Safety and feasibility of a tolerogenic dendritic cell-based treatment for multiple sclerosis (MS): a comparison of intranodal and intradermal cell administration in two phase I clinical trials

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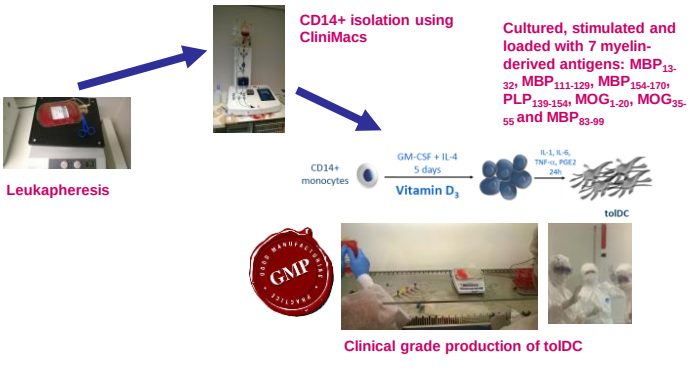
INTRODUCTION

Treatment options for multiple sclerosis (MS) have exponentially increased in the past decade. However, higher treatment efficacy brings treatment-related risks due to reduced immune competence. Hence, an unmet need for safer and more selective treatments targeted towards the cause of the disease remains. In this respect, antigen-specific tolerization with autologous tolerogenic dendritic cells (tolDC) is a promising approach.

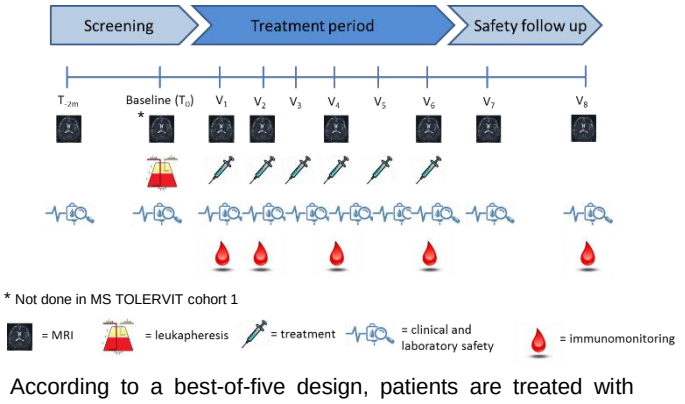
OBJECTIVES

We assess the safety and feasibility of the therapeutic use of autologous tolDC in a well-defined population of MS patients in two single-center clinical trials, comparing intradermal (i.d., MS-tolDC, NCT02618902, Antwerp, BE) and intranodal (i.n., TOLERVIT-MS, NCT02903537, Badalona, SP) administration.

MANUFACTURING PROCESS



STUDY OUTLINE



* Not done in MS TOLERVIT cohort 1

According to a best-of-five design, patients are treated with ascending doses of tolDC in 3 cohorts, with interim analysis of safety by an independent Data Safety Monitoring Board (DSMB). Here, interim results of the first-dose cohort, treated with 5 x 10^6 cells, are presented.

STUDY RESULTS: FIRST DOSE COHORT

	Belgium	Spain
# patients screened	8	7
# patients entered the trial	4	6
# products that did not comply with release criteria	1	2
# patients voluntary withdrew during the trial	0	1
# patients received tolDC treatment	3	3

PATIENT CHARACTERISTICS

Age (years)	30-43
Gender (M/F)	2/4
RRMS / SPMS / PPMS	4/0/2
EDSS	1,5-6
Disease duration (years)	2-13

ADVERSE EVENTS

To date, no serious adverse events (SAE) have been reported.

Most adverse events were considered to be treatment unrelated, except for mild-moderate local reactions seen at the injection site and variable pain during the injections.

MRI RESULTS: NEW T2 AND GD+ LESIONS

Patient ID	screening	baseline	V1	V2	V4	V6
R10106	0	N.D.	0	1	1+	
R10104	1	N.D.	1+	2+	0	1+
R10105	2+	N.D.	0	0	2+	5+
MStolDC003	0	0	0 *	0	0	0
MStolDC004	0	0	0	0	1+ *	0
MStolDC006	1+	0	0	0	0	0

* Mild MS relapse, not meeting protocol definition
+ The MRI T2 lesion was also a Gd+ lesion
N.D. = not done
patient ID: R= intranodal; MStolDC =intradermal

The on-study disease activity was not different as compared to pre-study activity according to the investigators.

CONCLUSION

Currently, the safety follow-up phase of the first dose cohort (n=6) is ongoing. While we consider the disease activity to be not significantly different from the pre-study phase, further follow-up is needed to demonstrate whether the observed MRI disease activity is treatment related or not.

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