Title of Study:

PReCedeNT trial: Phase III randomised-controlled open-label trial of Lutetium - 177 Peptide Receptor Radionuclide Therapy (PRRT) Plus Chemotherapy Versus PRRT alone in FDG-avid, Well-Differentiated Gastro-Entero-Pancreatic Neuroendocrine Tumors (GEP-NETs)

Date: 08.07.2019

Informed Consent form; Version 1.3

PARTICIPANT INFORMATION SHEET AND INFORMED CONSENT FORM

Title of Study	PReCedeNT trial: Phase 3 randomised open-label trial of Lutetium - 177 Peptide Receptor Radionuclide Therapy (Lu-177-PRRT) Plus Chemotherapy Versus Lu-177-PRRT alone in FDG-avid, Well-Differentiated Gastro-entero-pancreatic Neuroendocrine Tumors (GEP-NETs)		
Subject Number:		Subject Date of Birth:	

Introduction - You are invited to participate in the research project as titled above. This document gives you a description of the mentioned study in which you are being asked to participate. Your participation in this study is voluntary and you can enquire about all details before giving your written consent to participate in the study.

You have been diagnosed with a metastatic neuroendocrine tumor which has increased in spite of adequate treatment . At present, there are multiple treatment options present, which include Octreotide, PRRT and chemotherapy. However, whether a combination of such therapies is preferable is not yet known. The current available medical literature suggests that your tumor characteristics require radionuclide therapy, that is, PRRT, for the control of disease. However, in patients like you, we are trying to develop a treatment plan wherein chemotherapy can be added to the radionuclide therapy, which may be effective. For the development of this treatment we are doing this study and you're invited to be a part of it.

Purpose: The purpose of this study is to compare the combination treatment of chemotherapy and radionuclide therapy i.e PRRT, with PRRT, in metastatic locally advanced/inoperable neuroendocrine tumors

Overall Study information

What is PRRT ? : PRRT is a type of radionuclide therapy. Radionuclide is a radioactive element which emits radiation. For radionuclide therapy, we use radioactive elements which emit radiation which kills cancer cells and does not cause much effect on other cancer cells in the body. When the radionuclide is attached to a substance which is present on cancer cells, this compound (radionuclide and attached substance) attach to surface of cancer cells and kill the cancer cells by this radiation. There is a substance known as octreotide which binds on the cancer cells of your type of cancer. So when the radionuclide, that is, Lutetium-177 (Lu-177) is tagged to this octreotide, and is injected, it thereby binds to cancer cells.This is commercially available as Lu-177-DOTATATE. TATE is the octreotide- and DOTA is the substance which attaches Lu-177 to TATE.

This therapy shall be administered in a radionuclide therapy ward, where you shall have to stay for 24 hours, in keeping with the radiation safety protocol. It is the accepted treatment for cancer like yours

What is combination therapy ? : Patients like you who have higher grade of neuroendocrine tumor or in whom cancer has spread rapidly can also be treated with chemotherapy, in order to control the aggressive cancer cells. Hence, combination of PRRT and chemotherapy can be effective in patients like you.

Study Participation: The patients of metastatic neuroendocrine tumors will be invited to participate in this study. At the beginning of the study you will be evaluated for eligibility based on your age, pathology report, general condition, medical history and prior therapy for the disease. In addition some blood tests and scans like Ga-68 DOTATOC PET/CT scan shall be done.
Once you are eligible and willing to participate in the study, a computer program will decide which treatment you receive, as this is a randomized study. The assignment is purely on the basis of chance and is done by a process called 'randomisation'. No doctor or care-giver has control over this process.

You will be assigned to either of the following two groups:
PRRT group (often called Arm A):
In this group, you shall receive lutetium-177 labeled DOTATATE (radiotracer labeled to octreotide) only. It will be injected intravenously in a radionuclide therapy ward in Tata Memorial Hospital, Parel. After receiving the therapy you shall be observed and kept in the ward for 24 hours, as per the radiation safety guidelines.
You shall receive 4 cycles of PRRT with a gap of 8-12 weeks between the individual sessions of PRRT
PRRT plus chemotherapy group (often called Arm B):
In this group, you shall receive PRRT as described in PRRT group. In addition, after 14-21 days of completion of PRRT, you shall receive oral tablet chemotherapy, which will be a combination of Capecitabine and Temozolamide. The combination of these tablets will be repeated every 4 weeks (=1 cycle) and you will receive 2-3 such cycles after every session of PRRT. Post completion of PRRT and combination chemotherapy, further chemotherapy may or may not be continued depending on how you tolerate and respond to the treatment.
Risks / Benefits:

Risks:
PRRT
More common side effects include fatigue, nausea (30%) and vomiting (15%), usually on the first day. About 65% of patients receiving PRRT experience temporary hair loss (not baldness), but the hair will resume growing when the treatment is concluded.
PRRT does have some temporary side effects. The most frequent side effects are mild reductions in the number of white blood cells and blood platelets. A decrease in the white blood cell count may result in infections. Platelets assist in the clotting of blood, so a decrease in platelet concentration may increase the risk of internal bleeding. In a few cases the platelet count may fall to dangerous levels, which may require treatment and could lead to the postponement of the next treatment cycle.

