PERSONALIZED IMMUNOTHERAPY BY ADOPTIVE T CELL TRANSFER DURING CHEMOTHERAPY WITH OR WITHOUT INTERFERON-ALPHA IN PATIENTS WITH RECURRENT PLATINUM-SENSITIVE EPITHELIAL OVARIAN CANCER

¹Els Verdegaal*, ¹Marten Visser, ¹Lien van der Minne, ¹Linda de Bruin, ²Inge Roozen, ²Pauline Meij, ¹Sjoerd van der Burg, ²Judith Kroep. ¹Leiden University Medical Center and Oncode Institute, Leiden, Netherlands; ²Leiden University Medical Center, Leiden, Netherlands

Background Epithelial ovarian cancer (EOC) is considered an immunogenic tumor, as illustrated by the clear correlation between T-cell infiltration and overall survival. This suggests that patients with EOC may be eligible for immunotherapy including adoptive cell therapy with autologous Tumor Infiltrating Lymphocytes (TIL). However, immunosuppressive cells including myeloid derived suppressor cells and regulatory T cells are also abundant in EOC and may need to be targeted simultaneously to achieve the full potential of the infused TIL. Carboplatin-paclitaxel chemotherapy (CPC) reduces the number of immunosuppressive cells in cervical cancer patients,¹ creating a window-of-opportunity for TIL to exert their full effector function. Interferon-alpha further supports infused TIL. A phase I/II trial (NCT04072263) was initiated to study the feasibility and safety of TIL during CPC with or without additional interferon-alpha in patients with recurrent platinum-sensitive EOC.

Methods Fifteen patients with recurrent platinum-sensitive EOC received 6 cycles of CPC intravenously every 3 weeks and TIL intravenously 2 weeks after the 2nd, 3rd and 4th CPC cycle. Pegylated-interferon-alpha was added in the second cohort for 12 weeks, starting one week before the first TIL infusion. Patients who received 3 TIL infusions were evaluable. The primary endpoint was feasibility and safety of TIL administration during CPC with or without interferon-alpha. As secondary endpoints signs of activity, underlying mechanisms, immunomodulation, and T-cell reactivity were studied.

Results Thirteen patients were available for analysis. Median age 63 years (range, 29–77). TIL could be successfully expanded for all patients. Treatment with TIL during CPC was safe and did not add toxicity. Addition of IFN α resulted in grade 3 leucopenia and grade 3 thrombocytopenia in the first 2 patients and was therefore omitted in subsequent patients. CPC alleviated the immunosuppressive status, reflected by reduced plasma IL-6 levels and circulating myeloid-cell numbers, while lymphocytes numbers are not affected. This was most prominently at 1–2 weeks after the 2nd CPC and is suggested to reflect improved conditions promoting intra-tumoral T-cell reactivity. Objective responses were observed in 10/13 (77%) patients and 3 patients had stable disease. Interestingly, in at least one patient the ongoing platinum-free interval of 25 months far exceeds the first platinum-free interval of 8 months after similar CPC. In depth studies on immune modulation by chemotherapy and by TIL/Interferon-alpha, and correlations between TIL phenotype and clinical outcome are ongoing and will be presented.

Conclusions Combined treatment with CP chemotherapy and properly timed TIL may result in clinical benefit for patients with EOC.

Acknowledgements The unrestricted funding of the trial by Ovacure is greatly acknowledged.

Trial Registration The trial is registered at www.clinicaltrials.gov under number NCT04072263.

REFERENCE

1. . Welters MJ, van der Sluis TC, van Meir H, Loof NM, van Ham VJ, van Duikeren S, Santegoets SJ, Arens R, de Kam ML, Cohen AF, van Poelgeest MI, Kenter GG, Kroep JR, Burggraaf J, Melief CJ, van der Burg SH. Vaccination during myeloid cell depletion by cancer chemotherapy fosters robust T cell responses. *Sci Transl Med* 2016;**8**(334):334ra52. doi: 10.1126/scitranslmed.aad8307

Ethics Approval This study was approved by Leiden University Medical Center's Ethics Board; approval number L18-012 and the Central Committee on Research Involving Human Subjects; approval number NL63434.000.17.

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.356>