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 Bruyn¹, Annégé Vledder¹, Koen Brummel², Anneke Eerkens³, Rob Ten Pas², Hester van Zeeburg², Jeroen Rovers², Hans Nijman¹.
¹University of Groningen, University Medical Center Groningen, Department of Obstetrics and Gynaecology, The Netherlands
²Mendus AB, Stockholm, Sweden

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

Previous data in acute myeloid leukemia (AML) has shown that vividencel 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 vividencel 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 IFNy ELISPOT and multiparameter flow cytometry using Cytek Aurora, respectively.

VIVIDENCEL (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.

DESIGN OF THE CLINICAL TRIAL
Patients with HGSOC were screened for eligibility after primary debulking and chemotherapy. Vividencel dosing was started at a minimal at 6 weeks after the last chemotherapy cycle. Vividencel 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.

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.

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

MATERIALS & METHODS
IFNy 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.

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

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Number of patients with the adverse event-related A/E</th>
<th>Number of patients with the adverse event-related A/E</th>
<th>Grade 3-4</th>
<th>Grade 1-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>12</td>
<td>20</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Headache</td>
<td>12</td>
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<td>20</td>
</tr>
<tr>
<td>Nausea</td>
<td>12</td>
<td>20</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Tiredness</td>
<td>12</td>
<td>20</td>
<td>12</td>
<td>20</td>
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</tbody>
</table>

CONCLUSIONS
Intradermal vaccination of vividencel is safe and well-tolerated in ovarian cancer patients. Vividencel 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

IMMUNE RESPONSE EVALUATION
Immune responses have been evaluated in 5 patients by IFNy 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.

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.

Cytokine Flow cytometry
40-plex cytometry allowed robust and reproducible longitudinal tracking of all major and rare lineages, including CD11c and CD22. 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.