Objective: To develop an immuno-PET strategy for in vivo evaluation of CA125 expression in epithelial ovarian cancer.

Methods: CA125 targeting monoclonal antibody (MAb) was prepared from B43.13 hybridoma. p-isothiocyanatobenzyl-desferrioxamine (SCN-DFO) was conjugated to MAb-B43.13 for 89Zr-labeling. 89Zr was produced on a TR19/9 cyclotron at Memorial Sloan-Kettering Cancer Center, NY. Ovarian cancer cell lines OVCAR3 and SKOV3 were used for in vitro studies. Athymic nude mice were used to develop xenograft models for in vivo radiopharmacological evaluation by small animal PET.

Results: MAb-B43.13 specifically bound to CA125 overexpressing OVCAR3 cells in vitro. MALDI-TOF analysis revealed 3.4 DFO molecules conjugated per MAb. 89Zr-labeled MAB-B43.13 was obtained in 76% isolated radiochemical yields at >99% purity with a specific activity of 5.4 mCi/mg and > 91% immunoreactivity. The radioimmunoconjugate was > 95% stable in human serum at 37 °C over 168 h. In vivo evaluation of 89Zr-MAB-B43.13 in xenograft animals revealed a steadily increasing uptake > 20% ID/g in OVCAR3 tumors 120 h p.i, with highest signals in tumor proximal lymph nodes. EPR based uptake was seen for 89Zr-labeled MAB-B43.13 in SKOV3 tumors. 89Zr-MAB-B43.13 showed expected hepatobiliary clearance profile.

Conclusion: 89Zr-labeled MAB-B43.13 forms a suitable radiotracer for immuno-PET of epithelial ovarian cancer.

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Poster Communications

96 Development of HDD kit for preparation of liver cancer therapeutic agent Re-188-HDD/lipiodol

Vinay Kumar Banka, Sung-Hyun Moon, Sudhakara Reddy Seelam, Yun-Sang Lee, Jae Min Jeong

Nuclear Medicine, Seoul National University College of Medicine, Seoul, Korea

Lipiodol solution of 188Re-4-hexadecyl-2,2,9-tetramethyl-4,7-diaza-1,10-decanedithioacetate (188Re-HTDD) was developed for liver cancer therapy [1–3]. However, formulation of it is difficult due to multi-step syntheses and low labeling yield. We synthesized a new compound 4-hexadecyl-4,7-diaza-1,10-decanedithioacetate (HDD) to solve the problems. HDD was synthesized from N,N-4-hexadecyl-4,7-diaza-1,10-decanedithioacetate (HDD) to solve the problems. HDD was synthesized from N,N'-bis-(2-hydroxy-ethyl)ethylenediamine. BOC protection, thioacetate introduction, deprotection of BOC, and conjugation with 1-iodohexadecane afforded the final product. HDD was formulated into a kit and was labeled with 188Re by heating in a boiling water bath and successive extraction with lipiodol. The labeling yield was high (90.2%). A comparative biodistribution study of 188Re-HTDD and 188Re-HDD was performed after intravenous injection into normal mice. Data were obtained at 0.5, 1, 3, and 24 h post-injection. The major uptake site was lung due to capillary-blockage. 188Re-HDD/lipiodol showed significantly higher lung uptake than 188Re-HTDD/lipiodol (p < 0.05). In conclusion, newly synthesized 188Re-HDD/lipiodol showed improved radiolabeling yield and biodistribution results compared to 188Re-HTDD/lipiodol, and might be more adequate for liver cancer therapy.

References

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98 Novel, multivalent tracers targeting prostate cancer biomarkers

Rajendra Bandari, Tamila Stott Reynolds, Zongrun Ji, Charles Smith

The Truman VA Hospital
The University of Missouri

Gastrin-releasing peptide receptors (GRPR), prostate-specific membrane antigen (PSMA), and αvβ3 integrin are identifying biomarkers being investigated as possible tools for molecular targeting and diagnosis of prostate cancer via PET or SPECT scintigraphy. The aim of this study was to investigate and compare the usage of new multipurpose, bivalent [DUPA-6-Ahx-(64Cu-NODAGA)-5-Ava-BBN(7–14)NH2] and [RGD-Glu-[64Cu-NO2A]-6-Ahx-RM2] radioligands for prostate cancer imaging.

Methods: Conjugates were prepared by solid-phase peptide synthesis, purified by reversed-phase high-performance liquid chromatography, metallated with 64CuCl2 and 68CuCl2, and characterized by electrospray ionization—mass spectrometry. The binding affinity was evaluated in PC-3 (GRPR +), LNCaP (PSMA +), and U87-MG (αvβ3+) cells and the tumor-targeting efficacy determined by biodistribution and microPET/CT imaging in tumor-bearing mice.

Results: Competitive binding assays in PC-3, LNCaP, and U87-MG cells indicated moderate to high receptor binding affinity for the new tracers. MicroPET scintigraphy using [DUPA-6-Ahx-(64Cu-NODAGA)-5-Ava-BBN(7–14)NH2] in PC-3/LNCaP and U87-MG tumor-bearing mice indicated that xenografted tumors were visible at 18 h post-injection, with significant, background radiation also being observed in non-target tissue. On the