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POSTER ABSTRACTS

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL

Evaluation of the Safety and Efficacy for Oral Mucositis Prevention of MIT-001 in Auto HSCT

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Background: Oral mucositis (OM) is one of the most prevalent complications leading to severe pain, difficulty eating, prolonged hospitalization, and life-threatening septic condition in patients receiving chemotherapy containing conditioning regimen prior to autologous hematopoietic stem cell transplantation (auto-HSCT). MIT-001 is a novel small molecule functioning as a mitochondria-targeted radical trapping agent (RTA) that effectively inhibits cellular ferroptosis/necrosis and cytokine production via blockade of reactive oxygen species (ROS) generation and calcium accumulation in the mitochondria. The current clinical study was designed to evaluate the safety, efficacy by prevention of OM and pharmacokinetics of MIT-001 in patients with lymphoma or multiple myeloma (MM) undergoing chemotherapy prior to auto-HSCT.
Methods: This phase IIa study consists of two parts: part 1 is an open label dose-escalating study dosing from 5 mg, 10 mg and up to 20 mg of MIT-001 to determine the recommended Part 2 Dose (RP2D) via evaluating the efficacy of OM, safety and pharmacokinetic characteristics of MIT-001, whereas Part 2 is a placebo-controlled, double-blinded, and randomized study to find the optimal dose of MIT-001 regarding the efficacy of OM and safety for the next IIb/III clinical trials.
In Part 1, the total screening period was 28 days: conditioning chemotherapy/MIT-001 treatment for four to nine days followed by auto-HSCT and recovery for 14 days and discharge at 28 days following HSCT. MIT-001 was administered intravenously for 30 minutes once daily before conditioning chemotherapy for four to nine days, depending on the conditioning regimens including high-dose melphalan and BMT (intravenous busulfan, melphalan, thiotepa) for auto-HSCT.
Pharmacokinetic blood samples of MIT-001 was collected at 5 time points including before administration to 24 hours after the start of the first and last administration of MIT-001. WHO criteria and NCI-CTCAE (v5.0) for OM grading were used for the severity of OM, which was evaluated daily during hospitalization and twice a week or once a week after discharge by investigator's choice. Pain related to OM was collected from patients using the Oral Mucositis Daily Questionnaire.
Results: In part 1, total of sixteen patients were enrolled in which 5 patients were assigned in 5 mg and 20 mg group each, and six patients were assigned in the 10 mg group. Twelve lymphoma patients and four MM patients were pre-conditioned by BMT and Melphalan regimen, respectively. Severe OM (grade 3) were observed in two lymphoma patients treated with 10 mg and 20 mg MIT-001 (FAS: 13.3%, 2/16). Two patients with grade 3 OM had experienced radiation therapy of head and neck area within 1 year. Severe OM (> grade 3) did not occur in the four MM patients, while grade 2 was observed in two patients. None of the patients received total parental nutrition feeding due to OM. The median duration of grade 3 OM was 6 days (range, 3 to 9) and mean onset was 6 days (SD±1) after conditioning initiation.
The duration and incidence of OM were not significantly different among the 3 groups. Mean area-under-the-curve (AUC) score for patient-reported soreness of the mouth and throat was not proportional to the dose of MIT-001. Time to engraftment was observed at a median time of 13 days (range, 11˜ 26 days) determined by the neutrophil and platelet recovery time following auto-HSCT, which was within the normal range of period of auto-HSCT when compared to historical control. With the statistical analysis using the Kruskal-Wallis test, MIT-001 showed good PK profile with dose-proportionality in the range of 5 mg up to 20 mg. Two doses of 5 mg and 20 mg were determined as RP2D under steering committee. Serious adverse drug reactions were not reported.
Part 2 is currently ongoing to evaluate efficacy of OM and safety of MIT-001 in forty-five patients with lymphoma and MM, where fifteen patients were allocated in 5 mg, 20 mg, and placebo group.

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Conclusions: The phase IIa part 1 results strongly suggest the therapeutic potential of MIT-001 to prevent severe OM in the patients with lymphoma and MM undergoing melphalan-containing conditioning followed by auto-HSCT.

Disclosures Kim: *MitoImmuneTherapeutics:* Current Employment, Current equity holder in private company, Other: CEO, Patents & Royalties.

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