IRST189.03_ RENALVax-2

"Vaccination with dendritic cells pulsed with autologous tumor homogenate in combination with HD-IL2 and immunomodulating radiotherapy in metastatic RCC: a phase II trial"

IRST189.03 Report Conclusione Arruolamento

EudraCT number**: 2015-000556-14**

Title**: Vaccination with dendritic cells pulsed with autologous tumor homogenate in combination with HD-IL2 and immunomodulating radiotherapy in metastatic RCC: a phase II trial**

Protocol: **ID IRST189.03**

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

Coordinating Center: IRCCS IRST

Study Chair: Dr.ssa Laura Ridolfi

Study Activated: 03/03/2016

Target**: 37 patients**

Actual accrual: **0 patients**

Rationale	This study focused on the evaluation of immunomodulation interventions association with an autologous dendritic cell vaccine and verify if an improvement of its clinical activity occured. Scientific data described the role of radiotherapy in the enhancement of immunological treatment effects, including vaccines, performed in cancer patients. Moreover, Interleukin-2 (IL2) administered at high doses could determine long lasting complete objective responses. Combination between IL2 and radiotherapy associated to vaccine should increase its clinical and immunological efficacy. Autologous Dendritic Cell Vaccine was produced from tumor tissue, apheresis product and plasma sample obtained from patient and processed according GMP procedures in the IRST Cell factory, which was authorized by AIFA for cell therapy production in April 2012. Interleukin-2, a lymphokine, was produced by recombinant DNA technology using a genetically engineered Ionizing radiation therapy (RT) has the well-established ability to kill cancer cells and other cells within the tumor stroma, including endothelial cells and

	intratumoral lymphocytes. Tumor cells killed by RT could be a very good source of antigens for Dendritic Cell (DC) uptake and presentation of T cells. Optimal activation of T cells by DC could be achieved only in the presence of inflammatory or "danger" signals. These danger signals were generated by radiation exposure, although their nature remained largely undefined. Pro-inflammatory cytokins IL-1beta,and TNFalfa could be induced by radiation.
Treatment	Three daily doses boost radiotherapy (XRT) at 6-12 Gy to at least 1, and up to a maximum of 5, metastatic fields, were administrated on days -4 -3 -2 or -3 -2 -1 before the first and the third cycle of vaccine+IL-2. The first day of administration of vaccine is day +1 and of IL-2 is day +2. The intradermal autologous dendritic cell vaccine loaded with autologous tumor homogenate plus IL-2 (dose 18 MIU/m2/day in 500cc by continuous IV infusion for 72 hours) was administered every 3 weeks up to 6 cycles.
Worldwide Marketing Authorisation Status	Interleukin-2 is commercially available worldwide. Therapeutic autologous DC vaccine is produced in IRST Cell Factory (authorization AIFA n. aM -26.2015 of 13.02.2015). All the study drugs are provided to the participating center IRST.

This study was authorized by AIFA on 27/01/2016 and authorized by the Italian Ethical Committee on 17/02/2016.

Objectives

The primary objective of the study was the evaluation of Overall Response Rate (ORR) by immune-response criteria (irRC).

The secondary objectives were:

- Overall survival (OS)
- Duration of response
- Progression free survival
- ORR by RECIST 1.1 criteria
- Toxicity
- Prognostic and predictive marker response
- Immunologic response

Sample Size

The study protocol foresaw a minimax two-stage Simon design :

- Step 1: recruitment of 12 patients. A 5% response rate precluded further study, whereas a 20% response rate indicated that further study could be warranted. Using alfa and beta errors of 0.10, if

an objective response was observed in at least 1 of the 12 patients enrolled during the first stage the study would go on with the step2.

- Step 2: recruitment of an additional 25 patients

The treatments would be considered active if an objective response was observed in 4 out of 37 patients treated.

Conclusions:

The study was stopped due to lack of patient enrollment on the 17/09/2018.

The study included a target of 37 patients over a period of 3 years, but no subjects were recruited.
The study was therefore discontinued due to major difficulties in identifying eligible patients due to the availability of new highly effective therapies and competitive experimental studies (overlapping inclusion/exclusion criteria and line of treatment) and finally for the logistical and therapeutic complexity that involves the combined treatment proposed in the protocol.

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