Safety and Efficacy of alginate-preserved human limbus-derived mesenchymal stem cells for the treatment of superficial corneal pathologies

[1]Sayan Basu, [1]Vivek Singh
[1]Centre for Ocular Regeneration, L V Prasad Eye Institute, Hyderabad, Telangana, India

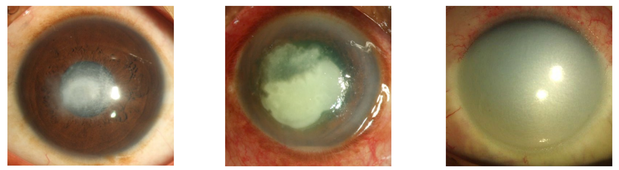
2360 - C0397

PURPOSE

- Conventional corneal transplantation is prone to failure in severe blinding pathologies like burns, ulcers and scars.
- Alternative strategies are being pursued globally to find better solutions.
- The human limbus-derived stromal/mesenchymal stem cells (hLMSC) have previously been shown to have anti-inflammatory and wound healing properties in pre-clinical studies.
- This study evaluated the clinical safety and efficacy of hLMSC for the treatment of superficial corneal pathologies.

METHODS

- This study was a prospective open-label phase 0 clinical trial.
- To establish the safety of hLMSC therapy in superficial corneal pathologies like formed scars, sterile non-healing ulcers, and burns.
- The hLMSC were derived from corneoscleral rims and manufactured according to current good manufacturing practice (cGMP) regulations.
- This trial was registered with CTRI (CTRI/2021/07/035034) on 22/07/2021.
- First CDSCO/DCGI approved (as per revised 2017 National Guidelines for Stem Cell Research and New Drugs & Clinical Trial Rules 2019) stem cell therapy clinical trials in Ophthalmology in India.
- Patient screening and recruitment was started on 19/Feb/2022. First patient treated on 9/Mar/2022, 20 patients recruited and treated by 30 December 2022.



Group I: Chronic Corneal Scars | **Group II:** Sterile Corneal Necrosis | **Group III:** Severe Corneal Burns

Figure I: Inclusion criteria were superficial corneal stromal pathologies such as scars, ulcers, and burns.

A. Preservation of hLMSCs in Alginate

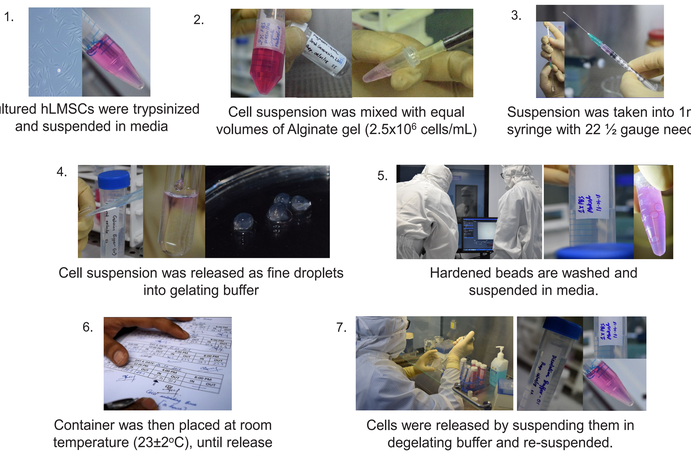
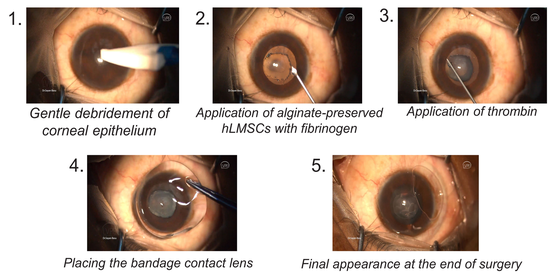


Figure 2: Encapsulation and preservation of hLMSCs: Alginate-encapsulated hLMSCs, in the form of beads were at room temperature for 24-48 hours, before clinical use.

B. Surgical application of alginate preserved hLMSCs



Clinical outcome assessment

- Uncorrected and best spectacle corrected visual acuity
- High-resolution anterior segment optical coherence tomography (OCT, RTVue, Optovue, Inc)
- Corneal densitometry using Scheimpflug imaging (WaveLight Oculyzer II, Alcon Surgicals)

Figure 3: Steps of the surgical procedure of administration of alginate-preserved hLMSC using commercially available fibrin sealant/glue.

