Topical Application Of Beremagene Geperpavec, An Engineered Herpes Simplex Virus Type I-based Gene Therapy Vector Expressing Type VII Collagen, Is Safe And Efficacious In A Murine Corneal Wound Model

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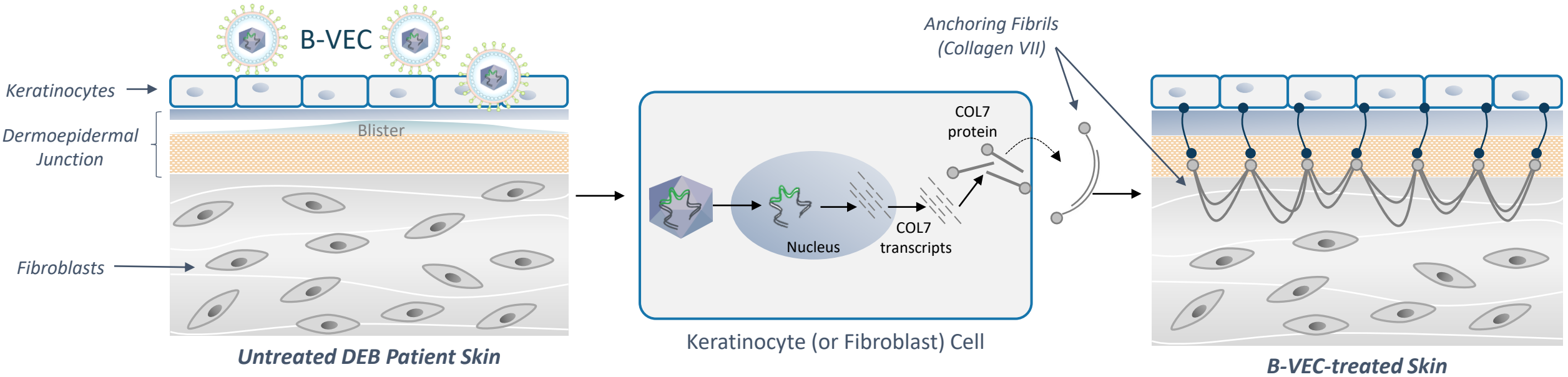
Beremagene geperpavec (B-VEC) for dystrophic epidermolysis bullosa (DEB)

B-VEC, a non-replicating, engineered herpes simplex virus type I (HSV-1)-based gene therapy vector

- Expresses the human *COL7A1* gene, which codes for the COL7 protein
- Formulated for topical application to DEB-associated skin lesions
- Phase I/II clinical trial data showed significant improvement in the healing of DEB-associated skin lesions over placebo and that repeat doses were well tolerated
- B-VEC is currently in Phase III clinical trials for treatment of DEB skin lesions, including chronic wounds



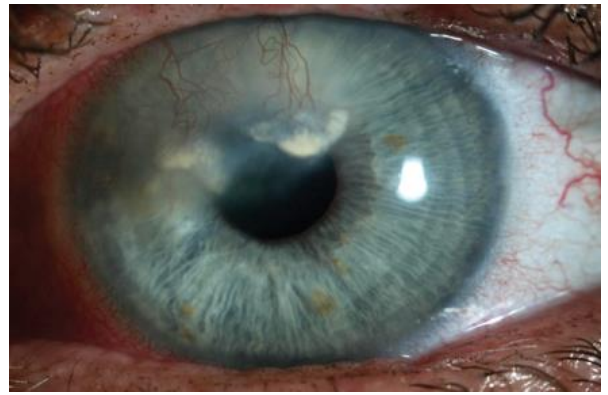
DEB-associated eye disease and potential ophthalmic use of B-VEC

Eye Disease in Epidermolysis Bullosa (EB) Patients

- EB can result in the development of abrasions, blistering, vascularization, and scarring of the cornea, conjunctiva, and eyelids
- Eye involvement can occur in most types of EB but is most common in RDEB[1]
- Current treatments are limited to ophthalmic lubricants and removal of scar tissue[2]
- Topical B-VEC could be a potential treatment for DEB-associated eye disease

Herpes Stromal Keratitis (HSK)

