IRST202.02

"PEPTIDE RECEPTOR RADIONUCLIDE THERAPY WITH 90Y-DOTATOC IN RELAPSED/REFRACTORY DIFFUSE LARGE B CELL AND MANTLE CELL LYMPHOMAS"

IRST202.02_ Report Conclusione Arruolamento

EudraCT number**: 2014-003418-10**

Title**: PEPTIDE RECEPTOR RADIONUCLIDE THERAPY WITH 90Y-DOTATOC IN RELAPSED/REFRACTORY DIFFUSE LARGE B CELL AND MANTLE CELL LYMPHOMAS**

Protocol: **ID IRST202.02**

Promoter: **IRCCS Istituto Romagnolo per la Cura dei Tumori "Dino Amadori" IRST S.r.l., Meldola (FC)**

Coordinating Center: IRCCS IRST

Study Chair: **Dr Maddalena Sansovini**

Study Activated: **09/02/2015**

First Patient Enrolled: 22/12/2016

Target**: 35 patients**

Actual accrual: **1 patient**

Rationale

90Y-DOTATOC	90Y- dotatoc consists of a somatostatin peptide analogue (Tyr-octreotide) conjugated to a metal complexing moiety (DOTA), and labeled with a tightly-bound beta-emitter (yttrium-90). DOTA-DPhe'-Tyr'-octreotide binds to high-affinity somatostatin receptors (Subtypes 2 and 3) and retains both its receptor binding properties and its physiological function when labeled with yttrium-90. Yttrium-90 is a high-energy-beta-emitter with a mean path length of approximately 4 mm in tissue and a decay half-life of 64.1 hours, making it particularly effective for tumor treatment. By targeting somatostatin-receptor positive tumors, 90Y-dotatoc may deliver a targeted tumoricidal dose of radiation. In heterogeneous tumor tissue, a 90Y-labeled peptide conjugate can also kill those tumor cells which fail to express the respective receptor but are located within the vicinity of the receptor-expressing cells.
Treatment	Each patient will receive a maximum cumulative 90Y-DOTATOC activity of 11.1 GBq (300 mCi), divided into 4 cycles (1.8 - 2.8 GBq for each cycle) with an interval of 6 – 8 weeks between cycles. The 90Y-DOTATOC will be slowly infused intravenously.

Indication and population	Patients with histologically confirmed relapsed or refractory DLBCL or MCL not suitable to other treatments and a diagnostic PET/CT with 68Ga-DOTATOC images demonstrate a significant uptake in the tumour (SSR-positive tumour).
Marketing Approval:	The radiopharmaceutical 90Y-DOTATOC had no marketing approval. Both components (90Y and Dotatoc) were commercially available. (The labelling procedure and quality control of 90Y-DOTATOC compound was performed at the Radiometabolic Unit in the radiochemistry lab, according to internal procedures referred to the current regulations (Decreto Ministero Salute 30 Marzo 2005 and further updates).

This study was authorized by AIFA on 01/12/2014 and authorized by the Italian Ethical Committee (CEROM) on 17/12/2014.

Objectives

The primary objective of the study was the overall response rate evaluation of Y-PRRT in relapsed or refractory DLBCL and MCL NHL, not suitable to other therapies, including HDCT, or patients relapsed after HDCT with ASCT.
The secondary objectives were the acute and late toxicity, the type and duration of lymphocyte toxicity, (B, T, NK lymphocytes), progression free survival, overall survival and Quality of Life.

Primary and Secondary Endpoints/Outcome Measures

The *primary endpoint* was the overall response rate [ORR = CR + PR].
For the ORR, each patient was assigned to one of the following categories: 1) complete response, 2) partial response, 3) stable disease, 4) progressive disease, 5) early death from malignant disease, 6) early death from toxicity, 7) early death because of other cause, or 8) unknown (not assessable, insufficient data). Patients in response categories 3-8 should be considered as failing to respond to treatment.
The safety profile of each treatment was summarized with the NCIC-CTG classification.

The *secondary end points* were the PFS and the OS.

The analysis was performed in the activity population. The late toxicity was recorded according to the CTC-AE, version 4.0 in the safety population until FUP would be completed (48 months).
Quality of life will be evaluated with Version 3.0 EORTC QLQ-C30.

Sample Size

It was estimated to enroll a maximum of 35 patients in 36 months; the treatment efficacy would have been tested in 18 patients in the first stage.

The study was conducted following the Optimal Two Stage Design proposed by Simon assuming the true response probability:

· under H0 (p0) <=10%

· under H1 (p1) >=30%

and considering alpha=0.05 and power=0.90.

After testing treatment efficacy on 18 patients in the first phase, the study would be stopped if 2 or fewer patients showed an objective response. If the study had progressed to the second phase, a total of 35 patients would have been studied. If the total number of responding patients is less than or equal to 6, the treatment would have been considered ineffective.

Each patient would receive a maximum cumulative 90Y-DOTATOC activity of 11.1 GBq (300 mCi) divided into 4 cycles (1.8 - 2.8 GBq for each cycle) with an interval of 6 – 8 weeks between cycles. The activity to be administered would be measured in a dose calibrator, properly calibrated for the 90Y-radionuclide.

Summary of overall safety assessment:

There were no safety findings that necessitated any action to be taken with regard to the conduct of the clinical trial.

Conclusions:

IRST202.02 study, authorized by AIFA on 01/12/2014, notified to the Ministry of Health in December 2014 and approved on 17/12/2014 by the Ethics Committee of Area Vasta Romagna and IRST (CE of the IRCCS IRST Coordinating Center), had been closed on the 23/02/2018 due to criticalities in patient enrollment.
The study planned recruit a target of 35 patients over a 3-year period, but only one subject has been recruited.

The study is therefore discontinued due to severe difficulties in identifying patients eligible for the study.

Firmato digitalmente da: Bernadette Beatrix Vertogen
Data: 06/12/2022 11:36:53