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ORAL ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Phase 1 Trial of Dendritic Cell/AML Fusion Cell Vaccine after Allogeneic Stem Cell Transplant in Acute Myeloid Leukemia

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Introduction

We have developed a vaccine in which patient-derived AML cells are fused with donor-derived dendritic cells (DCs). Vaccination after initial remission and consolidation was shown to elicit leukemia-specific immune responses. We hypothesized that donor-derived DC/AML vaccination post-transplant would elicit the durable expansion of leukemia-specific T cells within the donor T cell repertoire to effectively protect against disease relapse. We report updated results of a phase 1 clinical trial (NCT03679650) evaluating the use of DC/AML fusion vaccine following allogeneic transplant.

Methods

DC/AML fusion vaccine was generated with patient leukemia blasts, cryopreserved at the time of diagnosis, and donor-derived DCs, from leukapheresis of patients who achieved hematopoietic recovery and remained in CR 25-90 days after an allogeneic transplant. DCs were differentiated via culture of adherent mononuclear cells in the presence of GM-CSF, IL-4 and TNFa. Vaccine was administered starting day 70-100 post-transplant as long as the patient did not have active GVHD requiring therapy. Two doses of the vaccine were given subcutaneously at 3 week intervals, in conjunction with 100 mcg GMCSF daily at the vaccine site for 4 days. A booster vaccine was given 30-60 days following the taper of immune suppression, in the absence of GVHD. Longitudinal profiling of the immune landscape by single cell RNA sequencing and CyTOF from peripheral blood samples obtained before and after vaccination is underway. Immunologic response of leukemia-specfic T cells is being evaluated via IFN-gamma expression following stimulation with autologous tumor lysate. OS was calculated using Kaplan Meier Curve.

Results

27 participants have been enrolled with median age 59 years (range 23-74). 15 patients were transplanted with a matched unrelated donor, 10 with a matched sibling donor and two with a haplo-identical donor. One patient relapsed prior to leukapheresis and was ineligible. The median yield of leukemia cells was $218x10^6$ (range $62-818x10^6$)and mean viability was 97%. The median yield of DCs was $106x10^6$ (range $19-182x10^6$) and mean viability 81%. Fusion vaccine was successfully generated in 25 of 26 patients who underwent leukapheresis; one patient had insufficient DC. Mean fusion efficiency was 47% with viability of 79%. Mean fusion vaccine dose was $3.8 x10^6$ cells. 6 patients from whom vaccine was generated did not meet eligibility to initiate vaccination due to GVHD or COVID19 infection. 19 participants initiated vaccine administration and are evaluable for toxicity and immunologic response. The most common side effects were vaccine site reactions (n=10 grade 1, n=2 grade 2). 5 patients developed GVHD that was attributed as possibly related to vaccination, at a median time of 17 days after vaccination (range 5-70 days). Acute GVHD included two events of skin grade 2, one GI grade 2, one liver and skin grade 3. Chronic GVHD included a moderate event affecting 3 organs and severe event affecting 4 organs. There were 10 additional GVHD events with a median time of 108 days post vaccination (range 7-126 days), assessed as unlikely related or unrelated to vaccine based on pre-existing GVHD and timing of onset. Median time of follow-up is 23 months post-transplant (range 11-59 months). Amongst 19 vaccinated patients, 14 remained in CR and median overall survival estimate is 49 months post

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transplant. 3 died of relapsed disease, 2 died of GVHD and/or infection, and 1 died of unknown cause. Preliminary results of PB CyTOF from 4 patients in remission and 1 patient that relapsed indicate higher proportions of T cells and DCs in patients in CR. Interferon expression was higher in a patient with durable remission while absent from a patient with early relapse.

Conclusions

Vaccination using host-derived leukemia cells and donor derived DC was safe and feasible. Adverse events post vaccination have included injection site reactions as well as acute and chronic graft versus host disease. Vaccination may be a promising strategy to reduce relapse as 14 of 19 vaccinated patients remain relapse free. Albeit this approach is limited to patients who have not had early relapse or early GVHD. Immunologic response by interferon release upon lysate stimulation, CyTOF and single cell RNA sequencing of the immune milieu will be reported.

