

Abstracts Swiss Radiopharmacy Day 2025!

Terbium-149 for Targeted Alpha Therapy: Comparison of the Somatostatin Analogues [149Tb]Tb-DOTATATE and [149Tb]Tb-DOTA-LM3 (A. Katrina Mapanao, PSI)

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Background: Alpha-particle emitters are gaining interest for targeted radionuclide therapy due to the high energy and short tissue range of α -particles, which may result in improved treatment outcome. Terbium-149 is an appealing radionuclide due to its favorable decay properties ($T_{1/2}$: 4.1 h, E_{α} : 3.98 MeV), including the emission of β^+ -particles suitable for PET. In this study, we aimed to compare the somatostatin analogues [¹⁴⁹Tb]Tb-DOTATATE and [¹⁴⁹Tb]Tb-DOTA-LM3 with regard to their therapeutic efficacy and safety.

Methods: Terbium-149 was produced at ISOLDE/CERN by spallation reaction combined with online mass separation, followed by radiochemical separation by the Radionuclide Development Group at the Paul Scherrer Institute. [¹⁴⁹Tb]TbCl₃ was used to label the cell-internalizing (DOTATATE) and non-internalizing (DOTA-LM3) somatostatin analogues. Cell viability and DNA damage were investigated in somatostatin receptor-positive AR42J cells exposed to [¹⁴⁹Tb]Tb-DOTATATE or [¹⁴⁹Tb]Tb-DOTA-LM3. Treatment outcome was investigated after injection of AR42J tumor-bearing mice with 1×5 MBq of the radiopeptides. The tolerability of 20 MBq [¹⁴⁹Tb]Tb-DOTATATE or [¹⁴⁹Tb]Tb-DOTA-LM3 was investigated in immunocompetent mice without tumors.

Results: [¹⁴⁹Tb]Tb-DOTATATE and [¹⁴⁹Tb]Tb-DOTA-LM3 were prepared at molar activities up to 20 MBq/nmol at >98% radiochemical purity. Cell viability was reduced in an activity concentration-dependent manner, with a slightly more potent effect observed for [¹⁴⁹Tb]Tb-DOTA-LM3 than for [¹⁴⁹Tb]Tb-DOTATATE. The induced DNA damage was, instead, comparable between the two radiopeptides. Treatment of mice with 1×5 MBq [¹⁴⁹Tb]Tb-DOTATATE or [¹⁴⁹Tb]Tb-DOTA-LM3 delayed tumor growth, leading to longer median survival

times (16.5 and 19 days, respectively) compared to that of untreated mice (8 days). The application of the radiopeptides at 20 MBq/mouse was well tolerated.

Conclusion: ^{149}Tb -labeled somatostatin analogues demonstrated promising potential for targeted α -therapy. Subcellular localization appeared to be irrelevant on the treatment outcomes as the differences between the two radiopeptides were marginal. No relevant adverse effects were observed.

Optimizing FAP Radiopharmaceuticals: Key Insights from a Dose Escalation Study (E. Gourni, Inselspital)

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Introduction: FAPI-based radiopharmaceuticals show promise for pan-cancer targeting. However, significant challenges remain, particularly the high blood pool uptake.

This study examines key factors influencing FAPI-radiotracer effectiveness, focusing on dose variations of five tracers (two monomers, three dimers). It also assesses their FAP selectivity and expression in cellular and animal models.

Methods: A dose-escalation study in PC3-mice evaluated [^{68}Ga]Ga-labeled FAPI tracers (10–1500 pmol). Pharmacokinetics were assessed via biodistribution, PET/CT (1 h p.i.), and metabolite analysis. Selectivity for FAP, PREP, and DPP4 was tested using the relevant inhibitors. qPCR verified FAP expression in murine organs, while ELISA measured circulating FAP in PC3-mice, healthy mice, and human volunteers.

Results: The administered dose significantly impacted blood retention, tumor uptake, and overall in vivo performance, emphasizing the need to optimize the injected mass of FAPI-radiotracers. Increasing the dose from 10 pmol to 350–600 pmol reduced blood uptake 5–8-fold while maintaining tumor uptake at 12%–19% IA/g. For [^{68}Ga]Ga-DOTAGA.Glu.(FAPi)₂, blood uptake dropped from 25.8±3.2% IA/g (10 pmol) to 3.2±0.5% IA/g (600 pmol), with tumor uptake rising from 12.5±1.7% to 16.5±2.3% IA/g. Higher doses (1000–1500 pmol) significantly altered the pharmacokinetics.

The ^{68}Ga -labeled tracers showed high FAP selectivity and in vivo stability. qPCR analysis confirmed high FAP expression in bones, tumors, pancreas, salivary glands, and bone marrow, aligning with biodistribution. Circulating FAP was detected in plasma from PC3-mice, healthy mice (100–116 $\mu\text{g/mL}$), and human volunteers (112–180 $\mu\text{g/mL}$).

Conclusions: Precise mass administration is crucial for optimal in vivo performance. Successful diagnostics and therapy depend on circulating FAP and accurate radiotracer dosing, ensuring favorable FAPI-radiotracer outcomes and highlighting the need for careful administration.

Radioprotection: How to Perform Nuclear Medicine Examinations in Pregnant Women (M. Nicod Lalonde, CHUV)

Pregnant women may present with conditions, which require nuclear medicine diagnostic imaging involving ionizing radiation. The clinical justification for the procedure must be thoroughly assessed before deciding on whether it should be performed. Imaging during pregnancy poses unique challenges, as it must balance clinical benefits for the mother with potential risks to fetal development. When imaging is clearly indicated, imaging parameters are adjusted in collaboration with medical physicists to minimize fetal exposure. Additionally, the fetal radiation dose is carefully estimated and discussed with the mother, and informed consent is obtained after ensuring that the patient fully understands the potential risks.

^{99m}Tc supply chain: Overview and challenges (M. Willemin b.e.Imaging)

The supply chain to produce Mo/Tc generators will be explained considering the aspects of logistics/transport, production/chemistry and radiation protection. Past and current supply challenges for Mo/Tc generators will be discussed from different angles which allows an estimation of the future supply situation.

Towards GMP Production of ^{68}Ga -Labelled Radiopharmaceuticals using Gallium-68 from Cyclotron (A. Jordanova, M. Liechti, Swan Isotopen AG)

^{68}Ga -labelled radiopharmaceuticals play a key role in modern nuclear medicine for diagnostic PET imaging and are widely used on a daily basis. To overcome the limitations of $^{68}\text{Ge}/^{68}\text{Ga}$ generator-based production, SWAN Isotopen AG is developing an innovative alternative process. This process uses cyclotron-produced gallium-68, which is purified and subsequently used for the radiosynthesis of ^{68}Ga -labelled radiopharmaceuticals using a standard synthesis module. The process is established following the Quality by Design principle in accordance with relevant guidelines, enabling the production of GMP-compliant ^{68}Ga -labelled radiopharmaceuticals in high quality and quantity.

The presentation will focus on the development of GMP-compliant production of ^{68}Ga -labelled radiopharmaceuticals using cyclotron-produced gallium-68, addressing both the challenges and the progress made in implementing this process, with an emphasis on the technical and regulatory aspects.

To date no other abstracts available.