685 PRELIMINARY RESULTS OF MT-401 IN POST-TRANSPLANT MRD+ AML PATIENTS

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Background Measurable residual disease (MRD) testing has become more prevalent in AML. MRD positivity is associated with increased relapse risk and shorter survival in AML, and currently, there no approved therapies for these patients. Zedenoleucel (also known as MT-401) is a non-genetically modified allogeneic multi-tumor associated antigen (mTAA)-specific T cell therapy with selectivity to multiple tumor antigens, specifically preferentially expressed antigen in melanoma (PRAME), Wilms' tumor 1 (WT1), New York esophageal 1 (NY-ESO-1) and Survivin.

Methods A multicenter Phase 2 study (ARTEMIS) evaluating the safety, tolerability and efficacy of zedenoleucel in patients with AML, including MRD$^+$patients, post-HSCT is ongoing. The study explores this therapy in patients with no active disease [in complete remission (CR) and MRD$^-$] or in patients with active disease (frank relapse or MRD$^+$). Patients may receive up to 3 consecutive infusions of zedenoleucel as a monotherapy (50-200 $\times$ 10^6 cells every 2 weeks) at weeks 0, 2 and 4 during the Intervention Period, and enter Follow-up at Week 8. Primary endpoints include various safety measurements. Efficacy evaluations occur at weeks 8, 12, 18, 24, 48 and yearly for 4 years using ELN recommendations for standard AML response criteria. MRD testing was done by flow cytometry or molecular testing (e.g. RT-PCR).

Results No concerning safety signals arose, including any dose-limiting toxicities in safety lead-in patients. The MRD$^+$patients had a variety of genetic mutations/abnormalities. One patient with NPM1 mutation converted from MRD$^+$ to MRD$^-$ at week 8 evaluation. Another patient with RUNX1 genetic abnormality showed a decrease in MRD by PCR from a starting baseline of 0.8093% to resolution via peripheral blood at approximately 32 weeks post-treatment with MT-401. T cell composition of the product consisted of 71% CD4$^+$ and 24% CD8$^+$ T cells. T cell receptor (TCR) analysis identified 3,117 antigen-specific clones (881 Survivin, 783 NY-ESO-1, 750 PRAME, 709 WT1). Immune monitoring of this patient using biomarker analysis showed T cell specificity not only for the targeted antigens but also for non-targeted antigens over time, thereby demonstrating epitope spreading. Interestingly, the tumor antigen composition by RNASeq identified an antigen expression profile that changes over time and inversely correlates with the presence of antigen-specific T cells, demonstrating the interplay of tumor cell immunogenicity and antigen-specific T cells.

Conclusions The preliminary ARTEMIS results showed that administration of MT-401 converted MRD$^+$patients to MRD$^-$ indicating that early intervention with MT-401 administration at MRD$^+$ stage in post-transplant AML can be beneficial.

Ethics Approval Ethics approval has been obtained by the Western IRB and participants gave informed consent before taking part. IRB tracking number is 20192173.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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