IRST172.04_ ACDC

Complementary vaccination with dendritic cells pulsed with autologous tumor lysate in resected stage III and IV melanoma patients: a phase II randomized trial (ACDC adjuvant Trial)

IRST172.04_ Report Conclusione Arruolamento

EudraCT number**: 2014-005123-27**

Title**: Complementary vaccination with dendritic cells pulsed with autologous tumor lysate in resected stage III and IV melanoma patients: a phase II randomized trial (ACDC adjuvant Trial)**

Protocol: **ID IRST172.04**

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: **19/08/2015**

First Patient Enrolled: **17/09/2015**

Target**: 120 patients (60 each arm)**

Accrual: **18 patients**

Rationale	Currently after radical surgery for single metastasis from melanoma there is no standard complementary therapy, but only follow-up is provided. However, the probability of developing new metastases is high, so a therapy that can reduce the risk of relapse and with a low toxicity profile is sought. In this clinical trial the efficacy of autologous dendritic cell vaccine was tested. This vaccine, which was prepared using mononuclear cells from peripheral blood and autologous tumors, was used for years at this Facility with excellent results in metastatic patients. This personalized vaccine was effective especially when it induces specific immunological responses. The purpose of this research was to evaluate the clinical and immunological efficacy of the personalized vaccine, prepared with dendritic cells and autologous tumor cells, in reducing the risk of disease recurrence and thus

	increase survival. The proposed study was therefore designed to demonstrate with scientific method the validity of this hypothesis.
Treatment	Intradermal Autologous Dendritic Cell vaccine loaded with autologous tumor lysate or homogenate on weeks 1, 5, 9, 13, 17, 21 (6 vaccines every 4 weeks) each dose followed by IL-2 3 MU/day, days 2-6.

This study was authorized by AIFA on 14/08/2015 and authorized by the Italian Ethical Committee (CEROM) on 30/07/2015, amended to update the IMPD with AIFA authorization of 27/07/2017 and favorable opinion CEROM on 12/07/2017, finally amended to be able to make it multicenter (amendment 1.0 of 25/09/2018) and authorized by AIFA on 24/05/2019 and by CEROM.

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

Primary endopoint

Relapse-free survival (RFS), i.e. the time from the date of randomization to the date of the first relapse or the date of death from any cause or the date of the last restaging in non relapsed patients.

Secondary endopoint

- Overall survival
- *In vivo* and *in vitro* immunomonitoring
- Toxicity
- Prognostic and predictive marker response
- Immunologic response

Sample Size

A median relapse-free survival of 7.0 months was assumed for the standard group. With a two-sided tailed alpha of 0.10 and power of 80%, assuming a median relapse-free survival of 11.7 months in the experimental arm (hazard ratio 0.60), it was assumed that 60 patients per arm over a period of 24 months and 12 months of follow-up were necessary. In the context of data monitoring board activities, an interim analysis for futility, according to the Bayesian approach proposed by Fayers et al, was assumed to be performed at 18 months in order to control the safety.
The randomization list was stratified by stage (III and IV M1a-b and IVM1c), and time from primitive tumor to first metastasis (≤ 2 years versus > 2 years). Five randomization lists were initially defined, one for each stratum.

Conclusions:

It was decided to prematurely close this study for unethical reasons.
In light of the availability of therapies for the patient setting in this study, it no longer appears ethical to randomize these subjects to the observation arm of the study, so enrollment was discontinued on 23/01/2019 pending a possible amendment to the trial.
The study included a target of 120 patients over a 6-year period; to date, 18 patients were recruited. Following a careful evaluation of the possibility of effectively modifying the protocol to make it scientifically valid and ethical, an adequate solution for the purpose was not found, so it was decided to permanently close the study.

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