Topical beremagene geperpavec (B-VEC) for the treatment of recurrent cicatrizing conjunctivitis in a patient with dystrophic epidermolysis bullosa

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BACKGROUND/PURPOSE

- Dystrophic epidermolysis bullosa (DEB) is a rare genetic blistering skin disease caused by mutations in the *COL7A*1 gene. It can be inherited in an autosomal dominant (DDEB) or recessive (RDEB) manner.[1]
- A subset of individuals with DEB may develop ocular surface involvement, including abrasions, blistering and scarring, that can lead to impaired vision and eventual blindness. Current therapies are limited to removal of scar tissue and ophthalmic lubrication.[2-4]
- Using a replication deficient herpes simplex virus type 1 (HSV-1)-based gene delivery platform, beremagene geperpavec (B-VEC) has been engineered to deliver functional human type VII collagen (COL7).
- B-VEC was evaluated in a phase 3, double-blind, placebo-controlled trial of 31 patients with DEB. B-VEC treatment demonstrated a statistically significant improvement in complete wound healing at 3 and at 6 months compared with placebo. B-VEC was well tolerated and is an investigational topical gene therapy currently under review by the FDA.[5]
- Based on the mechanism of action of B-VEC and the biochemical and ultrastructural similarities between the skin and the cornea, it was hypothesized that B-VEC may also potentially provide a therapeutic benefit for the ocular manifestations in patients with DEB.
- We hereby present a case of a male with RDEB and a history of corneal blindness **(Figure 1A)**. Approval from the FDA for the compassionate use of B-VEC was obtained in 2021 (IND #27789), and in 2022 from the University of Miami's Institutional Review Boards (#20211165). **To our knowledge, our patient is the first human treated with a topical ocular gene therapy.**

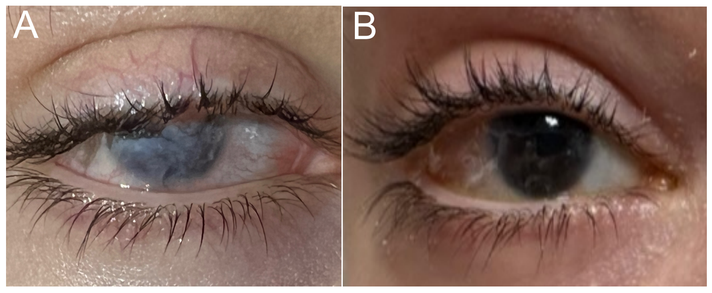


Figure 1: Slit lamp pictures of the right eye. **A:** Baseline ankyloblepharon. The visual acuity was hand motion (HM) **B:** Ocular surface of the right eye 6 months after the surgery and 23 B-VEC applications.

MATERIALS AND METHODS

- Compassionate use study in a 13-year-old male with RDEB at the Bascom Palmer Eye Institute (Miami, FL) who presented with bilateral advanced cicatrizing conjunctivitis (CC). The patient presented with blisters in the skin since birth, and the diagnosis of RDEB was confirmed via genetic analysis at age 7. There was no family history of the disease. He has bilateral contraction and syndactyly of hands and fingers, and to date, his whole body is always wrapped in elastic bandages, except for his face and neck .
- He developed conjunctival blisters at ages 4 and 6 in the left and right eye, respectively. He underwent repeated superficial keratectomy and symblepharon lysis surgeries with amniotic membrane transplantation in his left eye (x2). These resulted in temporary visual acuity improvement, with posterior recurrence and regression to baseline in less than 3 months. He also has bilateral limbal stem cell deficiency since age 8.
- The patient enrolled in the phase 3 trial of B-VEC in 2020 and received treatment of B-VEC on skin wounds. After completion of the phase 3 trial, patient continued receiving B-VEC for wounds in the open-label extension (OLE) trial.
- Surgical symblepharon lysis with pannus removal, immediate ophthalmic B-VEC drug product application (5×10^9 PFU/mL) and suturing of an amniotic membrane were performed on his right eye in August 2022. A bandage contact lens (BCL) was placed on top of the amniotic membrane. Simultaneously, he got an esophageal dilation with gastrostomy tube placement, as he was having severe dysphagia caused by esophageal strictures.
- After the surgery, topical B-VEC was instilled continuously: 3 times/week for the first 2 weeks; then once weekly until the corneal epithelium healed completely (assessed via slit lamp and anterior segment optical coherence tomography-OCT); and then, once monthly. The patient was concurrently using ophthalmic prednisolone, moxifloxacin, allogeneic immunosafe PRGF, insulin eyedrops and artificial tears.

