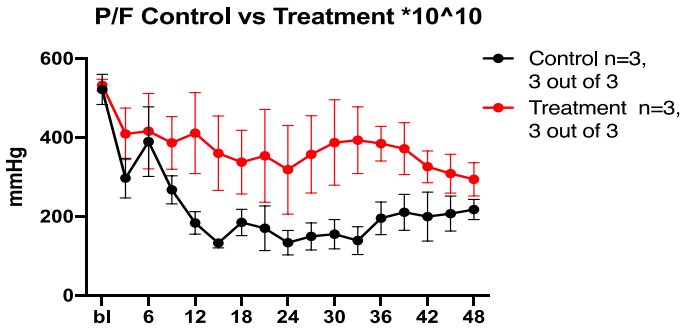
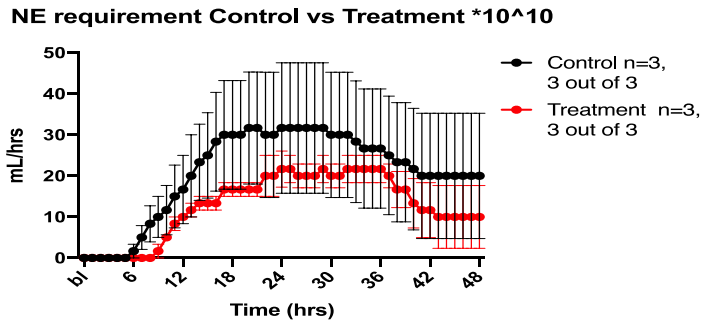
Interim Results: Very Strong Beneficial Effect of *i*-MSCs in Sheep Model of ARDS

P/F ratio



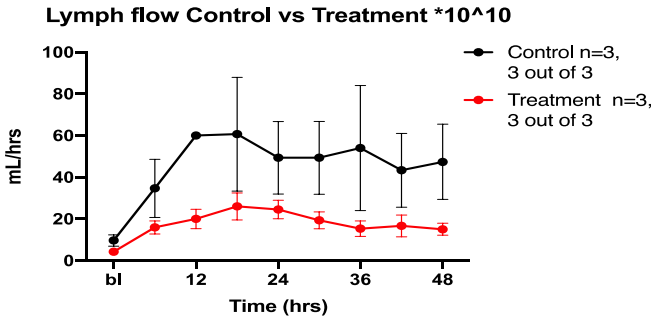
Improved Oxygenation

Norepinephrine Requirement

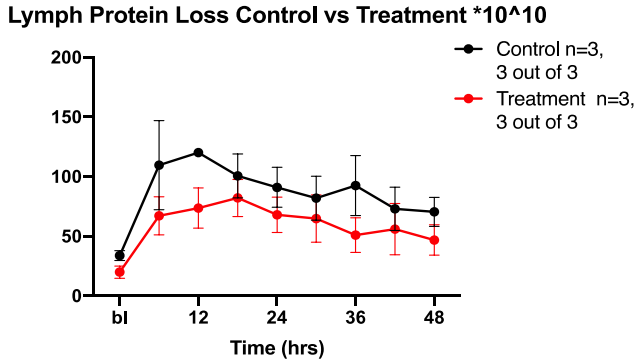


Less systemic shock

Pulmonary Lymph Flow



Pulmonary Lymph Protein Loss



Reduced Lung Vascular Injury

Overview of findings: In this ovine model of severe ARDS the animals receiving *i*-MSCs demonstrated clear improvement over control animals of several critical clinical parameters: 1) oxygenation (improved); 2) systemic BP (less shock/less pressor support); and 3) lung/alveolar permeability (decrease in production of excess lung lymph flow and associated protein loss) which persisted throughout the 48 hour course of the experiment

Our Solution – NoveCite *i*-MSCs

Description:

- Allogeneic (“off-the-shelf”) *i*-PSC-derived *induced* Mesenchymal Stem Cells
- High potency *i*-MSCs – *in vitro* data showing exponentially higher secretion of immunomodulatory proteins vs. BM-derived MSCs
- Footprint-free *i*-PSCs created using patented non-immunogenic mRNA process
- Clonal cells, telomere restored, unlimited supply, lower COGs
- “Superior” MSCs

How Supplied/Administered:

- Cells cryo-frozen 250 ml IV bag (saline), thawed and reconstituted with Plasmalyte prior to use
- IV infusion: will evaluate dosing range between 1-10 million cells/kg to determine OBD (optimal biological dose); a second dose may be given, at 48-96 hours, based on patient’s clinical status

Target Indication:

- Treatment of ARDS in Covid-19 patients

Future Indications:

- Treatment of acute inflammatory respiratory conditions

Clinical Development Plan (as of 12/2020)

Phase	Type	n	Description
1/2	Multi-center Phase 1 dose-finding study followed by a randomized placebo-controlled Phase 2 expansion phase to assess the safety, tolerability, and efficacy of iMSCs in patients with moderate to severe ARDS due to COVID-19	40 in phase 1 and 200 in phase 2	This is an adaptive design trial. The first part of the trial will serve as the phase 1 portion of the trial and will serve to establish safety in human subjects. The phase 1 portion will also serve as a dose-finding study. The phase 2 portion of the trial will take the selected dose forward into a larger patient population. The phase 2 portion will serve to establish safety of the selected dose in a larger population as well as an evaluation of efficacy endpoints. The results of this study will serve to establish the primary endpoint and help determine the sample size for the phase 3 study.
3	Multi-centered randomized placebo-controlled safety and efficacy evaluation of iMSCs for treatment of acute respiratory distress syndrome in patients with COVID-19	TBD	The primary objectives of the Phase 3 study are to confirm and expand on safety and effectiveness results from the Phase 1/2 studies of iMSCs as a treatment for subjects with moderate to severe ARDS due to COVID-19. The secondary objectives of this study are to evaluate tolerability, pulmonary function, mortality, and quality of life among survivors associated with iMSCs therapy as a treatment for subjects with moderate to severe ARDS due to COVID-19. This trial to serve as a pivotal trial for the NDA.