Technology Transfer and Process Development for an Autologous Cell Therapy Against Multiple Sclerosis

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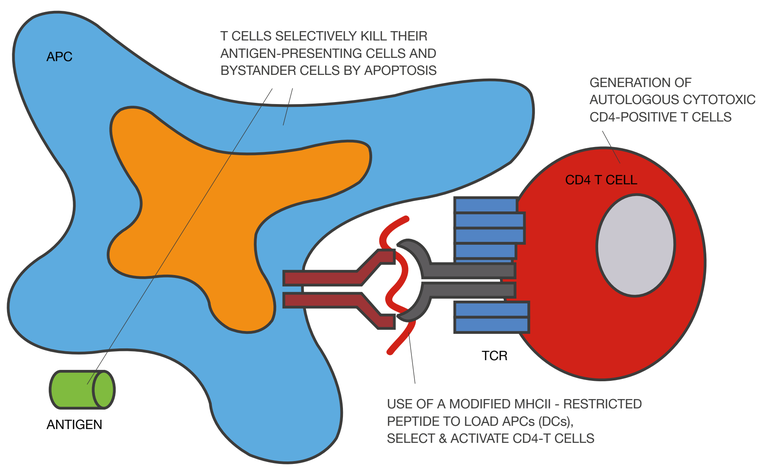
1: MaSTherCell, 2: Imcyse

Cell-based products intended for clinical use need to be manufactured in compliance with cGMP regulations. This requires important investments in facilities and people and has become one of the greatest challenges of young companies or laboratories aiming to obtain proof-of-concept in man. Contract Development and Manufacturing Organizations with cell therapy expertise offer expert personnel, accredited laboratories clean rooms and quality system to tackle these tasks in a time- and cost-efficient manner.

Here we present the results of a customer case study on the technology transfer and process development of an autologous T cell product against multiple sclerosis (Sclerolym, Imcyse).

BACKGROUND

Imcyse is targeting CD4+ T Cells, which trigger an immune reaction and are implicated in autoimmune diseases such as Multiple Sclerosis. More than treating symptoms, Imcyse's therapy halts and reverses course of the disease by converting pathogenic CD4+ cells to beneficial cytolytic CD4+ cells. In order to plan its First-In-Human-Therapy (FIHT), Imcyse has partnered with MaSTherCell for the manufacturing of GMP clinical batches for its T Cell therapy.



OBJECTIVES

Cell-based products are often complex mixes of cell types. Clinical performance depends on rigorous control of the manufacturing process and specifications which are in turn limited by the difficulty to design analytical methods to characterize cell mixtures. An additional hurdle is the need to upscale production while conserving the product characteristics when moving towards clinical studies.

Transfer of know-how

Scale-up (10-50x) & GMP compliance

Increase control & robustness

Specifications on QC results

APPROACH

Among all the parameters defining an outsourcing approach, the technology transfer step is key to succeed and is contingent upon a real collaboration between both partners. A global approach was implemented here based on a hypothetical large scale process. Several runs were achieved in order to perform back-to-back comparisons: one small-scale observation run at the client's facility and eight half large-scale runs at MaSTherCell's site. Three additional runs were performed in GMP conditions.

Optimizations in 4 rounds

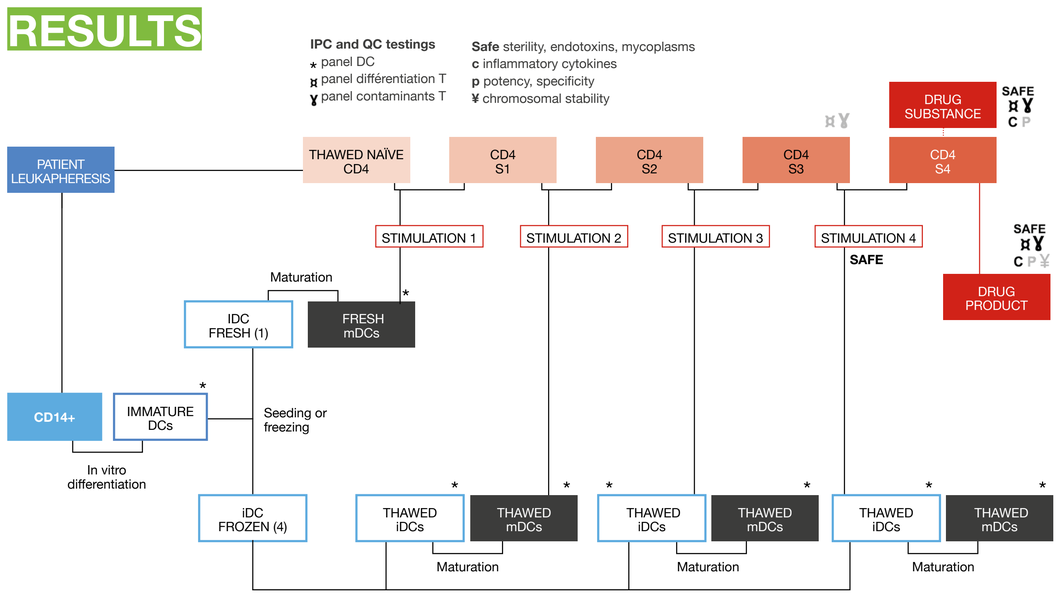
Engineering runs (GMP)

