

785 A phase I study of intralymphatic (IL) administration of ipilimumab (IPI) with intravenous nivolumab (NIVO) using the Sofusa® DoseConnect™ device in patients with advanced melanoma.

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Dimou, Anastasios & Suman, Vera & Denic, Kristina & Kottschade, Lisa & Montane, Heather & Finnes, Heidi & Franta, Kristina & Schimke, Jill & Yan, Yiyi & McWilliams, Robert & Block, Matthew & Jakub, James & Reid, Joel & Markovic, Svetomir. (2022). 785 A phase I study of intralymphatic (IL) administration of ipilimumab (IPI) with intravenous nivolumab (NIVO) using the Sofusa® DoseConnect™ device in patients with advanced melanoma. Journal for ImmunoTherapy of Cancer. 10. A816-A816. 10.1136/jitc-2022-SITC2022.0785.

Background

Pre-clinical studies of Sofusa® DoseConnect™ (DC) have shown that IL infusion of antineoplastic medications results in higher lymph node concentrations, more efficient tumor growth inhibition and less systemic exposure when compared to conventional systemic administration. We conducted a Phase I clinical trial to assess the safety of IL infusion of ipilimumab with DC followed by nivolumab IV in patients with advanced melanoma.

Methods

A 3+3 phase I clinical trial was conducted to assess the safety of IL infusion of IPI by DC over 12-24 hours followed by NIVO 3 mg/kg IV among patients with advanced melanoma. A maximum of four 21 day cycles were administered. Cycle 1 IPI was administered by DC; cycles 2-4 IPI were administered at 1 mg/kg IV. Dose levels (DL) of cycle 1 IPI included: DL1: 1 mg/kg; DL-1: 0.75 mg/kg; and DL-2: 0.5 mg/kg. All DL were given at 0.5 mL/hour. Dose limiting toxicities included the following if they were at least possibly related to DC: inability to administer at least 75% of the protocol-specified dose due to DC dislodgement, ≥ grade 4 hematologic toxicity, ≥ grade 3 non-hematologic toxicity or ≥ grade 3 infusion site reaction or infusion related reaction that does not resolve to Grade 0-1 within 2 weeks. IPI pharmacokinetics were characterized in all patients who participated in the study.

Results

Six patients (3 males and 3 females) were enrolled in this trial at DL1. The median number of prior therapies for metastatic disease was 1 (range 1-3). The most common sites of metastatic disease were distant lymph nodes and lung. No dose limiting toxicities were observed. Cycle 1 toxicities reported included grade 2 hypophysitis (N=1) and grade 2 abdominal pain (N=1). No adjustments to the DC flow rate were required. Two severe, DC unrelated, immune-related toxicities were reported: grade 3 maculopapular rash and grade 3 colitis (same patient, cycle 1 causing discontinuation). Four patients progressed on treatment (1-cycle 2; 3-cycle 4). One patient completed 4 cycles of treatment. The mean IPI serum concentrations at the end of the infusion and 15 days after the DC infusion in Cycle 1 were 4.13 ug/mL and 4.88 ug/mL, respectively.

Conclusions

IL administration of IPI with the DC device on the first cycle was well tolerated with no dose limiting toxicities. Safety and secondary efficacy of IL infusion of IPI through all 4 cycles will be assessed next.

Trial Registration

ClinicalTrials.gov: NCT04967196

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Mayo Clinic.

Consent

Informed consent was obtained from all individual participants included in this study.