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Ex vivo expanded hematopoietic progenitor cells (HPC) from cord blood in clinical trials for patients with hematological malignancies

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Abstract

Cord blood transplantation (CBT) is an acceptable treatment for patients with hematological malignancies who have no matched bone marrow graft. However, low cell dose has limited the use of CBT.

To overcome cell dose limitation we have developed a novel epigenetic technology for the ex vivo expansion of HPC based on the finding that cellular copper content modulates self-renewal and differentiation. The lead molecule of our technology is the copper (Cu) chelator tetraethylenepentamine (TEPA). TEPA's biological activity was attributed to its effect on overall cellular Cu levels as: (a) a treatment with TEPA resulted in the reduction of cellular Cu followed by the inhibition of HPC differentiation, and (b) the excess Cu reversed TEPA's activity and accelerated differentiation.

We applied this technology to develop a product called StemEx. A robust manufacturing process under GMP was developed. CD133 progenitor cells are selected from the small portion of a CBU and cultured for 21 days in media containing TEPA and cytokines. The cultured product is transplanted one day after the transplantation of the larger non-cultured portion containing a minimal safety cell dose of $1x10^7$ cells/kg. The processing of clinical batches demonstrates a robust expansion of progenitor cells, with a mean $CD34^+$-fold expansion in culture of 76 (range 9–149). Safety and feasibility of transplanting StemEx were demonstrated in a phase I/II trial. StemEx is now developed in an international pivotal registration study. One hundred patients with hematological malignancies—indicated for BMT with no family related donor match—will be transplanted with StemEx and compared to a historical cohort. The primary endpoint is overall survival at 100 days, with a follow-up of 180 days.

Keywords: cord blood transplantation, CBT, hematological malignancies, ex vivo expansion, copper chelator, tetraethylenepentamine, TEPA, progenitor cells, CD34+, CD133