Evaluation of immune response to tumor associated antigens in patients with high grade serous ovarian cancer vaccinated intra-dermally with DCP-001, an allogeneic, cancer cell-based vaccine.

Marco de Bruyn[1], Annegé Vledder[1], Koen Brummel[1], Anneke Eerkens[1], Rob Ten Pas[2], Hester van Zeeburg[2], Jeroen Rovers[2], Hans Nijman[1].

[1]University of Groningen, University Medical Center Groningen, Department of Obstetrics and Gynaecology, The Netherlands

[2]Mendus AB, Stockholm, Sweden

INTRODUCTION

Treatment of high grade serous ovarian cancer (HGSOC) after debulking and chemotherapy remains challenging. This phase 1 trial (NCT04739527) evaluates the use of a cell-based relapse vaccine, vididencel (DCP-001), to prevent disease recurrence after primary treatment.

Previous data in acute myeloid leukemia (AML) has shown that vidicencel induces immune responses to tumor associated antigens, like WT1 and PRAME, leading to clinical responses (7/20 MRD responses, of 5 with full MRD conversion) in AML patients with measurable residual disease and improvement of relapse free and overall survival (ASH2022 #713 van de Loosdrecht).

HGSOC expresses tumor associated antigens which are overlapping with those expressed in AML, like WT1, PRAME and Survivin. For this study, the safety and clinical effect of use of vididencel in HGSOC is investigated. Immunomonitoring for specific immune responses to tumor associated antigens and general immune cell composition during the vaccination period is assessed by IFNγ ELISPOT and multiparameter flow cytometry using Cytek Aurora, respectively .

VIDIDENCEL (DCP-001)

Vividencel is an allogenic, leukemic cell-based relapse vaccine and expresses co-stimulatory molecules, resembling activated dendritic cells, and tumor associated antigens such as WT1 and PRAME. It is injected intra-dermally and leads to an inflammatory response and indirect priming of the immune system.

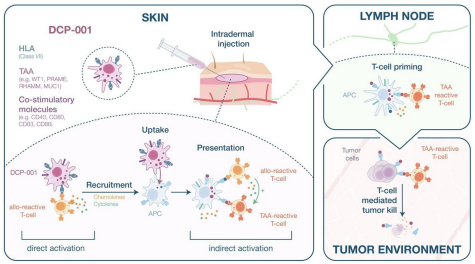

Figure 1. Schematic overview of the Mode of Action of vididencel (DCP-001)

DESIGN OF THE CLINICAL TRIAL

Patients with HGSOC were screened for eligibility after primary debulking and chemotherapy. Vididencel dosing was started at a minimal at 6 weeks after the last chemotherapy cycle.

Vididencel is given four times biweekly (week 0, 2, 4 and 6) at a dose of 25 million cells/vaccination (vc), followed by 2 monthly boosters (week 14 and 18) of 10 million cells/vc.

Blood for immunomonitoring was taken at the indicated visits (Figure 2).

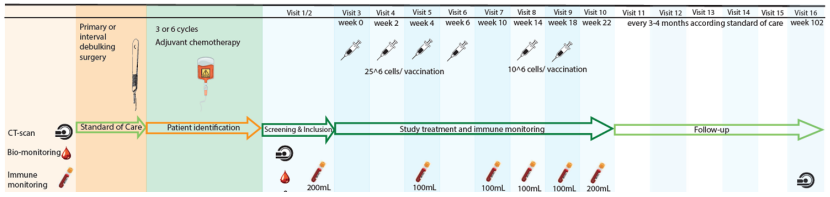

Figure 2. Schematic overview of the clinical trial, vaccinations and assessments

INTERIM RESULTS

At present (17Mar23) a total of 11 patients have been included, 7 have completed the full vaccination schedule (6 doses) and 4 patients are still on treatment. In total 4 patients recurred of which one died.

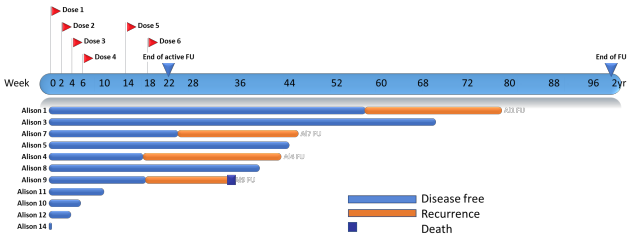

Figure 3. Swimmers'plot of the 11 included patients, as of 17MAR2023

Safety Vididencel is well-tolerated, with only mild to moderate adverse events; in all patients an injection site reaction was observed after administration of vididencel, which resolved after a few days.

Table 1. Overview of most frequent A/E related to vididencel

Adverse event	Number of patients with the event	Number of events	Grade 1 (n)	Grade 2 (n)
Fatigue	6	11	10	1
Headache	3	3	3	0
Nausea	2	7	7	0
Tiredness	2	3	2	1

MATERIALS & METHODS

IFNγ ELISpot is performed on peripheral blood mononuclear cells after restimulation with WT1, PRAME, MAGE-A3/4 and NY-ESO1. Vaccine induced T-cell responses (VIR) at any point after week 0 are calculated as at least a 2-fold increase of the mock-corrected baseline response.

MATERIALS & METHODS (continued)

Sustained VIR are counted if a VIR to the same antigen is observed in at least 2 time-points after start of DCP-001. Flow cytometry is performed using a 40-marker panel to evaluate the immune profiles of innate and adaptive immune system, as well as activation and exhaustion markers and memory profiles.

IMMUNE RESPONSE EVALUATION

Immune responses have been evaluated in 5 patients by IFNγ ELISPOT. VIR were detected in a range of 0-8, and all but 1 patient had at least one sustained VIR to either of the 4 antigens. One patient had no VIR, however this patient had already high baseline responses to all 4 antigens.

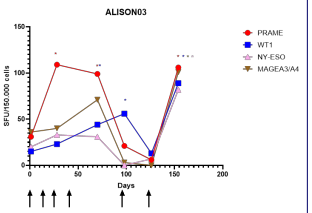

Figure 4. IFNγ ELISPOT analysis. Indicated are the mock corrected responses for either of the 4 antigens. The * indicate the vaccine induced responses (VIR). This patient has 2 sustained VIR, to PRAME and WT1

Cytek Aurora Flow cytometry

40-plex cytometry allowed robust and reproducible longitudinal tracking of all major and rare lineages, including cDC1 and cDC2.

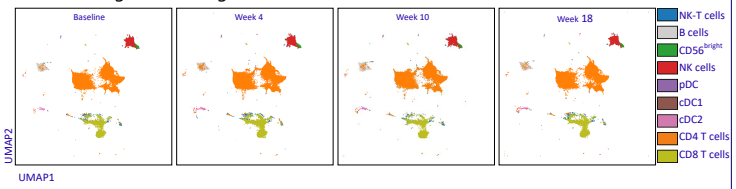

Figure 5. UMAP analysis of PBMC samples taken at baseline, week 4, 10 and 18. Indicated are the major are rarer immune subsets such as cDC1, cDC2 and pDC subsets

CONCLUSIONS

- Intradermal vaccination of vididencel is safe and well-tolerated in ovarian cancer patients
- Vidicencel induces durable T-cell responses to tumor associated antigens in OC patients
- Enrolment will be continued
- Disease free and overall survival analysis is ongoing
- Analysis of immune responses by Cytek Aurora followed by high dimensionality reduction is ongoing

Correspondence: a.vledder@umcg.nl