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Preclinical dosimetric studies of 177Lu-scFvD2B, 177Lu-PSMA-617 and 177Lu-iPSMA

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Targeted radionuclide therapy (TRT) combine selective uptake and high internalization in tumor cells with minimal risk to healthy tissues. Consequently, internal dosimetry has become a very important tool for evaluating the risks and benefits of new TRT agents.

The aim of this study is to estimate the tumor-absorbed doses produced by a single chain(scFv)-based construct, 177Lu-scFvD2B, and to compare it with those produced by two low molecular weight (LMW) agents currently used in prostate cancer therapy, 177Lu-PSMA-617 and 177Lu-iPSMA.

The three radiopharmaceuticals (RFs) were prepared and their radiochemical purity determined. Biodistribution studies of each RF were then carried out in healthy mice to calculate the number of disintegrations in the main organs per unit of administered activity. Organs absorbed dose were then calculated with OLINDA/EXM 2.1.1 for each 177Lu-RF using both adult male and mouse phantoms. Tumor-absorbed dose was calculated for different tumor size using tumor uptake values, obtained from 3D SPECT image reconstruction of mice bearing LNCaP micro-pulmonary tumors treated with the 177Lu-agents.

All 177Lu-agents were obtained in high yield (>98%). Dosimetric studies with mouse and human phantoms demonstrated that organ absorbed doses of 177Lu-scFvD2B were higher than those of 177Lu-LMW agents. However, tumor-absorbed doses of 177Lu-scFvD2B for all tumor sizes investigated were 2.8 to 3.0 times higher than those of 177Lu-iPSMA and 177Lu-PSMA-617, respectively.

In conclusion, this study demonstrated the potential of 177Lu-scFvD2B as a therapeutic agent for PSMA-expressing tumors, due to its higher tumor-absorbed dose compared to 177Lu-LMW agents.