Currently one standard-of-care therapy option in women with early, high-risk or locally advanced breast cancer. While some patients respond excellently to preoperative therapy, in other patients significant tumor shrinkage cannot be achieved. We investigated the impact of NAC on circulating immunomodulatory parameters. We also examined whether changes in these parameters correlate with the response to NAC measured by the Residual Cancer Burden (RCB) score determined after neoadjuvant treatment.

**Materials and Methods**

To detect drug-specific effects, two different RCB regimens in primary breast cancer patients scheduled for pre-operative therapy were compared. 39 patients with conventional anthracycline/taxane sequence (E>C>D, n=39) and 40 patients with reverse sequence (D->E/C) were included. Blood plasma samples were collected at three time points - ‘baseline’ (before NAC), ‘midterm’ (after the first six cycles of NAC) and ‘surgery’ (after NAC before operation).

The plasma levels of uPA, uPAR, TIM-3, MCP-1, MCP-2, OPG, IP-10, CD 27, Eotaxin, Tweak, TRAIL, PD-L2, M-CSF and VEGF-A were determined either by using ELISA or a multiplex bead array immunosassay.

**Results**

OPG, CD27, MCP-1, MCP-2, CGG19, Tweak, TRAIL, PD-L2 and M-CSF decreased between baseline and midterm in E/D->D patients. However, the majority of patients treated with the reverse sequence showed such effect. These drug-induced changes correlated with the RCB score. Non-responders (RCB ≥ 1.36) showed a significantly different pattern than responders.

**Conclusion**

These data confirm that NAC affects the immune system in a drug-specific manner. Factors correlating with the RCB-score might represent promising biomarkers to predict the response to therapy.

**Disclosure Information**


**Abstracts**

**P06.09**

ANTI-HPSMA CAR ENGINEERED NK-92 CELLS: AN OFF-THE-SHELF CELLULAR THERAPEUTIC FOR TARGETED ELIMINATION OF PROSTATE CANCER CELLS

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**Background**

Adoptive cell therapy of malignant diseases takes advantages of the cellular immune system to recognize and destroy cancer cells. Despite the remarkable success in B cell malignancies after adoptive transfer of CD19 CAR T cells, CAR T cell therapy in solid tumors has shown less encouraging clinical results, above all caused by tumor escape mechanisms.

**In order to overcome such limitations, NK-92, a permanent and IL-2-dependent cell line with a high cytotoxicity in vitro, has been engineered in preclinical models with CAR.** In this project, we exploited a CAR directed against the human antigen hPSMA that is overexpressed in prostate tumors. This project aimed at transducing NK-92 cell line to obtain a hPSMA-specific CAR NK-92 cell population, to be thereafter characterized in vitro and in vivo for antigen-specific functional activity.

**Materials and Methods**

NK-92 cell line was transduced with a lentiviral vector (LV) carrying a CAR anti-hPSMA. The cell population obtained was then sorted and analyzed for degranulation capacity, IFNγ production and lytic activity against hPSMA+ (PC3-hPSMA, LNCaP) or hPSMA+ prostate tumor cells. In vivo therapeutic efficacy of CAR-transduced NK-92 was evaluated initially using Winn-Assay and then in subcutaneous and orthotopic tumor models.

**Results**

CAR-expressing LV efficiently transduced NK-92 cells, which in turn produced cytokines, degranulated and exerted a relevant cytotoxic upon challenge with PSMA+ prostate tumor cells, irrespective of 10 Gy γ-irradiation. In all the in vivo, tumor models CAR-transduced NK-92 shown a statistically significant inhibition of tumor growth.

**Conclusions**

Chimeric antigen receptor-engineered NK-92 could offer a valid and cost-effective alternative to primary CAR NK or T cells, in particular in cases, where a suitable donor is not available or the sophisticated infrastructure needed for cell isolation, expansion and genetic modification is missing. This work demonstrates that CAR-engineered NK-92 cells display a high and specific recognition of hPSMA+ PC both in vitro as is in vivo, and could represent an efficient strategy as a new therapeutic intervention against prostate carcinoma, thus paving the way to an Off-The-Shelf cellular therapeutic for targeted elimination of cancer cells and induction of protective antitumor immunity.

**Disclosure Information**