Induction of specific T-cell responses to tumor associated antigens and induction of B-cell responses in ovarian cancer patients by intradermal injection of vididencel

Annegé Vledder1, Hester van Zeeburg2, Satwinder Kaur Singh2, Jeroen Rovers2, Marco de Bruyn1, 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 surgery and chemotherapy remains challenging. This phase 1 trial (NCT04739527) evaluates the use of a cell-based relapse vaccine, vididencel, to prevent disease recurrence after primary treatment. Vididencel expresses Tumor Associated Antigens (TAA), such as WT1 and PRAME, and induces immune responses to these antigens correlated with clinical responses in a study of AML patients leading to clinical responses (ASH2022 #713 van de Loosdrecht). As these antigens are also frequently upregulated in HGSOC, vididencel is evaluated in this patient population. Immunomonitoring for specific immune responses to tumor associated antigens (TAA) and general immune cell composition during the vaccination period is respectively assessed by IFNγ ELISPOT and multiparameter flow cytometry using Cytek Aurora.

VIDIDENCHEL (DCP-001)

Vididencel 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 surgery and chemotherapy. Vididencel dosing was started at a minimum of 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).

MATERIALS & METHODS (C'tnd)

Flow cytometry was being performed using a 40-marker panel on the Cytek Aurora to evaluate the immune profiles of innate and adaptive immune system, activation and exhaustion markers and memory profiles. Unsupervised analysis using flowsom was used for analyses of changes during vaccination.

RESULTS

As of October 2023, in total 16 patients have been enrolled, of which 11 had completed the treatment phase (up to week 22). Four patients have died, of which three patients showed disease recurrence before week 22. In general the vaccine was safe and well-tolerated, with fatigue and redness and swelling at the injection site as main side effects.

IMMUNE RESPONSE EVALUATION ELISPOT

Immune response assessment showed VIRs to all antigens analysed, including NY-ESO1 which is not expressed by vididencel. In 6/8 patients VIR were detected (range 0-8 VIR). As of high baseline responses to all 4 antigens, in 1 patient no VIR could be detected (2-fold increase over baseline). In 5 of 8 patients the VIR detected were sustained over multiple timepoints (range sVIR 0-2) (Table 1).

CONCLUSIONS

Intradermal vaccination of vididencel is safe and well-tolerated in ovarian cancer patients

Broad T-cell responses to commonly shared tumor associated antigens expressed by vididencel like PRAME and WT1

NY-ESO1 T-cell responses are induced, although not expressed by vididencel, possibly due to tumor cell lysis and antigen spreading

Humoral immune responses are induced, observed as increase in B-cell memory and plasmablast frequencies after vaccination

Vididencel can induce a broad cellular and humoral immune response

Follow-up for clinical outcome and immune response assessments of all patients is ongoing.

Correspondence: a.vledder@umcg.nl or jeroen.rovers@mendus.com