These can be managed by symptomatic treatment and in some cases may require decrease in dose of the drug. You would be monitored at each visit for these side effects and corrective measures would be taken as soon as these are noticed.
The worrisome side effects would be seen in below 10% of patients.
Rarely, patients with extensive, diffuse liver metastases, a deterioration of liver function leading to encephalopathy may occur in the weeks following PRRT therapy. This could be reversible or in very rare cases, irreversible leading to death.
Chemotherapy
The above mentioned chemotherapy regimens are standard of care. The risk of side effects and toxicities are well known and will be managed as a part of standard protocol.

Benefits:. You may or may not directly benefit from taking part in this study. Future patients like you would benefit from what is learned. This information would help doctors in future to decide whether to give this treatment in patients like you.

Costs: Cost of treatment of side effects in will be borne by patient.

Confidentiality: The information in the study records will be kept confidential and the clinical charts will be housed in the TMH/CRS. Data will be stored securely and will be made available only to persons conducting the study and to the regulatory authorities. The data will not be made available to another individual unless you specifically give permission in writing. No reference will be made in oral or written reports which could link you to the study. Result of the study will not be communicated unless deemed necessary.

Compensation for Injury: Since both arms are standard of care, you will not be entitled to any compensation

Participation: Your taking part in this study is entirely voluntary. You may refuse to take part in the study or you may stop your participation in the study at any time, without a penalty or loss of benefits. Your participation also may be stopped by the study doctor without your consent. This may happen if there untoward side effects of chemotherapy or in case if your tumor unfortunately comes back on it. If any new information about this treatment becomes available, you will be informed about it.
If you withdraw from the study prior to its completion, you will receive the usual standard treatment and your non participation will not have any adverse effects on your subsequent medical treatment or relationship with the treating physician.
If you withdraw from the study before data collection is completed, your data will not be entered in the study report.

Your Responsibilities: You need to come regularly to the hospital as per the scheduled visits and report about any adverse effects.

Site Information and Contact Details: If you have questions at any time about the study or the procedures, or to report any health related information and experienced adverse effects as a result of participating in this study, you may contact the study doctor.

Study Doctor's Name	:	Dr Ameya Puranik
Address	:	Dept of Nuclear Medicine, Main Building Basement, Tata Memorial Hospital Dr. E. Borges Marg, Parel, Mumbai – 400012
Contact No.	:	022-24177151/7019

If you have any questions about the informed consent process or your rights as a participant, contact the Member Secretary of Institutional Ethics Committee (IEC).

IEC Contact Person's Name:		Dr. Umesh Mahantshetty/ Dr. Girish Chinnaswamy
Address	:	
Contact No.	:	022-24177262

Informed Consent Form

Study Title: Phase 3 randomised open-label trial of Lutetium - 177 Peptide Receptor Radionuclide Therapy (Lu-177-PRRT) Plus Chemotherapy Versus Lu-177-PRRT alone in FDG-avid, Well-Differentiated Gastro-entero-pancreatic Neuroendocrine Tumors (GEP-NETs)

Study Number:

Subject's Initials:_____ **Subject's Name**:_____

Date of Birth / Age:_____

To become a part of this study and to authorize use and disclosure of your personal health information, you or your legal representative must sign this consent form and date the signature page.
Please read this section carefully and if in agreement please sign and date at the bottom of the page.

1. I confirm that I have read and understood the information mentioned in the information sheet dated __/ __/ ____ for the above mentioned study and have had the opportunity to ask questions.
2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I understand that the study doctor, others working on the doctor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
5. I agree to take part in the above study.

I have read the above information and agree to participate in this study. I have received a copy of this form.

Participant’s name	
Participant’s signature/thumb impression & date	
Legal Acceptable Representative name	
Legal Acceptable Representative signature/thumb impression & date	
Address (Capital letters) Phone Nos.	
Impartial Witness’s name	
Impartial Witness’s signature & date	
Address (Capital letters) Phone Nos.	
Name of P/I or Co-PI/Co-I:	
P/I or Co-PI/Co-I Signature & date	