Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Cytotherapy 23 (2021) 1–39

Contents lists available at ScienceDirect

CYTOTHERAPY

journal homepage: www.isct-cytotherapy.org

International Society ISCT Cell & Gene Therapy®

1

A PHASE I CLINICAL TRIAL ON INTRAVENOUS ADMINISTRATION OF IMMATURE HUMAN DENTAL PULP STEM CELLS (NESTACELL HDTM) TO HUNTINGTON'S DISEASE PATIENTS

J Macedo[1,*], E Pagani[2], CV Wenceslau[3], L Ferrara[1], I Kerkis[4]
[1]Azidus Brasil, [2]Cellavita and Azidus Brasil, [3]Cellavita Pesquisas científicas, [4]Instituto Butantã

Background: Huntington's disease (HD) is a neurodegenerative condition caused by an increase in the CAG repeats of the huntingtin (HTT) gene at chromosome 4. It is a rare disease; whose prevalence varies from 0.4 to 5.7 cases per 100,000 habitants. The clinical manifestations usually start by the fourth decade of age with motor, cognitive and behavioral features, that typically evolve for 10 to 20 years until death. Currently, there is no curative treatment. Nestacell HD is an allogeneic cell therapy manufactured from the human immature dental pulp stem cells by the Brazilian company Cellavita. This study aimed at assessing the safety, tolerability, and preliminary data on the efficacy of intravenous injections of Nestacell HD. It was approved by the local IRB, CONEP, and ANVISA.

Methods: This is a first-in-human, uncontrolled, open-label, Phase I clinical trial with six HD participants. The study started following the patients for 4 months to collect baseline data. Then, they received 3 administrations with a 1-month interval of either 1 million cells per Kg (first 3 patients) or 2 million cells per kg (last 3 patients) by the intravenous route. The patients were then followed for 2 years. The safety was evaluated based on the adverse events (AV) incidence, severity, and causality. The efficacy was evaluated using the Unified Huntington's Disease Rating Scale – UHDRS. The immunological response was evaluated by CD4+ and CD8+ proliferation, and inflammatory markers (cytokines).

Results: All participants completed the treatment and the two-year follow-up period. The treatment was well tolerated. There were no treatment-related serious adverse events (SAE), nor any AE led to dropout. No patient increased the cytokines or the CD4/CD8. Five patients had improvement to the UHDRS motor domain, which started two weeks after the first administration and remained for six to nine months after the last administration. All patients were entitled to additional infusions to maintain clinical improvement.

Conclusion: The treatment with Nestacell HD was well tolerated and might have improved the HD motor manifestations; thus justifying further Phase 2 clinical trials.

2

ACE2 OVEREXPRESSION CHANGES THE SARS-COV-2 INFECTION PROFILE IN BEAS-2B CELLS

CS Bartolomeo[1,2,*], TN Alves[1,2], RMR Lemes[3,4], GZ Ivanov[2], RLT Morais[4], AJ Costa[5], MS Nishino[3,4], TB Bassani[3,4], GJS Pereira[5], SS Smaili[5], RMB Maciel[3,4,6], LH Okuda[7], CT Braconi[8], JT Maricatto[8], LMR Janini[8], RP Ureshino[3,4], CM Prado[9], RS Stilhano[2]
[1]Department of Biosciences, UNIFESP, [2]Department of Physiological Sciences FCMSCSP, [3]Department of Biological Sciences UNIFESP, [4]Laboratory of Molecular and Translational Endocrinology UNIFESP, [5]Department of Pharmacology UNIFESP, [6]Department of Medicine UNIFESP, [7]Biological Institute, [8]Department of Microbiology Immunology and Parasitology UNIFESP, [9]Department of Biosciences, UNIFESP

Background: COVID-19 is a pandemic disease caused by the novel coronavirus SARS-CoV-2, which spread worldwide, revealing uphill repercussions. The infection is mediated by coronavirus spike protein and host cell receptor ACE2 (Angiotensin Converting Enzyme 2). Several cell lines have been used as an in vitro model to test potential drugs and to study the viral kinetics. Since lungs are one of the first organs affected by the virus, pulmonary cell lines such as: A549 (lung cells) and BEAS-2B (Bronchial epithelium cells) are the most studied. However, these cells present a slow viral replication profile which complicate the testing of new antiviral drugs and viral replication studies. High levels of ACE2, which is observed in some groups of patients, is associated with the increase of viral replication and severe symptoms. Thus, the development of a BEAS-2B cell line overexpressing ACE2 would be a useful model to study SARS-CoV-2 infection and to study new drugs.

Aims: Develop a BEAS-2B cell line overexpressing ACE2 and evaluate the role of ACE2 on SARS-CoV-2 viral kinetics.

Methods: BEAS-2B were transfected with pCEP-ACE2-myc and selected with hygromycin (125ng/ul) for 20 days, creating BEAS-2B-ACE2 cell line. ACE2 expression was quantified by RT-qPCR. Western Blotting and Immunofluorescence were used to quantify the ACE2 protein levels. ACE2 activity was evaluated using (MCA-Ala-Pro-Lys (Dnp)-OH) substrate. Cells were infected with SARS-CoV-2 (MOI=0.2). Viral kinetics were analyzed by RT-qPCR. Proliferation analysis was performed by MTT assay.

Results: Long-term overexpression ACE2 in BEAS-2B-ACE2 was confirmed by RT-qPCR, Western Blotting and Immunofluorescence. Compared to BEAS-2B, ACE2 mRNA expression was 100-fold higher ($p<0.05$), ACE2 protein levels increased 12X ($p<0.05$) and the immunofluorescence showed that ACE2 protein was more abundantly in BEAS-2B-ACE2. A 50X ($p<0.0001$) increase in the ACE2 activity was observed 2 months after the transfection. There was no difference in proliferation between BEAS-2B-ACE2 and BEAS-2B. Overexpression of ACE2 increased the viral kinetics. BEAS-2B-ACE2 presented 1000X ($p<0.05$) more SARS-CoV-2 RNA in cells and supernatant compared with BEAS-2B, 48 and 72 hours after infection.

Conclusion: Here we show for the first time that overexpression of ACE2 in BEAS-2B drastically changes the infection profile of SARS-CoV-2 and increases viral load – making it an useful cell line for future studies of SARS-CoV-2.

3

ACELLULAR LIVER SCAFFOLD PROMOTES CELL RECRUITMENT AFTER HETEROTOPIC TRANSPLANTATION

ML Dias[1,*], CMP Batista[1], R Martins-Santos[1], AC Silva[2], CBV Andrade[3], MF Leite[4], RCS Goldenberg[1]
[1]Carlos Chagas Filho Biophysics Institute, Federal University of Rio de Janeiro, [2]Clementino Fraga Filho University Hospital, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, [3]Department of Histology and Embryology, State University of Rio de Janeiro, UERJ, Rio de Janeiro, RJ, Brazil, [4]Department of Physiology and Biophysics, Federal University of Minas Gerais, UFMG, Belo Horizonte, MG