



Abstract 971 Figure 2

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NK CELL-MEDIATED ERADICATION OF OVARIAN CANCER CELLS WITH A NOVEL CHIMERIC ANTIGEN RECEPTOR DIRECTED AGAINST CD44

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Introduction/Background* Disease recurrence and chemoresistance are major causes of poor survival rates in ovarian cancer patients. Ovarian cancer stem cells (CSC) were shown to represent a source of tumor recurrence owing to the high resistance to chemotherapy and enhanced tumorigenicity. Chimeric antigen receptor (CAR)-based adoptive immunotherapy represents a promising strategy to reduce the risk for recurrent disease. We developed a third-generation CAR to specifically target CD44, a widely accepted ovarian CSC marker.

Methodology We used ovarian cancer cell lines A2780, SKOV3, and OVCAR3 as well as primary ovarian cancer cells (P1, P2 and P3) harvested from ascites samples of an ovarian cancer patient. An anti-CD44 CAR was generated based on a third-generation CAR design containing CD28 and 41BB as codomains. NK-92 cells were equipped with CAR constructs by lentiviral transduction. IFN γ release assays were performed to demonstrate specific activation of engineered NK cells. Live cell impedance analysis with xCELLigence was used to estimate the anti-tumor activity of NK cells. For a chemotoxicity assay NK cells and cisplatin were added to A2780 or primary ovarian cancer cells. After treatment, analysis was done by the CellTiter 96[®] Aqueous One Solution Cell Proliferation Assay.

Result(s)* NK92 cells equipped with the anti-CD44 CAR (CD44NK) showed specific cytotoxic activity against CD44-positive ovarian cancer cells and primary ovarian cancer cells (figure 1). Specific activation of engineered NK cells was demonstrated by IFN γ secretion assays. Interestingly, CD44NK cells demonstrated cytotoxic activity under cisplatin treatment. The simultaneous treatment with CD44NK and cisplatin showed higher anti-tumor activity compared to a sequential treatment as shown in figure 2.

Conclusion* The new anti-CD44 CAR proved specific killing in ovarian cancer cell lines and primary ovarian cancer cells. We showed that CD44NK retained cytotoxicity during cisplatin incubation. The most potent anti-tumor effect was achieved by simultaneous treatment with CD44NK cells and cisplatin. This study will be the basis for further *in vivo* studies and future clinical developments.

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MUCINOUS BORDERLINE OVARIAN TUMORS : PATHOLOGICAL AND PROGNOSTIC STUDY

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Introduction/Background* Mucinous borderline ovarian tumors (MBT) are characterized by an epithelial proliferation similar to those of well-differentiated adenocarcinomas but are distinguished by the absence of stromal invasion. They are often difficult to diagnose histologically. On the one hand, the invasion of the stroma is not always easy to highlight, and on the other hand, the indirect criteria of invasion are not