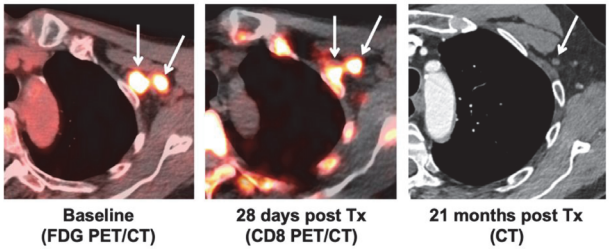
establish safety and optimal scanning parameters and a dose expansion phase focusing on two API doses (0.5 mg (n=4) or 1.5 mg (n=5) API). All patients were monitored for drug-related adverse events with blood chemistry, hematology, cytokine assay and anti-drug antibodies (ADA). Biodistribution, radiodosimetry and SUV PET uptake was performed in all patients.

Results 15 subjects (31–82 years, M/F = 9/6) with metastatic melanoma (n=8), NSCLC (n=6), and HCC (n=1) were enrolled. Treatment histories included naïve (n=2), discontinued prior IOT (n=3), active IOT (n=10). No drug-related AEs nor abnormal laboratory tests were noted except for a transient increase in ADA in 1 subject. The CD8-tracer accumulated in tumors and CD8 rich tissues (e.g. spleen, marrow, nodes) with maximum uptake at 24–48 hours post injection along with low background activity in non-T cell rich tissues (e.g. muscle, heart). More favorable dosimetry was seen at 1.5 mg versus 0.5 mg API (effective dose=0.64 mSv/MBq versus 0.67 mSv/MBq, respectively). Comparison of 1.5 mg and 0.5 mg API in expansion cohorts demonstrated similar uptake in nodes but with reduced uptake in marrow and spleen at the higher API. Tracer-uptake in tumors was noted in 10/15 (67%) subjects, favoring slightly higher tumor uptake in the 1.5 mg cohort. One patient with advanced melanoma on IOT had increased CD8-tracer uptake in several metastases on an early post treatment scan, which correlated with response (figure 1).



Abstract 294 Figure 1 71 year old man with locally advanced stage III melanoma
FDG PET/CT imaging (left) shows two FDG avid metastases in the left axilla. CD8 PET/CT imaging (middle) performed 28 days after starting immunotherapy demonstrates increased tracer activity in both metastases, suggestive of tumor infiltration by CD8 T cells. Follow-up imaging via CT (right) confirmed a complete response to therapy.

Conclusions 89Zr-IAB22M2C targets CD8+ rich tissues and visualizes whole-body biodistribution of CD8+ cells in tumors and reference tissues and may predict early response to IOT. A 1.5 mg protein dose provides similar distribution to 0.5 mg dose, with more favorable dosimetry and is used in the ongoing Phase 2 study.

Acknowledgements None

Trial Registration ClinicalTrials. gov Identifier: NCT03107663

Ethics Approval The study was approved by Institutional Review Boards of MSKCC (IRB #16-1109), Honor Health (West IRB #1179278) and University of Pennsylvania (IRB # 828992).

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.

REFERENCE

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295 FIRST-IN-HUMAN PHASE I TRIAL OF IBI188, AN ANTI-CD47 TARGETING MONOCLONAL ANTIBODY, IN PATIENTS WITH ADVANCED SOLID TUMORS AND LYMPHOMAS

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Background IBI188 is a humanized IgG4 monoclonal antibody targeting CD47, an antiphagocytic ('don't eat me') signal present on cancer cells. Blockage of this myeloid checkpoint, IBI188 enhances tumor cell phagocytosis and cross priming of T-cells. We conducted a first-in-human phase 1a trial to evaluate the tolerability, safety and PK/PD characteristics of IBI188. (NCT03763149).

Methods Patients with advanced/refractory solid tumors or lymphoma were enrolled in this two-part dose-escalation study: Part A for testing optimal priming doses at 0.1, 0.3, and 1 mg/kg and Part B for optimal maintenance doses at 3, 10, 20, 30 mg/kg weekly. An accelerated titration followed by traditional 3+3 design was used in this study with a 28-day dose-limiting toxicity (DLT) observation period. Primary endpoint was safety profile; secondary endpoints included PK parameters and PD markers, i.e. CD47 receptor occupancy.

Results As of June 18, 2020, 20 patients have been enrolled, 6 in Part A and 14 in Part B. There was no DLT reported at any dose level. The median treatment duration was 1.8 months (0.2–5.5) months. The most common treatment-related adverse events (TRAEs) were nausea (n=7), back pain (n=7), fatigue (n=6), vomiting (n=4) and blood bilirubin increased (n=4). Three patients had ≥ Grade 3 TRAEs (Grade 3 blood bilirubin increase, Grade 4 platelet count decrease and Grade 3 anemia, each in 1 patient). Three of 20 patients (15%) had anemia, an expected TRAE associated with the mechanism of IBI188. Majority of the patients (65%) had infusion related reactions (IRR). All IRRs were Grade 1–2 and able to be managed with standard IRR treatment. The clearance of IBI188 decreased with the increasing dose from 3 to 20 mg/kg and IBI188 can overcome the sink at 10 mg/kg or higher dose level. The PK analysis at 30 mg/kg is ongoing. The 10 mg/kg maintenance dose resulted in T cells receptor occupancy above 80%. After multiple administrations (≥ 3 times, including the priming dose), the RBC and T cells receptor occupancy tends to be stable and maintained around 90%. The receptor occupancy analysis at 20 mg/kg and 30 mg/kg is ongoing.

Conclusions IBI188 was well tolerated at 1 mg/kg priming dose following by the maintenance dose up to 30 mg/kg.

Trial Registration NCT03763149

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