High dimensional analysis of peripheral blood mononuclear cells in AML patients shows a beneficial tumor reactive T-cell environment at treatment start in patients responding to treatment with an allogeneic leukemia-derived cancer vaccine (vididencel)

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Introduction

- Persistence of measurable residual disease (MRD) is a poor prognostic factor and predicts relapse in patients with acute myeloid leukemia (AML). New treatment modalities to treat residual disease and detect early responses are urgently needed
- Vididencel is an allogeneic, leukemic cell-based relapse vaccine. Vididencel 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
- A phase 1 study showed that vididencel is safe and can induce both humoral and cellular immune responses1 leading to unexpectedly long survival times
- The current phase 2 study aims to investigate the ability of vididencel to generate an anti-leukemia response in patients with AML in CR, but MRD positive (Clinicaltrials.gov: NCT03697707).

Clinical study design and outcome

STUDY DESIGN
- AML patients in Complete Remission (CR1), ineligible for HSCT and minimal residual disease (MRD) positive by flow cytometry and/or-qPCR
- Patients are given 4 bi-weekly vaccinations with vididencel intradermally followed by 2-booster vaccinations at week 14 and 18
- Primary endpoint: MRD responses & immune response assessment

CLINICAL OUTCOME
- 20 evaluable patients for MRD response assessment
- 14 patients remained in complete remission (CR)
- 5 patients (25%) converted to MRD negative
- 2 patients (10%) had at least a 10-fold increase in MRD levels
- 7 patients (35%) had stable MRD levels
- 6 patients (30%) relapsed in the first 32 weeks

Mode of Action vididencel (DCP-001)

Figure 2.

Baseline immune cell composition impacts clinical response and outcome

Peripheral blood mononuclear cells analyzed by flow cytometry before start of vididencel vaccination showed a differentiating immune profile at baseline for patients whom remain in complete remission (CR) versus those who relapse in the first 32 weeks.

ISNE of full immune cell composition at baseline

Baseline immune cell composition shows a higher relative level of B-cells, and relative lower CD8 CM in patients who remain in CR. Statistical analysis shows a significant difference on the level of CD19+B-cells (p<0.0031) and CD8+CD56-CCR7+ central memory T-cells (p=0.0287).

ISNE of dendritic cell compartment (CD14 HLA-DR*)

Higher relative levels of CD14+DR+ cells are observed at baseline in CR patients. In particular the frequency of cDC1 and cDC2 is higher at baseline in patients who remain in CR. Analysis on these DCs during treatment with vididencel show an increase of these subsets in patients who remain in CR (Figure 5).

Conclusion

- Vididencel induces durable T-cell responses, as measured by IFNγ ELISPOT towards relevant TAs, with the highest number of responses in patients who remain in complete remission
- Patients who remain in CR have a higher relative level of tumor reactive T-cells, like CD4 PD1+ICOS+ and CD8 PD1+ICOS+, and lower levels of LAG3 expressing CD4 and CD8 T-cells
- Lower relative levels of CD8 CM, higher levels of B-cells and cDC1 and cDC2 at baseline are present in patients remaining in CR
- Vididencel induces an increase of cDC1 and cDC2 during vaccination
- In depth analysis of induced immune response during the vaccination with vididencel in relation to the clinical response is ongoing.

References