RESULTS

A. Characterization of alginate-encapsulated hLMSCs released for clinical use

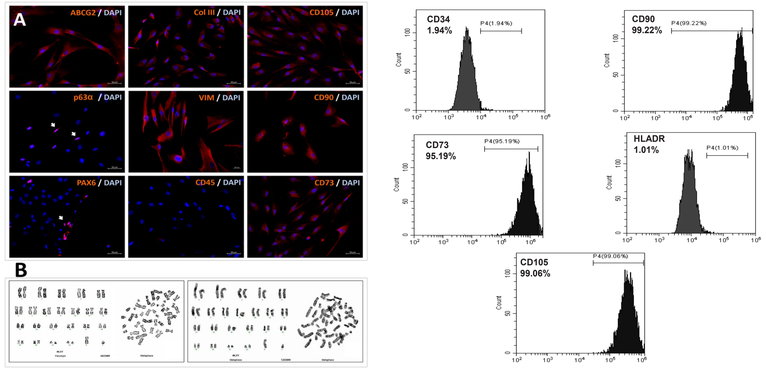


*Figure 4: hLMSC phenotyping and stability. **(A)** Immunostaining assessment of the hLMSC phenotype before clinical use. The panel shows stem-cell biomarkers (p63+, Pax6+, ABCG2+) and mesenchymal biomarkers (VIM+, CD45−, CD73+, CD90+, and CD105+) stained red against DAPI, nuclear stain (blue). 40×; 50 µM. **(B)** Karyotyping of hLMSCs before and after encapsulation and preservation. Both groups showed no numerical or significant reforms. **(C)** The expression of MSC markers in hLMSCs preserved in alginate was quantified using flow cytometry.*

B. Clinical outcomes of alginate-preserved hLMSC therapy

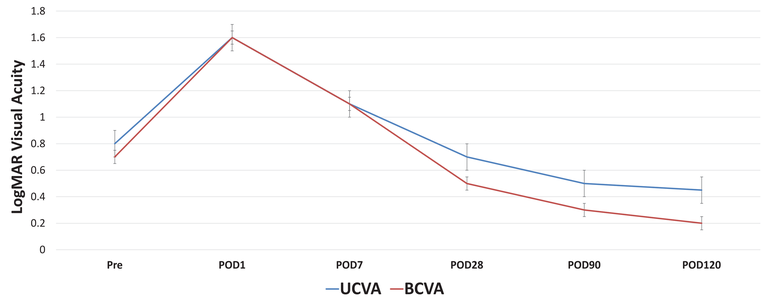


Figure 5: Serial change in LogMAR Visual acuity at different time points.

C. Clinical examination post alginate-preserved hLMSC therapy

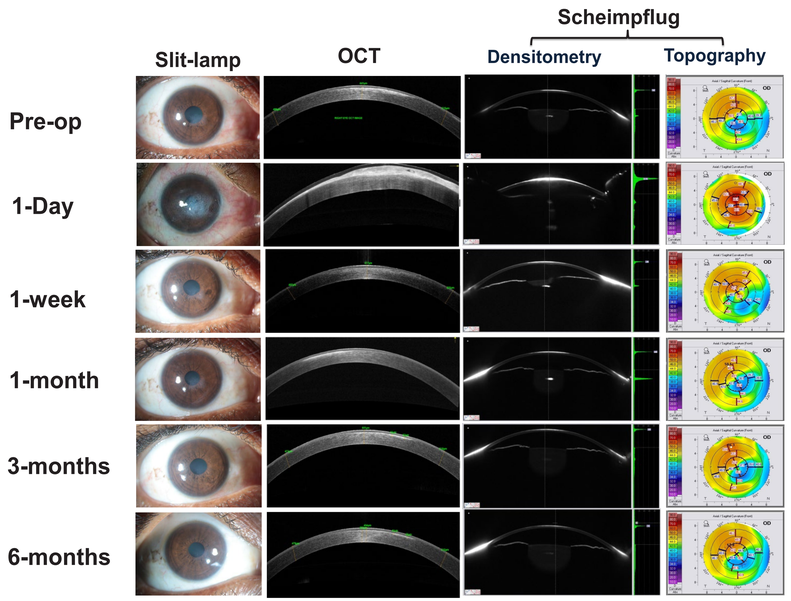


Figure 6: Serial documentation of changes seen on slit-lamp photography, AS-OCT, corneal densitometry, and topography after alginate-preserved hLMSC therapy.

- Follow-up ranged from 3.5 to 12 months.
- None of the eyes developed any serious adverse events.
- All eyes epithelized between 7-10 days post-application of hLMSC.
- 14 (70%) of the eyes showed significant improvement in uncorrected and best spectacle-corrected vision
- All eyes showed reduced corneal reflectivity on objective imaging metrics

CONCLUSION

- This study established safety and next step is to establish efficacy in multi-centric trials
- Future Applications:
  - Low-cost cell-therapy for corneal opacities
  - Anti-inflammatory therapy for ocular surface diseases
  - Cell-incorporated corneal hydrogel for wounds and volume replacement

ACKNOWLEDGEMENT

This work was supported by Hyderabad Eye Research Foundation. We thank the Centre for Ocular Regeneration (CORE), Brien Holden Eye Research Centre (BHERC) for infrastructural support and Ramayamma International Eye Bank for generously providing us the donor corneas.

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Competing interests & Financial disclosures: None

LVPEI-IC-SCR Ref No 05-21-017 (Ethics Ref No LEC 09-19-318)

Email: sayanbasu@lvpei.org