



Meeting Report | Oncology: Basic, Translational & Therapy: Radiopharmaceutical Therapy

[¹³¹I]MIP-1375, a small molecule prostate-specific membrane antigen (PSMA) inhibitor for targeted therapy of prostate cancer (PCa)

Shawn Hillier, Ross Merkin, Kevin Maresca, Craig Zimmerman, John Barrett, Mathias Tesson, William Eckelman, Rob Mairs, John Joyal and John Babich

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Article

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Abstract

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Objectives [¹²³I]MIP-1072, (S)-2-(3-((S)-1-carboxy-5-(4-[¹²³I]iodobenzylamino)pentyl)ureido)pentanedioic acid is a high affinity ligand for PSMA (*Can Res* 2009) which has been shown to localize to radiologically-proven metastatic PCa in man. The high expression of PSMA in PCa has led us to evaluate the ¹³¹I analog of MIP-1072, MIP-1375, for therapeutic efficacy in human PCa tumor model.

Methods High specific activity MIP-1375 was prepared with Na¹³¹I via iododestannylation. LNCaP spheroids were treated with 0-37 MBq/mL MIP-1375 for 0-8 hours. Mice with PSMA(+) (LNCaP and transfected PC3-PSMA) or PSMA(-) (PC3-vector) xenografts were administered 35 MBq as a single dose or two doses one week apart. To determine whether PSMA binding was specific, a cohort of mice were co-injected with 10 mg/kg PMPA to block

Fusion Pharmaceuticals, Inc.
Exhibit 1009.001

PSMA binding. Radiotherapy was initiated when tumors reached 300 mm³. Tumor growth and body weight were monitored three times per week. LNCaP tumors were stained for KI-67, a marker of cellular proliferation.

Results MIP-1375 was synthesized to a radiochemical yield of 67%, a radiochemical purity of >98% and specific activity of >75 GBq/mmol. MIP-1375 inhibited the growth of LNCaP spheroids in a dose and time dependent manner, and significantly delayed the growth of PSMA(+) tumors as compared to controls. MIP-1375 treated LNCaP tumors exhibited decreased KI-67 staining compared to controls. PSMA-dependent efficacy was evident since tumors in mice co-injected with MIP-1375 and PMPA or PSMA(-) tumors grew at a rate equivalent to the vehicle groups. No significant change in body weight was observed in any group.

Conclusions MIP-1375 inhibited the growth of tumor xenografts in a PSMA-specific manner at ¹³¹I doses that are clinically relevant. These data support further investigation of MIP-1375 as a targeted radiotherapeutic for treatment of PCa in man

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