Expanded CD34+ cells for cardiac cell therapy

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Background: We previously demonstrated that intra-cardiac delivery of autologous peripheral blood-CD34+ stem cells, mobilized by granulocyte-colony stimulating factor (G CSF) and collected by leukapheresis after myocardial infarction, structurally and functionally repaired the damaged myocardial area. When used for cardiac indication, CD34+ cells are now considered as ATMP (Advanced Therapy Medicinal Product). We have industrialized their production by developing an automated device for ex-vivo CD34+ stem cell expansion, starting from a whole blood sample.

Method: Blood samples were collected from healthy donors after G-CSF mobilization. Manufacturing procedures included: (1) isolation of total nuclear cells (2) CD34+ immunoselection (3) expansion and cell culture recovery in the device and (4) expanded CD34+cell immunoselection and formulation. The assessment of CD34+ cell counts, viability and immunophenotype and sterility tests were performed as quality tests.

Result: We established graft acceptance criteria and performed validation processes in three cell therapy centers (CTCs). 59.4±36.8×106 viable CD34+ cells were reproducibly generated as the final product from 220 mL whole blood containing 17.1±8.1x106 viable CD34+ cells. CD34+ identity, genetic stability and telomere length were consistent with those of basal CD34+ cells. Gram staining and mycoplasma and endotoxin analyses were negative in all cases. We confirmed the therapeutic efficacy of both CD34±cell categories in experimental AMI (Acute Myocardial Infarct) in immuno-deficient rats during pre-clinical studies.

Discussion: This reproducible, automated, and standardized expansion process produces high numbers of CD34+ cells corresponding to the approved ATMP and paves the way for a phase I/IIb study in AMI, which is currently recruiting patients.

Biography

Claire after a Phd. in cell biology, she joined the team of founders of CellProthera in 2009 and participated with her team to scientific works including the design and development of the StemXpand and the surrounding process. As project manager, and in collaboration with the CMO, she is an active element in the preparation of international clinical trials and participates to discussions with various regulatory authorities. In collaboration with the CDO, she is currently involved in the development of the future commercial device and the complete characterization of the process.

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