

Radiolabeled polyethyleneiminomethyl phosphonic acid as a molecule with potential for diagnosis and therapy. Comparative study on models of bladder cancer and osteosarcoma.

Ferreira S^{1,2,3}, Abrantes AM^{1,4}, Brito A¹, Laranjo M^{1,4}, Gonçalves AC^{4,5}, Sarmiento-Ribeiro AB^{4,5}, Metello L³, Zeevart J⁶, Louw W⁶, Dormehl I⁷, Botelho MF^{1,4}

¹Biophysics Unit, Institute for Biomedical Research on Light and Image, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

²School of Sciences, University of Minho, Braga, Portugal

³Nuclear Medicine Course, High Institute of Allied Health Technologies of Porto's Polytechnic Institute, Porto, Portugal

⁴Centre of Investigation on Environment, Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

⁵Applied Molecular Biology and Hematology Group, Faculty of Medicine, University of Coimbra, Coimbra, Portugal.

⁶Radiochemistry Department, NECSA, Pretoria, South Africa

⁷Department of Internal Medicine, University of Pretoria, South Africa

Introduction: The polymer PEI-MP (polyethyleneiminomethyl phosphonic acid) that might be labeled with ^{99m}Tc and ¹⁸⁸Re, have a strong potential for diagnosis and metabolic radiotherapy, respectively. The aim of this study was to evaluate the efficacy of ^{99m}Tc-PEI-MP for diagnosis and ¹⁸⁸Re-PEI-MP as therapeutic agent, in a comparative study using in vitro and in vivo models of bladder cancer and osteosarcoma.

Material and Methods: In vitro studies were performed using the cell lines of bladder cancer (CRL-1472) and of osteosarcoma (MNNG-HOS). Cytotoxicity of PEI-MP was investigated using

the MTT test and flow cytometry. Radiochemical purity of ^{188}Re -PEI-MP and $^{99\text{m}}\text{Tc}$ -PEI-MP was achieved using ascending microchromatography. Cellular uptake studies were performed using the complexes ^{188}Re -PEI-MP, $^{99\text{m}}\text{Tc}$ -PEI-MP, $\text{Na}^{188}\text{ReO}_4$ and $\text{Na}^{99\text{m}}\text{TcO}_4$. Cell samples were collected during four hours, centrifuged to separate supernatant and pellet. Subsequently, the radioactivity of each portion was counted to determine percentage of uptake. The in vivo studies were performed using twelve groups of Balb/c nu/nu mice: four normal groups injected with $\text{Na}^{188}\text{ReO}_4$, ^{188}Re -PEI-MP, $\text{Na}^{99\text{m}}\text{TcO}_4$ and $^{99\text{m}}\text{Tc}$ -PEI-MP, four with bladder carcinoma xenotransplants and four with osteosarcoma xenotransplants injected with the same complexes. After injection of the radiopharmaceuticals, were acquired dynamic and static images for 2 and 4 hours. For biodistribution proposes, mice were euthanized 2 and 4 hours after injection and organ samples where weighted and counted in a well-counter to obtain percentage injected activity per gram of organ (%ID/g).

Results: The MTT assay and flow cytometry tests showed that PEI-MP is not cytotoxic. The radiochemical purity of ^{188}Re -PEI-MP and $^{99\text{m}}\text{Tc}$ -PEI-MP was $\geq 85\%$. The uptake studies demonstrated that the uptake was higher for ^{188}Re -PEI-MP and $^{99\text{m}}\text{Tc}$ -PEI-MP in relation to their controls, and higher for ^{188}Re -PEI-MP e relation to $^{99\text{m}}\text{Tc}$ -PEI-MP. Biodistribution results, with $\text{Na}^{188}\text{ReO}_4$ and $\text{Na}^{99\text{m}}\text{TcO}_4$, showed a higher uptake by the thyroid, bladder and stomach, following a normal biodistribution. The biodistribution with ^{188}Re -PEI-MP and $^{99\text{m}}\text{Tc}$ -PEI-MP showed that the excretion of these complexes occurs primarily through the renal system, with a small fraction being eliminated by the hepatobiliary system. Tumor/muscle ratio for ^{188}Re -PEI-MP was >1 for the xenotransplants of osteosarcoma and >1.5 to xenotransplants of bladder cancer.

Conclusions: Considering the results, ^{188}Re -PEI-MP seems to be promising in the treatment of both types of cancer, but with a greater potential for bladder cancer. $^{99\text{m}}\text{Tc}$ -PEI-MP seems to be optimal for diagnosis of both types of cancer.



It has been decided that it would not be shown the entire version of this document.

To obtain more informations:

www.nucmedonline.net

cursomedicinanuclear@gmail.com



Referencial: SC-HESD 090