Disclosures Stone: *Abbvie:* Consultancy. **Soiffer:** *Astellas:* Consultancy; *NMPD - Be the Match, USA:* Membership on an entity's Board of Directors or advisory committees; *Jasper:* Consultancy; *Juno Therapeutics/ BMS/Celgene USA:* Other: Data Safety Monitoring Board; *Bluesphere Bio:* Consultancy; *Neovii:* Consultancy; *Vor Bipharma:* Consultancy; *Smart Immune:* Consultancy. **Ho:** *Jazz:* Consultancy, Research Funding; *Alexion:* Consultancy; *Omeros:* Consultancy; *CareDx:* Research Funding; *Allovir:* Consultancy. **Romee:** *Inndura:* Consultancy; *Biohaven:* Research Funding. **Neuberg:** *Madrigal Pharmaceuticals:* Current equity holder in private company. **Ebert:** *Neomorph Inc.:* Current equity holder in private company, Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Consultancy; *Exo Therapeutics:* Current equity holder in private company, Membership on an entity's Board of Directors or advisory committees; *Skyhawk Therapeutics:* Current equity holder in private company, Membership on an entity's Board of Directors or advisory committees; *TenSixteen Bio:* Current equity holder in private company, Membership on an entity's Board of Directors or advisory committees; *Calico:* Research Funding; *Novartis:* Research Funding. **Avigan:** *Takeda:* Consultancy, Other: Advisory role; *Chugai Pharma:* Consultancy, Other: Advisory role; *Celgene:* Consultancy, Other: Advisory role, Research Funding; *Paraxel:* Current Employment; *Legend Biotech:* Consultancy, Other: Advisory role; *Juno Therapeutics:* Consultancy, Other: Advisory role; *Karyopharm Therapeutics:* Consultancy, Other: Advisory role; *Kite/Gilead:* Consultancy, Other: Advisory role, Research Funding; *Bristol-Myers Squibb:* Consultancy, Other: Advisory board; *Aviv Med Tech:* Consultancy, Other: Advisory board; *Partner Therapeutics:* Consultancy, Other: Advisory board; *Janssen:* Consultancy, Other: Advisory board; *Sanofi:* Consultancy, Other: Advisory board; *Kowa Pharmaceutical:* Consultancy, Other: Advisory board; *Pharmacyclics:* Research Funding; *Kite, a Gilead Company:* Research Funding. **Rosenblatt:** *Parexel:* Consultancy; *Bioclinica:* Consultancy; *Advare:* Consultancy; *Karyopharm:* Membership on an entity's Board of Directors or advisory committees, Other: Karyopharm; *Sanofi:* Research Funding; *Bristol Myers Squibb:* Research Funding.

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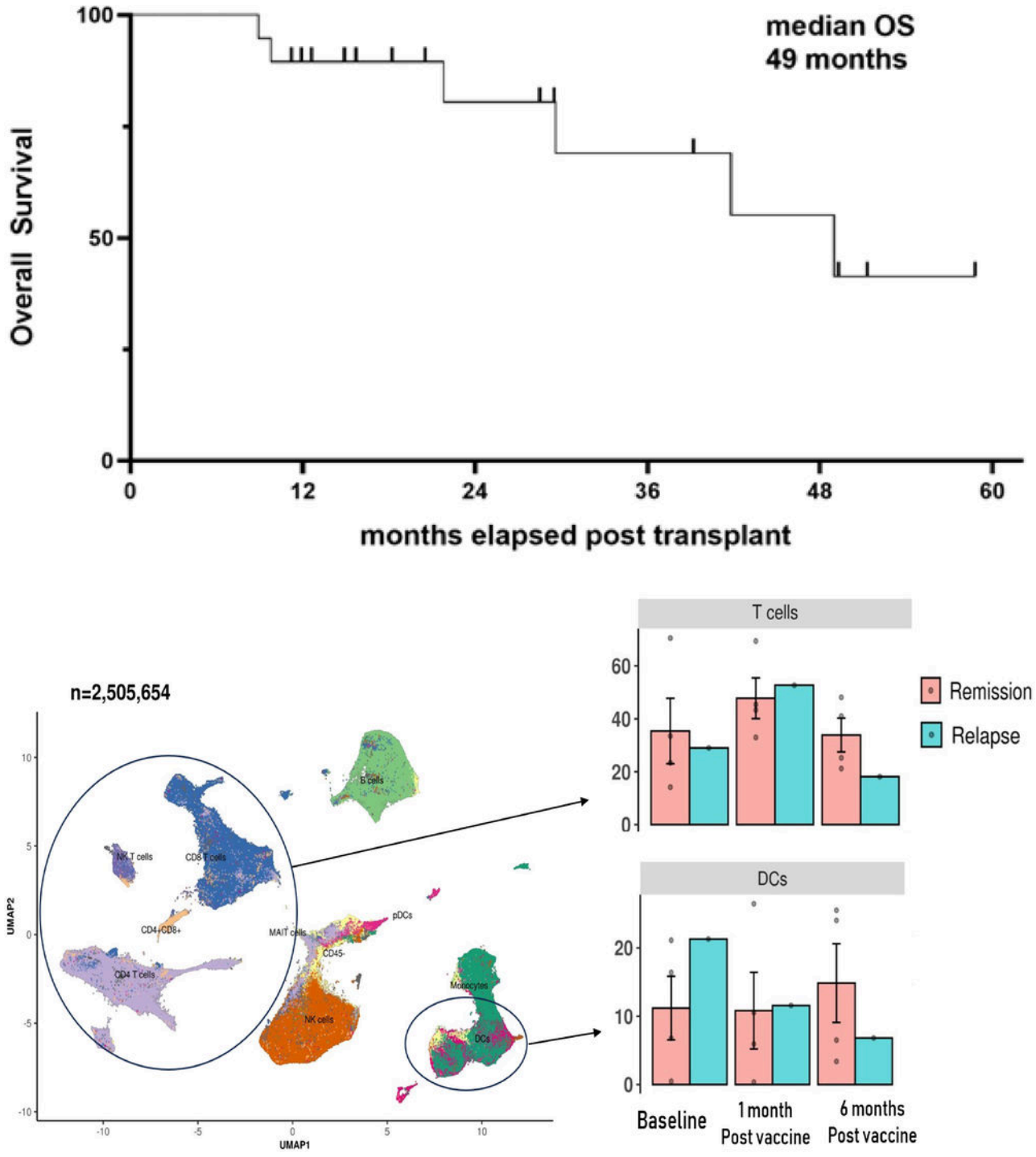

Figure 1

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