RESULTS

Corneal epithelium healing: Full corneal epithelial healing was observed at 3-months after the surgery with topical B-VEC applications (19 doses). 6-months after the surgery and continuous B-VEC therapy (23 doses), there were no signs of symblepharon recurrence or corneal scarring. **(Figures 1B and 2)**

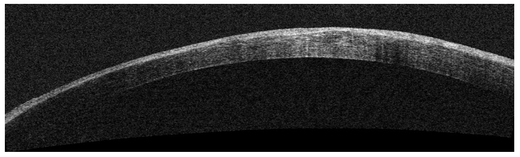


Figure 2: Anterior segment OCT, with no evidence of corneal scarring or infiltrates.

Retina: After 7 months and 24 doses of B-VEC, no abnormalities were observed in the retina **(Figure 3).**

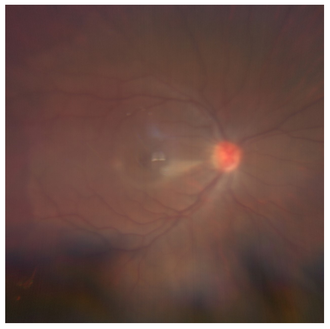
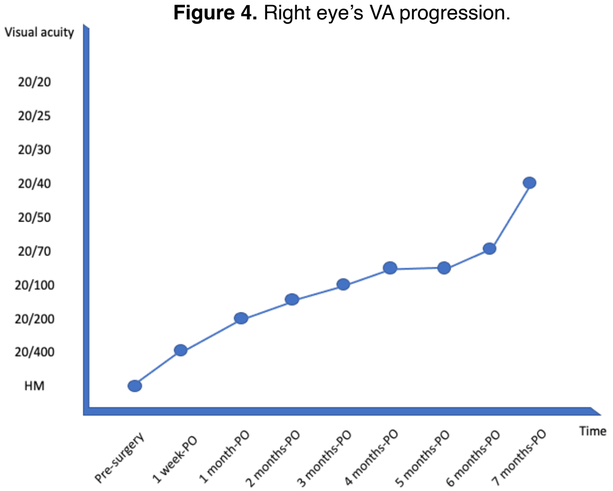


Figure 3: Fundoscopic image of right eye's retina.

Visual acuity (VA)

The patient's right eye VA went from hand motion (HM) prior to the interventions to 20/40 7 months post-surgery and 24 doses of B-VEC **(Figure 4).**

Figure 4. Right eye's VA progression.



Safety: No drug-related adverse events (AE) have been observed.

Two non-related, serious AEs were reported:

1) Prolonged hospitalization due to complications post-gastrointestinal surgery, and
2) Prolonged hospitalization due to complications post-esophageal dilation

B-VEC treatment was not interrupted during either event.

CONCLUSIONS

- Topical ocular application of B-VEC in this 13-year-old patient with RDEB was well-tolerated with no signs of ocular HSV-1-like disease. VA improved without recurrence of symblepharon through 7 months of B-VEC use.
- Based on this first case, B-VEC has the potential to be a safe and effective treatment for recurrent cicatrizing conjunctivitis in patients with DEB. Longer follow-up and future, larger studies are required for further and consistent evidence

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DISCLOSURES

Commercial Relationships Disclosure: Alfonso Sabater: Commercial Relationship(s);Code C (Consultant/Contractor):Abbvie;Code C (Consultant/Contractor):GlaxoSmithKline;Code C (Consultant/Contractor):Brill Pharma;Code C (Consultant/Contractor):Laboratorios Sophia;Code O (Owner):TissueCor;Code O (Owner):LyoDrop;Code O (Owner):PlasmaCord I Arianna Tovar: Commercial Relationship: Code N (No Commercial Relationship) II Jennifer Gomez: Commercial Relationship: Code N (No Commercial Relationship) I Trevor Parry: Commercial Relationship(s);Code E (Employment):Krystal Biotech I Hubert Chen: Commercial Relationship(s);Code E (Employment):Krystal Biotech I Brittani Agostini: Commercial Relationship(s);Code E (Employment):Krystal Biotech I Suma Krishnan: Commercial Relationship(s);Code E (Employment)):Krystal Biotech