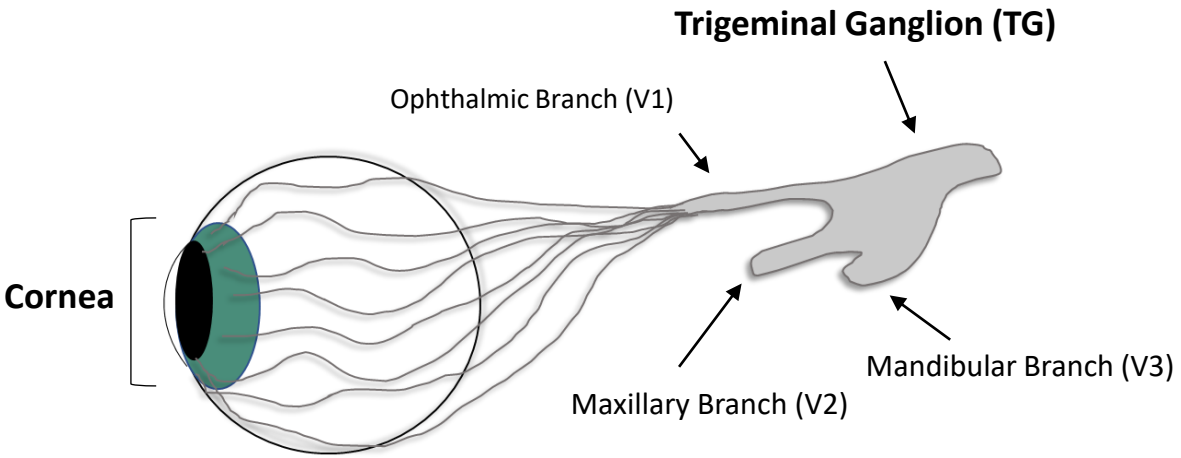
- Immunopathological condition that can occur after a corneal HSV-1 infection
- Can cause inflammation, irreversible scarring of the cornea, and blindness
- HSK manifests as progressive:
  - Opacity
  - Neovascularization
  - Loss of corneal sensitivity
- Mice can be used to study the development of HSK[3]

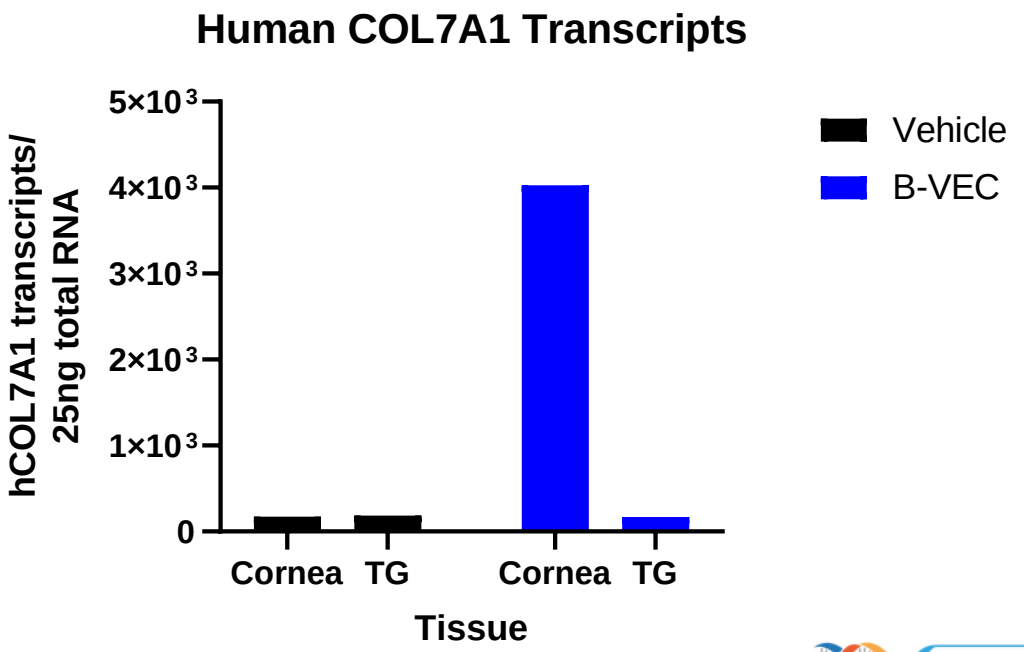


https://www.reviewofcontactlenses.com/article/rccl1117-treating-herpes-simplex-virus