Qualification runs

	Small-scale process IMC	Large-scale process MTC
Starting material	Buffy coat	Leukapheresis
Cell subset selection	MACS Positive selection of CD4+ cells followed by depletion of CD45RO+ cells on MACS	CliniMACS Negative selection of CD4+ by depletion of monocycles, B cells, DCs, hematopoïetic precursors, NK cells, CD8+ cells and APCs by CliniMACS
T cells cryopreservation	Vials in Mister Frosty	Large bags in CryoMed
Culture medium	AIM-V	DendriMACS and TexMACS
Use of antibiotics	Yes, gentamyein	No
Raw materials	R&D grade cytokines and peptide	GMP or pharmaceutical grade reagents, peptide safety controlled
Culture support for DC differentiation	6-well plates	Differentiation bags (Miltenyi)
Culture support for T cells / DC coculture	6-well plates	Expansion bags (Miltenyi)
Final dose	NA	5-50 million cells

Main differences between client's small-scale process & MaSTherCell's large-scale process.

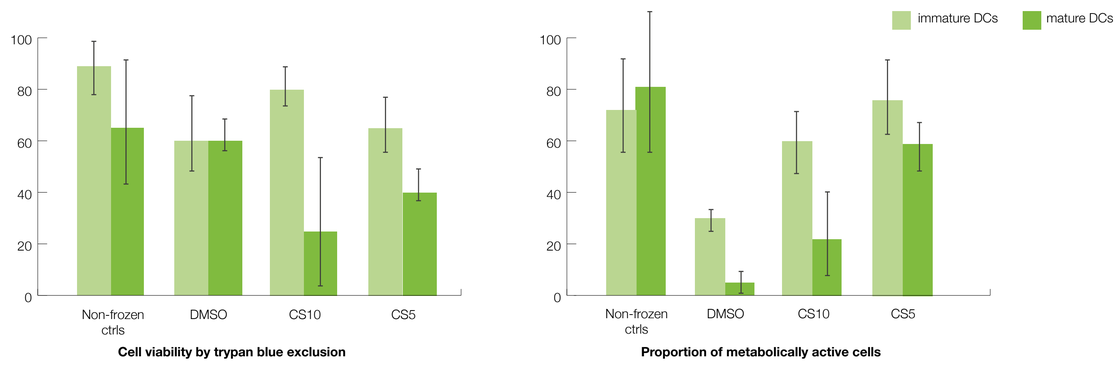
RESULTS



Cryopreservation followed by in vitro maturation of dendritic cells (DC).

- Cryopreservation seriously affects DCs functionality
- Maturation of thawed DCs leaves only a few percent live cells

Optimization of recovery and maturation of cryopreserved DCs.



Switch to cryostore solutions dramatically improved survival of mature DCs.

CONCLUSION

Sclerolym process was scaled-up, developed and qualified as to allow timely start in phase 1 clinical studies.

- Scaled-up & GMP-compliant process
- "In process" & final product quality QC
- GMP or pharma grade raw materials
- Change cell culture vessels to ps plastic flasks
- Freeze DCs in cryostore 5
- Avoid platelet contamination in T cells

MaSTherCell is a dynamic and global Contract Development and Manufacturing Organization (CDMO) on a mission to deliver optimized process industrialization capacities to cell therapy organizations. The heart of MaSTherCell is a team of highly dedicated experts. A validated and flexible facility located in the strategic center of Europe.

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