

Clinical and Pre-clinical Evaluation of Theranostic Pair (Terbium-161 and Terbium-155) for Imaging and Radionuclide Targeted Therapy of Tumors

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Introduction & background: (state of the art and goal/motivation for the project)

The idea of theranostic approach is rapidly gaining momentum among the academia and practitioners in nuclear medicine community and there is considerable interest to commercially produce these isotopes for clinical applications. The approach combines diagnosis and therapy with suitable radiotracers. One of the most promising theranostic pair comes from the quadruped of terbium isotopes e.g., Terbium-161 (quite often referred to as the Swiss knife of nuclear medicine) and Terbium-155. Reactor produced Terbium-161 emits beta particles for therapeutic applications while accelerator produced Terbium-155 emits gamma rays for SPECT diagnosis. Both of the isotopes have suitable comparable half-lives for therapy as well as imaging for the required extended period of time. Isotopes of the same element as theranostic pair offers excellent mapping due to the same biological pathways and distribution. Global capability of Tb-155 production is limited owing to limited numbers of high energy particle accelerators.

PINSTECH and MEDICIS facility at CERN has already signed an active collaboration agreement in the field of novel theranostic isotopes production. As part of the collaboration, one PINSTECH scientist is deputed on secondment at MEDICIS for the radiochemistry experiments for one year. Three scientists from PINSTECH have already completed the assignment at CERN while the fourth one is currently in MEDICIS for the experimentation. Three consignments of Actinium-225, a promising alpha emitter for targeted radionuclide therapy, have been received at PINSTECH from MEDICIS. Radiolabelling of Ac-225 has successfully been demonstrated at INMOL-Lahore while the work on the Generator System for Ra-225/Ac-225 is currently underway at IPD-PINSTECH. Irradiation facility at PARR-1 is used for enriched Platinum-194 and the irradiated sample as Platinum-195m is shipped back to MEDICIS for clinical studies.

Project description:

Counterparts	Proposed Roles and Contribution
MEDICIS-CERN	<ul style="list-style-type: none">• Provision of mass separated Terbium-155 and required chromatographic resins for purification
PINSTECH	<ul style="list-style-type: none">• Production and purification of Terbium-161• Purification of Terbium-155 imported from CERN• Radiolabelling of Terbium-161 and Terbium-155 with suitable bio-molecules
NORI-Islamabad and IRNUM-Peshawar Cancer Hospitals	<ul style="list-style-type: none">• Clinical trials/Patient studies on R&D basis

In order to further strengthen this collaboration and use it for the full benefit of cancer patients, it is suggested that stakeholders in CERN-MEDICIS will provide Terbium-155 isotope to PINSTECH for R&D purposes. The said isotope, Tb-155 will be used in combination with Tb-161 as a perfect theranostic pair for pre-clinical and clinical evaluation of different types of tumors. In order to materialize the proposal, different types of resin (LN, AMINEX, and DGA) will be required from CERN-MEDICIS for purification of these promising isotopes. As a joint venture between PINSTECH and MEDICIS, Terbium-161 will be produced in Pakistan Research Reactor-1, PARR-1, for therapeutic applications while Terbium-155, currently produced and collected at MEDICIS' facility, will be provided by MEDICIS. The two isotopes making the Theranostic Pair will be evaluated for pre-clinical studies (radiolabelling with suitable ligands, biodistribution and toxicity) at IPD-PINSTECH while clinical trials/patient studies will be performed at the two cancer hospitals in IRNUM-Peshawar and NORI-Islamabad.

Materials and Methods: Therapeutic isotope Terbium-161 will be produced by irradiating enriched Gadolinium-160 at Pakistan Research Reactor-1 and purified on the LN chromatographic resin. After purification, the isotopes will be labeled with DOTA-TATE and PSMA followed by bio-distribution and toxicity studies on mice. The diagnostic counterpart Terbium-155 will be imported from MEDICIS either after mass separation from the Cerium-139 or on the Sodium Chloride layer on the Aluminum backing. After required purification, both the isotopes will be sent to the cancer hospitals for patient studies and collection of efficacy data.



Project proposal to the MEDICIS Collaboration board



References and Funding: The project will be a joint venture on the terms and conditions of the already signed agreement between MEDICIS and PINSTECH with mutually agreed details.

Isotope requests: Human grade purified isotope of Terbium-155 in MBq quantity for diagnostic purpose.