**DC Vaccination Induces Antigen Specific Immune Responses in AML Patients: A 1-Year Interim Assessment**

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**Introduction**

- Acute Myeloid Leukemia (AML) is the most common acute leukemia in adults. The backbone of therapy is a combination of cytarabine- and anthracycline-based regimens, followed by hematopoietic stem cell transplantation (HSCT) for eligible candidates. Unfortunately, elderly patients and patients with co-morbidities are often unable to tolerate such regimens and develop minimal residual disease (MRD) persisting after HSCT, resulting in long-term relapses.

- In animal models, dendritic cells (DCs) loaded with tumor antigens elicit both cellular and humoral immunity, and induce tumor-specific T cell responses and tumor regression. Therefore, DC-based vaccines have emerged as a promising approach to eradicate MRD in AML patients, particularly in patients not eligible for HSCT and/or at high risk of relapse.

- The Wilm’s tumor protein (WT-1), and the preferentially expressed antigen in melanoma (PRAME) have been identified as leukemia-associated antigens (LAAs). The importance of these antigens has been corroborated by the detection of immune response to these antigens in AML patients.

- The present first-in-human study (EUDRA CT No. 2014-003250-44) was conducted to assess the safety and feasibility of an autologous, patient-derived DC vaccine for the LAAs WT-1 and PRAME, in AML patients in CR.

**Fast-DC Vaccine Characterization**

- Patient-derived DCs were obtained using a Fast 3-day ex vivo culture protocol, after patient leukapheresis and monocyte enrichment. DC differentiation and maturation was carried out in the presence of GM-CSF and IL-4, with or without IFN-γ, and IL-12.

- WT-1 and PRAME-expressing DCs showed high surface levels of costimulatory molecules (i.e. B7-1, B7-2, CD40, CD80), but low levels of immune inhibitory molecules (i.e. PD-L1 and PD-L2). Mature DCs also expressed CCR-7.

**MRD Levels and WT-1/PRAME-specific Peripheral T Cell Responses**

- PRAME and WT-1 mRNA levels in the bone marrow (BM) were monitored by qPCR at multiple timepoints to assess MRD. The diagrams depict the kinetics of PRAME and WT-1 mRNA in representative patients with early (A) or late relapse, or in remission. Relapses were associated with a sharp increase in WT-1 and/or PRAME mRNA levels in the BM.

- IFN-γ production was assessed in vitro upon stimulation of peripheral T cells with a pool of WT-1 or PRAME peptides (IFN-γ ELISPOT) and used as an indicator of vaccine-induced Ag-specific T cell responses.

- Early relapse : PRAME and/or WT-1-specific IFN-γ T cell responses were observed in 2/4 (50%) patients with early relapse and correlated with a sharp increase in PRAME and/or WT-1 mRNA in the BM.

- Late relapse : PRAME and/or WT-1-specific IFN-γ T cell responses were observed in 4/4 (100%) patients and were concomitant to the increase in WT-1 and/or PRAME mRNA in the BM.

**Clinical Follow-Up (1-year)**

- A total of 20 AML patients (WT-1 expressing AML blasts) in morphologic remission (CR), with or without hematologic recovery (CRi) following induction chemotherapy, were treated.

- Patients (pts) received up to 16 DC injections in yr 1 and 12 in yr 2. At each time point, both PRAME and WT-1 DCs (2.5 – 5 x 10^6 / DC type) were administered intradermally.

**Summary and Conclusions**

- The Fast-DC protocol reproduced a high number of patient-derived, autologous DCs, which expressed WT-1 or PRAME, showed an immune-stimulatory phenotype and produced IL-12. The WT-1/PRAME DC vaccine exhibited a favorable safety profile.

- The WT-1/PRAME DC vaccine was administered to a total of 20 AML patients in complete remission: 12/20 (60%) patients remained in complete remission, 8/20 (40%) relapsed within one year from the first vaccine administration.

- AML relapses were associated with an increase in the serum levels of IFN-γ, but also of IL-4, IL-5 and IL-6.

- Patients in remission exhibited higher levels of CD3+ HLA-DR+ T cells in the BM and peripheral blood; however, peripheral T cells capable of producing IFN-γ in response to intravenous stimulation with WT-1 or PRAME were only detected in 3/12 (20%) patients.

- In contrast, in vitro T cell production of IFN-γ in response to WT-1 or PRAME (ELISpot) was observed in 50% and 100% of patients with early and late relapses, respectively. Such responses were associated with increased levels of PRAME and/or WT-1 mRNA in the BM.

- The impact of WT-1 and/or PRAME-specific T cell responses on AML remission warrant further investigation and will be further explored in the upcoming 2-year follow-up data analysis.