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POSTER ABSTRACTS

617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Vaccination Using an Allogeneic Leukemia-Derived Dendritic Cell Vaccine, Maintains and Improves Frequencies of Circulating Antigen Presenting Dendritic Cells Correlating with Relapse Free and Overall Survival in AML Patients

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Background. Active immunotherapy relies on the patient's immune system for induction of an effective immune response. Not only the frequency, number and exhaustion or activation status of CD8 T cells is important for an efficacious tumor cell lysis, but the quality, number and distribution of different antigen presenting cells is of equal importance. Vididencel is an allogeneic leukemia-derived dendritic cell vaccine used in AML patients in first complete remission (CR1/CRi), but with MRD positivity, to mount an immune response through intradermal vaccination (ADVANCE-II, Clintrials.gov: NCT03697707). Intradermal vaccination is known to induce a specific immune response, by recruitment of skin and blood derived dendritic cells, which process antigen and present them to the immune system (Zuo et al., 2021). In this study circulating dendritic cells and monocytes have been investigated before and during vaccination to investigate the effect of vididencel treatment on the composition of antigen presenting cells in relation to clinical responses.
Methods. A total of 20 evaluable AML patients, in CR1/CRi, with measurable residual disease (MRD $^{+}$) and ineligible for HSCT at inclusion, received 4 biweekly doses of vididencel, followed by 2 booster doses at week 14 and 18.
Peripheral blood mononuclear cells were taken at baseline, week 6, 11, 14, 18, 20 and 32, ficoll isolated and cryopreserved in liquid nitrogen. Analysis of immune cell composition was performed by spectral flow cytometry, using a single 40-marker panel. Immune subset analysis of dendritic (live, single, CD45+, Lin-(CD3, 56, 19), CD16-, CD15-) cells was performed and correlated to clinical response, relapse free and overall survival, by high dimensional analysis using FlowSOM.
Results. Dendritic cell subsets increased upon vaccination, with levels before and during vaccination being the highest in patients remaining in CR. Gating of the dendritic cell subsets by spectral flow cytometry analyses could be hampered by presence of leukemic blasts in the peripheral blood, expressing for example CD123, a marker required for gating of pDCs. Using gating on the lineage negative, CD15-, CD16- and HLA-DR+ cells, a deep immunophenotyping was performed on dendritic cells in peripheral blood. Baseline analysis showed a significantly higher frequency of CD45RA+, HLA-DR+ cells in patients who remain in CR. Using tSNE and UMAP plots generated to analyse changes in the Lin-, CD14-, CD15-, CD16- and CD11b-, HLA-DR+ population; changes and increases in several subsets were observed, most notably in subsets with cDC1, cDC2 and pDC characteristics, like expression of CD141, CLEC9A, CD1c and CD123. Higher frequencies at baseline of dendritic cells (cDC1 and cDC2) correlated positively with both relapse-free and overall survival. In patients remaining in CR, vaccination further increased or maintained dendritic cell subset frequencies, of which classical cDC1 and cDC2 correlated with longer overall survival ($p<0.05$).
Conclusion: Patients who remain in CR after vididencel treatment had highest baseline levels of HLA-DR+ CD45RA+ cells, which could be myeloid cells able to differentiate into dendritic cell subsets, as in general CD45RA+ is lost during maturation

from precursor to matured dendritic cells. Vaccination might improve and induce maturation of dendritic cell subsets, such as cDC1, cDC2 and pDC, which enhance antigen capturing, processing and presentation to tumor-reactive T cells, ultimately leading to improved survival.

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