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 deepen responses are urgently needed.

Vididencel is an allogeneic, leukemic cell-based relapse vaccine and expresses multiple immunomodulatory antigens to treat residual disease and deepen responses. Persistence of MRD is poor for the population of patients in CR, but MRD positive patients benefit from the vaccine.

Clinical study design and outcome

STUDY DESIGN

AML patients in Complete Remission (CR1), ineligible for HSCT or MRD positive by flow cytometry and/or RT-PCR or NGS

Patients are given 4 bi-weekly vaccinations with vididencel intradermally followed by two booster vaccinations at week 14 and 18.

Primary endpoint: MRD response & immune response assessment

CLINICAL OUTCOME (22NOV22)

20 evaluable patients for MRD response assessment

14 patients remained in CR

5 patients (25%) converted to MRD negative (MRD response)

2 patients (10%) had at least a 10-fold decrease in MRD levels (MRD response)

7 patients (35%) had stable MRD levels (MRD stable)

6 patients (30%) relapsed in the first 32 weeks

Median RFS is not yet reached; estimated 12 months RFS 64% (41-90%)

Median OS = 30.9 months; estimated 12 months OS 85.3% (65-94%)

Methods

Immunoa4onitoring of peripheral blood mononuclear cells was performed frozen PBMC, which were isolated using a standardized protocol by trained staff.

IFNγ ELISPOT

Samples were analysed by restimulation with WT1, PRAME or RHAMM peptide pools. Vaccine Induced Response (VIR) was defined as at least a 2-fold increase of the specific, mock-corrected baseline response.

Flow cytometry

Multiparameter flow cytometry was performed using a 40-marker panel using Cytex Aurora on frozen PBMC samples. Flow sens analysis on subsets was performed on concatenated files (using the plug-in as provided, based on the method described by Sophie van Gassen1), with added metadata on visit number and clinical response (MRD responder, stable MRD and relapse at week 32). ISNE plots were generated for the full immune samples, and on separate immune subsets, CD4, CD8, monocytes. Overlay of ISNE plots, with 2% and 5% contour plots were used to identify the largest differences in populations.

Confirmation of the identified subsets was performed on the original .fcs data files and statistical analysis was performed using JMP1.

Results

Baseline immune cell composition shows differences related to clinical response

A higher relative level of B cells, and relative lower CD8 CM in patients who remain in CR is observed at baseline (Figure 2). Statistic analysis shows a significant difference on the level of CD19+ B cells and CD6+CD45RA-CCR7+ central memory T cells.

At baseline, T cell subset differences were observed across the response groups (Figure 4). More tumor-reactive subsets were identified in patients remaining in CR, whereas more suppressive subsets were identified in relapsed patients, like CD4+ LAG3+ and CD8+ LAG3+ T cells (Figure 5).

Higher number and durable functional T-cell responses in patients with MRD response

Viddencel expresses WT1, PRAME and RHAMM and IFNγ ELISPOT towards these antigens shows responses in 17/20 patients (85%) in this study. The highest number of vaccine induced responses are observed in patients who had a MRD response. At several timepoints vaccine induced responses to the same antigen were observed, indicative for a durable T cell response.

Improvement in immune cell subsets across all patient categories

After vaccination, levels of B-cells increased in the majority of patients, CDC1 levels increased, especially in those low at baseline, whereas inhibitory CD8+ LAG3+ T cells decreased, most notably in patients who relapsed.

Conclusion

Innate and adaptive immune responses are observed after vididencel to allow for a beneficial environment for tumor control or eradication.

Increasing levels of CDC1 and B-cells

Reduced or decreasing levels of inhibitory CD8+ LAG3+ T cells

Functional T cell responses towards frequently expressed antigens in AML, i.e. WT1, PRAME and RHAMM, were observed in the majority of patients

Vaccine induced responses are higher in patients with clinical response, especially in those with a MRD response

RFS and OS indicate a durable disease control in this patient population which is at high risk for relapse

References


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