360 HARNESSING THE POTENTIAL OF AUTOLOGOUS NK CELLS FOR IMMUNOTHERAPY OF PATIENTS WITH ADVANCED BLADDER CANCER

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Background Advanced bladder cancer is associated with significant morbidity and poor overall survival. Despite the introduction of checkpoint-inhibitors as part of the standard treatment the median overall survival is only about 2 years. The development of more efficient therapeutic approaches is necessary. Cell-based immunotherapy has shown potential for treating bladder cancer and may have synergistic effect with checkpoint-inhibitors. We investigated the ex vivo expansion and activation capacity of autologous NK cells derived from patients with advanced BC.

Methods Blood samples from patients were collected before and after first line platinum-based chemotherapy. Peripheral blood mononuclear cells (PBMCs) from six patients with unresectable locally advanced/metastatic bladder cancer were extracted from peripheral blood and cultured in medium supplemented with IL-2. T cells were activated with an anti-CD3 monoclonal antibody to assist NK cell proliferation. Samples from two healthy donors were cultured in parallel as a control group. Total cell number, cell population phenotype and cytotoxicity of NK cells were evaluated during cell culture. In the second stage of this study, PBMCs from post chemotherapy treatment of the same patients will be expanded and analyzed.

Results PBMCs collected from patients before chemotherapy treatment were cultured and achieved a fold expansion of 361 ±186 while the fold expansion of cells from healthy donors was 290±37. NK cells, our target population, showed 2071 ±995 and 2837±2225 fold expansion during culture in patients before treatment and in the healthy donors respectively. More than 90% of this population co-expressed the NK cell activation markers CD16 and NKp30. The cytotoxicity of the expanded NK cells was tested against K562 cell line in patients and healthy donors and demonstrated 58±4% and 51±11% NK cell degranulation respectively. Preliminary data from two post treatment samples showed a total cell and NK cell expansion of 470±196 and 3125±1319, respectively.

Conclusions Our results show that autologous NK cells from bladder cancer patients, both before and after chemotherapy, can be expanded and activated ex-vivo. Further, we demonstrated that the expanded NK cells are cytotoxic and degranulated against tumor cells. Ex-vivo activated autologous NK cells may complement existing therapies in bladder cancer.

Ethics Approval This study was approved by the Swedish Ethical Review Authority; approval number: Dnr 2022–02090-01 and amendments Dnr 2022–03397-02 and Dnr 2022–06613-02. The participants has given informed consent before taking part in this study.

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