

Title: Prospective, multicenter, first-in-human phase 1/2 study of ^{64}Cu PSMA I&T investigating dosimetry, safety, and efficacy in men with biochemically recurrent metastatic prostate cancer

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Background: Prostate-specific membrane antigen (PSMA) is an established target for imaging prostate cancer (PC). This study demonstrates the safety, biodistribution, and efficacy of ^{64}Cu PSMA I&T, a novel tracer in men with biochemically recurrent metastatic PC.

Methods: 38 patients with biochemically recurrent metastatic PC were enrolled in this Phase 1/2 trial. The first 12 patients were randomized to receive either 5, 7, or 9 mCi ^{64}Cu PSMA I&T and underwent sequential positron emission tomography (PET) to assess the pharmacokinetics, radiation dosimetry, and image quality. Radiation dose to selected organs was estimated using OLINDA/EXM. The remaining 26 patients were enrolled in the Phase 2 portion of the trial and underwent PET/CT 1 and 4 hours after ^{64}Cu PSMA I&T administration. Images were assessed by three independent reviewers for presence or absence of disease. Results were compared to composite reference standards of histopathology, conventional imaging, or other FDA approved PSMA-PET to determine patient-level correct detection rate (CDR) and region-level correct localization rate (CLR) for the diagnostic performance of ^{64}Cu PSMA I&T ($H_0 = 60\%$ for both endpoints).

Results: There were no drug-related adverse events reported in any patients. Phase 1 dosimetry results identified the liver and right colon as the critical organs both with mean absorbed doses of 0.25 mGy/MBq. The average effective dose was 0.061 mGy/MBq. Image quality assessment in Phase 1 revealed 9 mCi as the optimal dosage, with an acceptable range of 7-9 mCi. In Phase 2, the CDR for 1-hour images was 77% to 84%, and 80% to 84% for 4-hour images. The CLR for 1-hour images was 77% to 87%, and 80% to 87% for 4-hour images.

Conclusions: ^{64}Cu PSMA I&T injection is safe and well tolerated and yields clinically relevant, high-quality images at a dosage range of 7-9 mCi. The co-primary endpoints of CDR and CLR were successfully met demonstrating ^{64}Cu PSMA I&T as a potentially safe and effective radiopharmaceutical for diagnostic PET in men with biochemically recurrent PC.

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Conflicts of Interest Statement: DRD, AB, and AM are employees of Curium.

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