COST EFFECTIVENESS ANALYSIS OF JUST-IN-TIME EXPANSION OF MESENCHYMAL STEM/STROMAL CELLS (MSCs) WITH PLUS™ HUMAN PLATELET LYSATE (hPL) FOR AN ALLOGENEIC CLINICAL TRIAL

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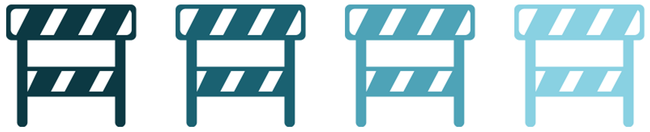
Introduction

Challenges in mesenchymal stem/stromal cells (MSCs) manufacturing



Meeting scale demands | Variability with culture conditions | Replacement of animal origin components | Management of production costs

Ethical, safety and regulatory considerations discourage the use of animal origin reagents, such as the culture medium supplement fetal bovine serum (FBS). Human platelet lysate (hPL) has been gaining popularity as a xeno-free supplement for MSCs expansion.

It is estimated that the total costs of bringing a new therapy to market are $2.8 billion. Manufacturing costs are a significant expenditure of clinical trials for cell therapies, since the processes involved are highly manual and with low production volumes. One of the most relevant manufacturing expenses is the cost of culture medium. More than 75% of recent trials use FBS as a culture medium supplement, while hPL is used in 11% of them.

Is hPL replacement of FBS as a culture medium supplement cost-effective?

Computational Methodology

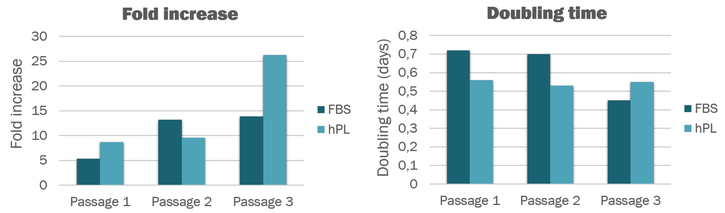
Open source simulation tool | Simulate a good manufacturing practice (GMP) facility | Insert biological variability to cutlure conditions | Calculate the manufacturing costs per dose

Case Study Definition

Safety and Tolerability Study of Allogeneic Mesenchymal Stem cell Infusion in Adults with Cystic Fibrosis (NCT02866721)

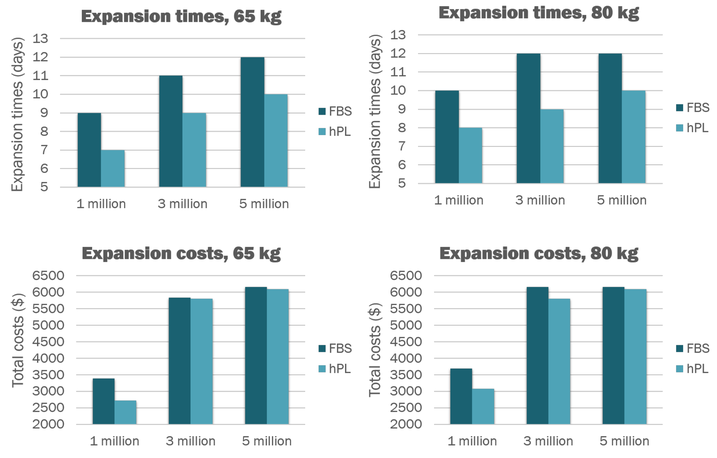
Parameter	Value
Cell source	Bone marrow
# cells/kg	1, 3 or 5 million
Patient weight	65 to 80 kg
Culture medium	DMEM + 10% FBS vs DMEM + 5% PLUS™
Price supplement/ml	FBS: $1.30 PLUS™: $3.00
# P0 cells plated	2 million

hPL enhances proliferation of MSCs



For the same MSCs donor, expansion using PLUS™ as the culture medium supplement yielded, in general, more cells per passage and faster times to confluence in comparison to FBS (Reese et al, 2014). These findings might influence expansion costs.

hPL is a cost saving option for MSCs expansion



For the same simulated patient, expansion using PLUS™ as the culture medium supplement on the computationally simulated expansion process yielded total cost savings per dose of up to 20% in comparison with FBS. These differences are particularly noticeable for the doses with lower numbers of cells, since they require only 2 passages instead of 3 for the 3 million and 5 million cells/kg doses.

The savings are particularly noticeable by saving days of process time, leading to a reduction in total process costs of $321 per day saved in the basis of reduced equipment and building utilization contributions, in parallel with less labor contribution. This difference in productivity compensates for the 12% higher cost per culture medium volume when it is supplemented with PLUS™

Considerations for clinical trial modeling

PLUS™ is a viable and cost effective alternative to FBS, under the assumption that bone marrow MSCs potency is maintained

Full manufacturing costs (initial estimates from full model are $20,000/dose.

Health economics model: cost-effectiveness of MSCs with disease modulators vs modulator therapy only.

Usefulness of a stem cell specific decision support tool

- Lack of flexibility of tools for small drugs/biologics
- Evaluate impact of donor variability of MSCs
- Forecast cost--effectiveness of MSCs for a clinical application
- Simulation of autologous and allogeneic processes
- 2D and 3D culture platforms available
- Expansion to a pluripotent stem cell model under development

Additional resources

Detailed references and parameters used
Previous applications of the computational model
Take part in the development of this open source tool
Be notified when the tool will be available for general use online (estimated in the final quarter of 2018).

Acknowledgements

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