Comparison of preclinical dosimetric studies of ^{177}Lu-scFvD2B, ^{177}Lu-PSMA-617 and ^{177}Lu-iPSMA.

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Aim: The efficiency of targeted radionuclide therapy (TRT) is mainly based on the potential of endoradiotherapeutic agents to combine selective uptake and high tumor cell internalization with minimal risk to healthy tissues[1]. Consequently, internal dosimetry has become a very important tool to evaluate the risks and benefits of new endoradiotherapeutic agents. Currently, the low molecular weight (LMW) Glu-ureido Prostate-Specific Membrane Antigen (PSMA) inhibitors, labelled with ^{177}Lu-DOTA are the most successful TRT agents to treat prostate cancer (PCa) and its metastasis[2]. However, it has been demonstrated that the DOTA chelating moiety reduces their internalization and so their radiation dose to the tumor[1]. Previously, we developed the antibody-based construct ^{177}Lu-scFvD2B, wich demonstrated statistically significant higher cell uptake and internalization in LNCaP cells (PSMA-positive) when compared to two of the endoradiotherapeutic agents currently used in PCa therapy, the ^{177}Lu-PSMA-617 and the ^{177}Lu-iPSMA[3]. The aim of this study is to estimate the ^{177}Lu-scFvD2B organ and tumor-absorbed doses and to compare the values with those of ^{177}Lu-LMW agents**.**

Methods: ^{177}Lu-scFvD2B, ^{177}Lu-PSMA-617 and ^{177}Lu-iPSMA were prepared and their radiochemical purity determined. Biodistribution studies of each radiopharmaceutical were then carried out in healthy mice to define the main source organs (SO) and to calculate the number of disintegrations in each source organs per unit of administered activity (N_{SO}). Absorbed dose in the main organs were then calculated for each ^{177}Lu-conjugate by means of OLINDA/EXM 2.1.1 software, using as program inputs the calculated N_{SO} for both adult male and mouse phantoms. Tumor standardized uptake values (SUV) obtained from the 3D SPECT image reconstruction of mice bearing micro-pulmonary tumors injected with ^{177}Lu-conjugates, were used to calculated the number of disintegrations in a tumor site per unit of administered activity (N_T) of each conjugate. Then, tumor-absorbed dose was calculated using the electron S-values published for sphere models with diameters ranging from 10 μm to 10 mm, considering a tumor density equivalent to water density and uniform activity distribution.

Results: All ^{177}Lu-labelled agents were obtained in high yield (>98%). Dosimetric studies carried out using mouse and human phantoms demonstrated that organ absorbed doses of ^{177}Lu-scFvD2B were from 1.4 to 2.3 times higher than those for ^{177}Lu-iPSMA and from 1.5 to 2.6 times higher than those for ^{177}Lu-PSMA-617. However, the ^{177}Lu-scFvD2B values of tumor-absorbed doses for all investigated tumor sizes were higher, from 2.8 to 3.0 times greater than those calculated for ^{1177}Lu-LMW agents. Moreover, ^{177}Lu-scFvD2B showed the highest tumor/kidney ratio when compared to those reported for ^{177}Lu-PSMA albumin conjugates[4].

Conclusion: In this study, we demonstrated the potential of ^{177}Lu-scFvD2B as a therapeutic agent for PSMA-expressing tumors, due to its higher tumor-absorbed dose when compared with ^{177}Lu-LMW agents.

References:

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