Figure 4. CD8 cell population in tumor sections by IHC

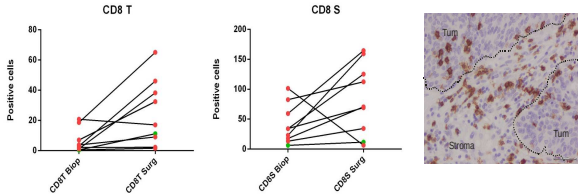
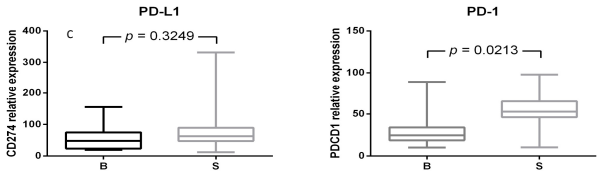


Figure 5. PD-L1 and PD-1 mRNA expression in biopsy and surgery samples



CONCLUSION

- NACT may promote an immune modulatory effect that could improve or favour the further use of specific immunotherapy in HGSOC patients.
- Further Next-Generation Sequencing analyses is ongoing.