ISCT abstract ISCTSF2o22

To submit in section Tissue engineering or tissue specific cells

Basic science and manufacturing (maybe also regulatory)

Title: HEPATICAN™ - A COMBINED CELL THERAPY AND MEDICAL DEVICE TO TREAT PATIENTS WITH LIVER FAILURE.

Authors: Clare Selden, Eloy Erro, Tom Brookshaw, Elizaveta Zotova, Joana Mendonca Da Silva, Suzanne Farid, Jeremy Opie, Barry Fuller

Background and Aim: HepatiCan™ is a bioartificial liver established from our previous fundamental research aimed at treating patients with severe liver failure, at the bedside, buying time for the patient's own liver to recover. This combined ATMP-medical device, a cryopreservable cell therapy, can be delivered to patients within hours of a clinical request.

Methods: To achieve a functional dose, we developed the ATMP production in GMP-like conditions and the device for delivery to patients, concurrently. Clinical scale production at a cell dose of >60 billion cells as organoids is in a bioreactor suitable for patient-facing use. Device design encompassed hardware, software and materials to meet regulatory requirements (MDR/MDD and subsequently FDA). Our targeted cost of good analysis (COG) ensures that production remains cost effective, and meets the UK National Institute for Health and Care Excellence guidelines. Additionally we performed a usability study according to IEC 62366-1, for bedside treatment.

Results: ATMP production: Full clinical scale protocols yielded 62.3±12.5 billion cells (n=3) in 2.5L of hydrogel biomass, and viability >98%. After cryopreservation and storage at <-150C, post-thaw recovery delivered 100% of biomass with >95% viability (n=2).

Biomass assessed for up to 72 hours continuously in the device in human plasma, maintained viability of >90%. Technical device aspects of HepatiCan™, indicated all components remained stable with minimal flow-pressure changes throughout. Biomass glucose consumption and protein production interrogated throughout the process indicated good, stable functional capacity.

COG analysis of ATMP production, cryopreservation, recovery and delivery to patient bedside, using best known purchase price costs indicated a cost of ~£45,000 between 1500 and 30,000 preps/year. In contrast, lifetime costs of liver transplantation in UK in 2020 was half a million pounds ($577,000).

Human factors engineering (usability) of use-errors during laboratory-simulated patient use met IEC62366-1, for HepatiCan™ delivery at the bedside.

Conclusions: HepatiCan™, a novel bioartificial liver cell therapy and medical device can be produced under conditions meeting relevant medical device guidelines, with GMP-like methodology, cost-effectiveness and suitability for patient treatment.

Acknowledgements: Work funded by NIHR (i4i award II-LA-0417-20002) UK, The liver Grop Charity, and UCL innovation and Enterprise

Could not add these refs but use them in poster or presentation

1. Selden C et al; Sci Rep. 2017 7(1):14518. doi: 10.1038/s41598-017-15021-4.

2. www.nss.nhs.scot/media/1080/commissioning-transplantation-to-2020.pdf

248o characters (2500 allowed)

Characters 2348 (not spaces) but also including words like **Title, Authors etc (I assume these headings may not count in any case)**

I wrote established from fundamental research before I started tracking

If the headings **Title, Authors etc** do not count towards characters you might be able to use COG paper as in

Our targeted cost of good analysis (COG) [2]

With 2. Mendonça da Silva J et al; Cytotherapy. 2021 23(8):683-693.