Simultaneous Auger e^- and β^--Particle Therapy of Metastasized NET Using ^{161}Tb-DOTATOC

Roger Schibli[1,3], Cristina Müller[1], Nicholas P. van der Meulen[1], Richard P. Baum[2]
[1]Center for Radiopharmaceutical Sciences, Paul Scherrer Institute, 5232 Villigen-PSI, Switzerland, [2]Institute of Pharmaceutical Sciences, ETH Zurich, 8093 Zurich, Switzerland, 3 THERANOSTICS Center for Molecular Radiotherapy and Molecular Imaging, ENETS Center of Excellence, Zentralklinik Bad Berka, 99438 Bad Berka, Germany

Background: Targeted radionuclide therapy using radiolabeled somatostatin analogues is currently among the most successful treatment options for patients suffering from somatostatin receptor-positive metastasized neuroendocrine tumors (NET). Recurrence of the disease based on single cancer (stem) cells that have escaped the therapy is, however, still a critical point in the disease management. The aim of this project is to develop a new concept of radionuclide therapy of NET, based on the radionuclide terbium-161.
Experimental Approach: ^{161}Tb has similar decay properties (β^-, γ) as the clinically-established ^{177}Lu (β^-, γ), however, it also emits Auger-e^- (12 e^-/decay) which are particularly effective for the treatment of smallest lesions and even single cancer cells. We have established an elegant production route via ^{160}Gd(n,γ)^{161}Gd→^{161}Tb which leads to carrier-free ^{161}Tb in quantities >10-20 GBq.
Results: In vitro and in vivo studies demonstrated superior therapeutic efficacy of ^{161}Tb compared to the effect of ^{177}Lu in combination with various tumor targeting molecules including DOTATOC. We have also established the production of ^{161}Tb-DOTATOC on an automated system (Eckert&Ziegler) according to GMP.
Conclusions & next steps: A pilot clinical study in three patients will be performed with ^{161}Tb-DOTATOC. These data should serve as the basis for a further multi-center clinical study. We believe that killing single cancer (stem) cells and destroying micro-metastases with Auger-e^-, while maintaining the effect of β^--particles, will result in a paradigm shift in the treatment of neuroendocrine cancer.