



COST ACTION CA21151 - HAPLO-iPS

Working Group 7: Clinical Application

D7.1: Summary of Safety, Clinical and Regulatory Requirements for Cell Therapy with hiPSC-Derivatives

Safety and Quality Requirements, Clinical Translation and EU Regulatory Roadmap

Final Version - Month 48 (September 2026)

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D7.1 SOPs for the recommended differentiation protocols and their scaling.

IMPORTANT NOTE: During the implementation of this deliverable, the approach initially foreseen was adapted to better address the objectives and needs identified during the course of the Action. A decision is taken to not to produce this deliverable in the original formulation and to change the focus from differentiation protocols to QC attributes of the differentiated product and to fuse the recommendations with those of D7.2. Nevertheless, a review of the literature on clinical trials was performed as part of the tasks to address this deliverable, and the findings and conclusions from such review are described below, together with the rationale for the modified approach.

Screening of the iPSC-ATMP clinical trials landscape

A thorough search of all available documentation on iPSC-derivatives clinical trials was conducted and updated up to May 2026. For this task all the publicly available information (see Methodology) was revised and the main information was structured. The main focus was to identify the therapeutic cellular products, the type of iPSC that was used as a source (autologous, allogeneic or HLA homozygous matched) and the clinical indications. Although the manufacturing process is not accessible for all the iPSC-products in clinical trials, some provided information on the therapeutic product formulation. The idea of this screening was to select the main iPSC-derivatives that are being currently produced and select some of them to produce the recommended differentiation protocol.

Methodology

Sources and references:

- Revision article: Kirkeby et al. Pluripotent stem-cell-derived therapies in clinical trial: A 2025 update. Cell Stem Cell, 2025. <https://doi.org/10.1016/j.stem.2024.12.005>
- hPSC Reg data base: <https://hpscereg.eu/>
- Clinicaltrial.gov database (NIH): <https://clinicaltrials.gov/>
- Japanese Registry of clinical trials: <https://jrct.mhlw.go.jp/en-top>
- Scientific articles describing specific clinical trials results
- Other publicly available information on the clinical trials like company's web pages or press releases.

The information was collected in an Excel file and organized by the following fields:

Clinical trial code / Sponsor / Country / Autologous or allogenic/ iPS cell line code / cellular product name / Final cell or product / Cell type / Tissue or organ / Application / Start year / N. patient targeted / N. Patient treated / Phase / Overall status / Active or Not active.

In addition, a graphical representation was produced. The updated version of the Excel file and the graphs were made available to all HAPLO-IPS participants.

Results

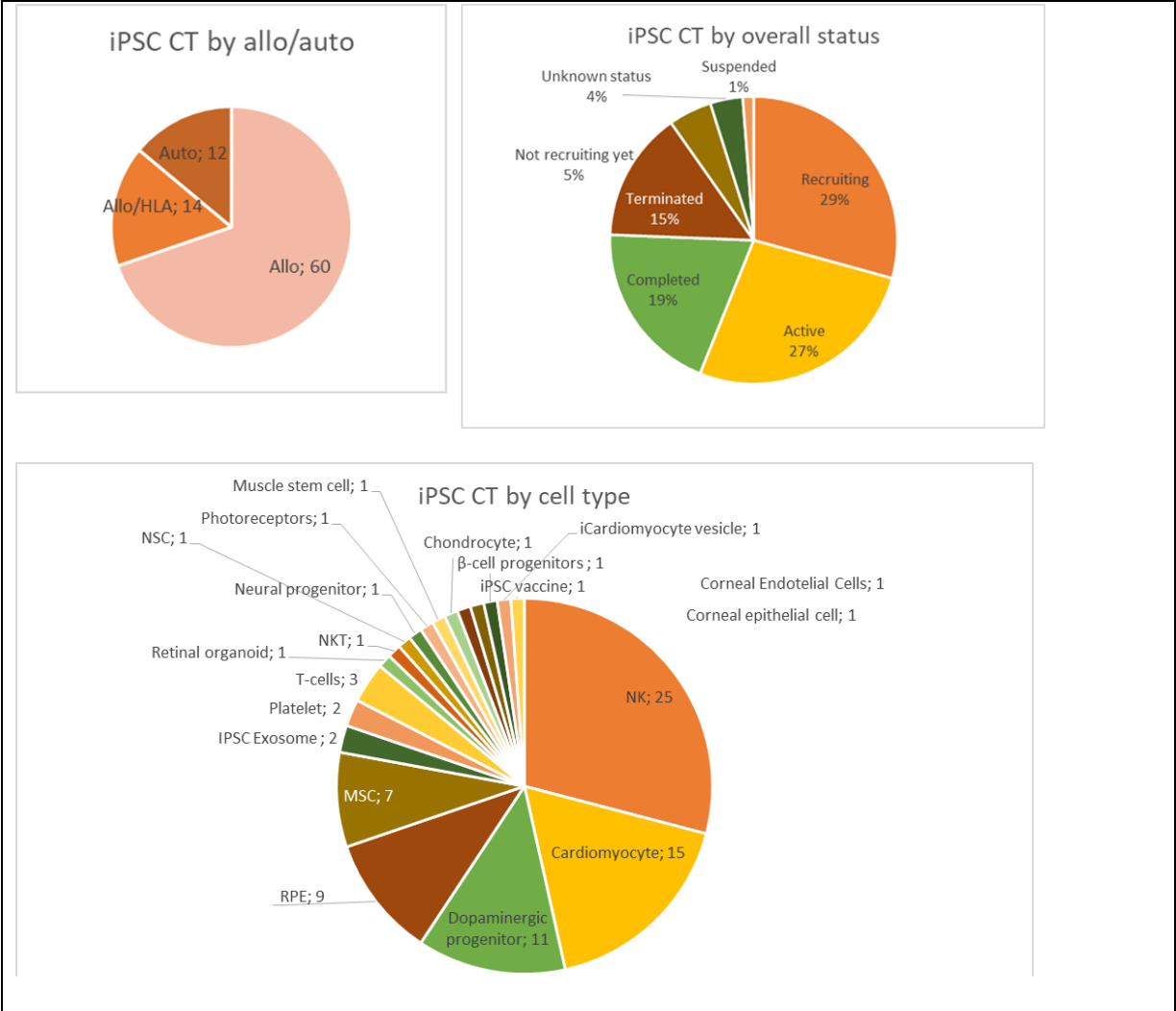
We found 86 clinical trials with iPSC-derivatives, most of them with an allogeneic or HLA-matched approach, and mostly still active with different stages of development (Fig. 1).

