

AB022. Biosynthetic implants for corneal regeneration in patients at high risk of rejecting donor transplantation

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Background: Patients with inflammation or severe corneal pathology are often at high risk of rejecting the human donor corneas that they receive during transplantation. Our goal was to determine whether cell-free implants incorporating phosphorylcholine-based polymer, 2-methacryloyloxyethyl phosphorylcholine (MPC), which has inflammation suppressing properties, can support repair and regeneration of ulcerated, high-risk corneas.

Methods: Interpenetrating networks of recombinant human collagen and MPC (RHC-MPC) were fabricated into corneal implants in a certified and monitored cleanroom. An open-label, first-in-human observational study was conducted following ISO 14971 and 14155:2011, the Declaration of Helsinki and relevant laws of Ukraine and India, after respective ethical approval and trial registration. Seven unilaterally blind patients, aged 36 to 76 years old, diagnosed with conditions putting them at high risk of rejecting conventional corneal transplantation, and capable

of providing informed written consent were grafted and followed up for an average of two years. However, RHC like native collagen is a large macromolecule and difficult to process and is non-customisable. Hence, small, customisable analogs to collagen comprising collagen-like peptides (CLP) conjugated to polyethylene glycol (PEG) were developed. These CLP-PEG analogs like RHC were combined with MPC into implants and tested in mini-pig models with alkali burned corneas, a high-risk condition.

Results: One patient had an unrelated infection that necessitated re-grafting and was excluded from the study. The RHC-MPC implants in the remaining six patients were stably integrated throughout the entire observational period. There was regeneration of the cornea epithelium and stroma. Significant vision improvement was observed in patients with damaged corneas due to infection. By two weeks post-operation, RHC-MPC implanted corneas of patients with active ulcers were free from the symptoms of pain, irritation and photophobia. Over the two-year follow-up period, sensitivity to touch improved, suggesting that the implants were able to promote nerve regeneration. The results seen in the clinical trial were reproduced in corneal grafts comprising MPC and the CLP-PEG collagen analog. Both CLP-PEG-MPC and control CLP-PEG only implants promoted regeneration of corneal epithelium, stroma and nerves. However, the alkali-burned corneas grafted with CLP-PEG-MPC implants retained the thickness of their healthy contralateral controls. Control corneas with CLP-PEG implants without the MPC however, were significantly thicker.

Conclusions: These results demonstrate that collagen or its synthetic analog comprising CLP-PEG, can promote regeneration. The incorporation of MPC appears to suppress inflammation in pathologies that constitute conditions with a high-risk for graft rejection. Regeneration was able to occur in inflamed corneas as evidenced by CLP-PEG only grafts, but long-term follow-up is needed to determine if the chronic inflammation may influence graft failure over time.

Keywords: Cornea; inflammation; implant; clinical trial; pigs

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