

In-vivo comparison of thorium-227 and zirconium-89 labeled 3,2-HOPO mesothelin antibody-chelator conjugate

Targeted thorium conjugates (TTCs) represent a new class of therapeutic radiopharmaceuticals for the targeted alpha therapy (TAT) of cancer. Cell surface glycoprotein mesothelin is highly expressed in many human cancers. Mesothelin targeted thorium-227 conjugate (MSLN-TTC, BAY 2287411), comprising a mesothelin targeted antibody (MSLN-Ab), covalently attached to 3,2-HOPO chelator, enabling specific complexation and delivery of the alpha particle emitter thorium-227 (^{227}Th) to tumor cells, is currently in a phase 1 clinical trial (NCT03507452). 3,2-HOPO systems are also very efficient chelators for zirconium-89 and it has therefore been suggested that positron emission tomography (PET) imaging provides a useful surrogate for understanding ^{227}Th radio-immunotherapy. Hence, we describe the radiolabeling of the conjugated MSLN-Ab conjugate with the PET isotope zirconium-89 (^{89}Zr) and show data from a biodistribution study comparing both thorium and zirconium conjugates.

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