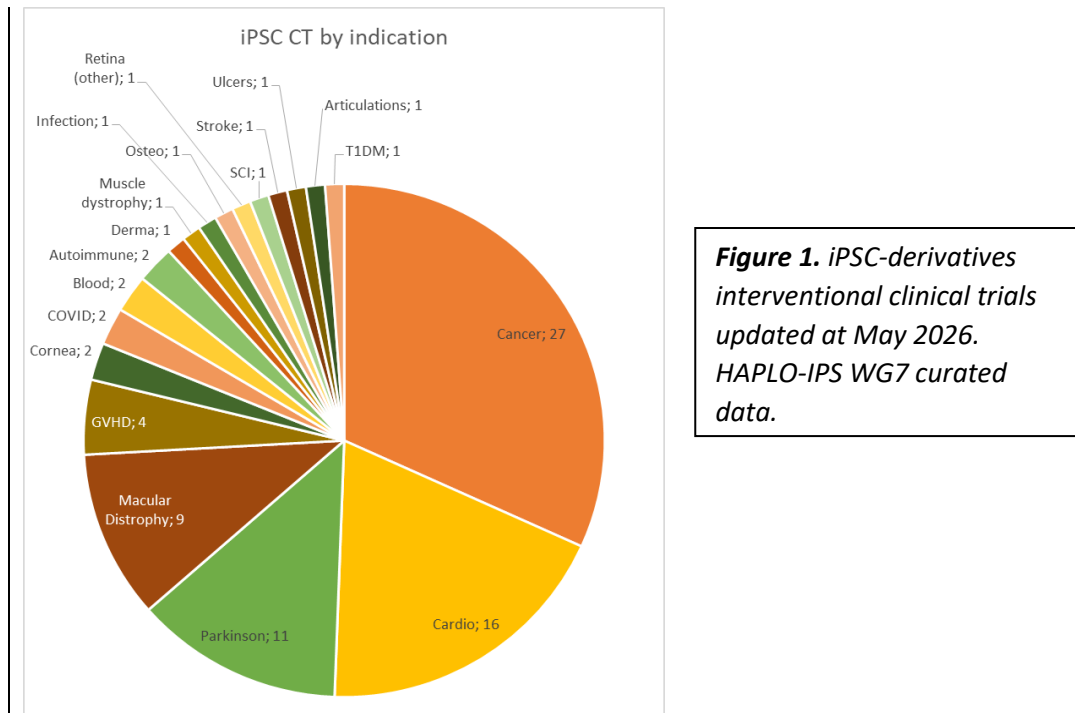
Broadly, 20 different cell types and 20 different indication were identified (Fig. 1).

For each cell type not all products or preparations were the same. For example, for cardiomyocytes we found: cells, sheet, patch, spheres or engineered human myocardium.

Conclusion

We reach to the conclusion that providing recommended differentiation protocols for each cell type and product variation was not a feasible or practical task and that providing recommendations for quality control attributes would be a much more interesting goal to help developers, manufacturers reach harmonization and optimize the process development and fast track regulatory approval.





Justification for a change in focus and fusion with D7.2

After extensive deliberation, WG7 decided that Deliverable 7.1: *Summary of manufacturing process for selected iPSC-ATMP*, was not a good aim for a deliverable, since the number of iPSC-ATMP is too large to allow a focused and detailed description, and the fact that each manufacturer is likely to develop their own unique processes attending to facilities expertise, intellectual property and others. Instead, it was decided to incorporate in D7.2 more detail and focus in safety requirements and to introduce quality characterization and requirements. The rationale was that harmonizing quality attributes would be a much achievable goal than harmonizing manufacturing protocols, and it would produce much more useful guidance for manufacturers and regulatory agencies.