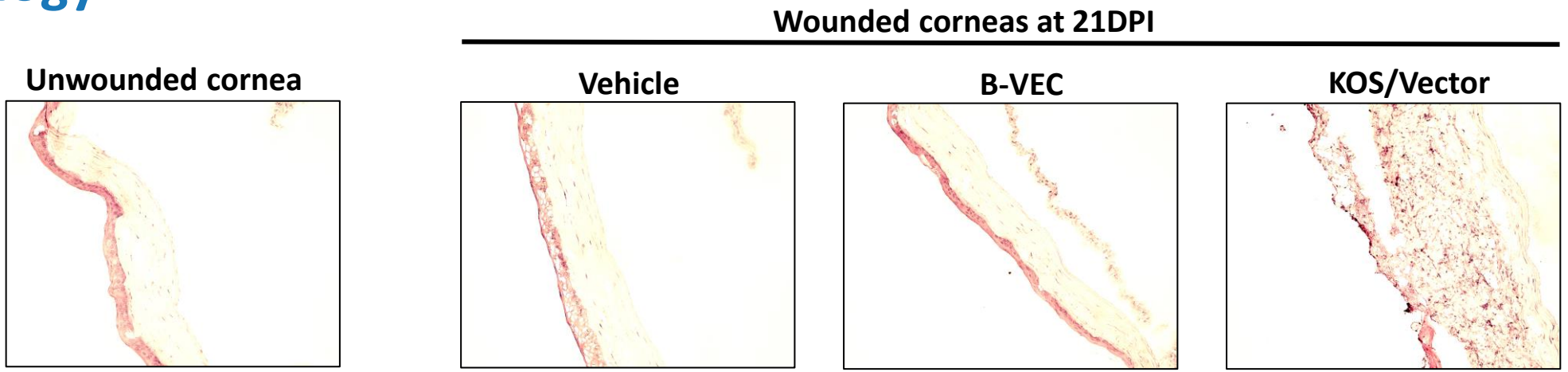
1. Fine JD, et al., Eye involvement in inherited epidermolysis bullosa: Experience of the National Epidermolysis Bullosa Registry. American Journal of Ophthalmology, 2004;138(2):254-262.
2. Tong L, et al., The eye in epidermolysis bullosa. British Journal of Ophthalmology, 1999;83:323-326.
3. Yun H, et al., Reversible nerve damage and corneal pathology in murine herpes simplex stromal keratitis. Journal of Virology, 2014;88(14):7870-7880.

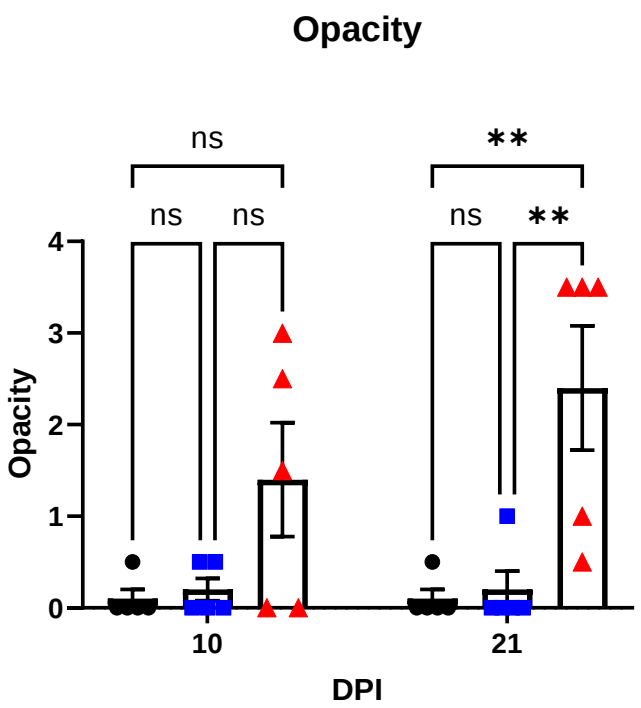
Topical B-VEC delivers human *COL7A1* to the cornea, but not the underlying sensory nerves, in a murine corneal wound model

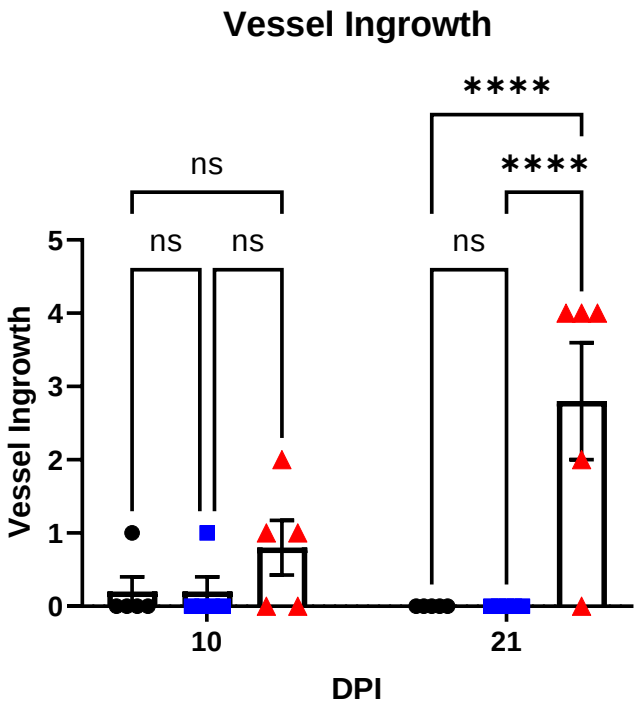


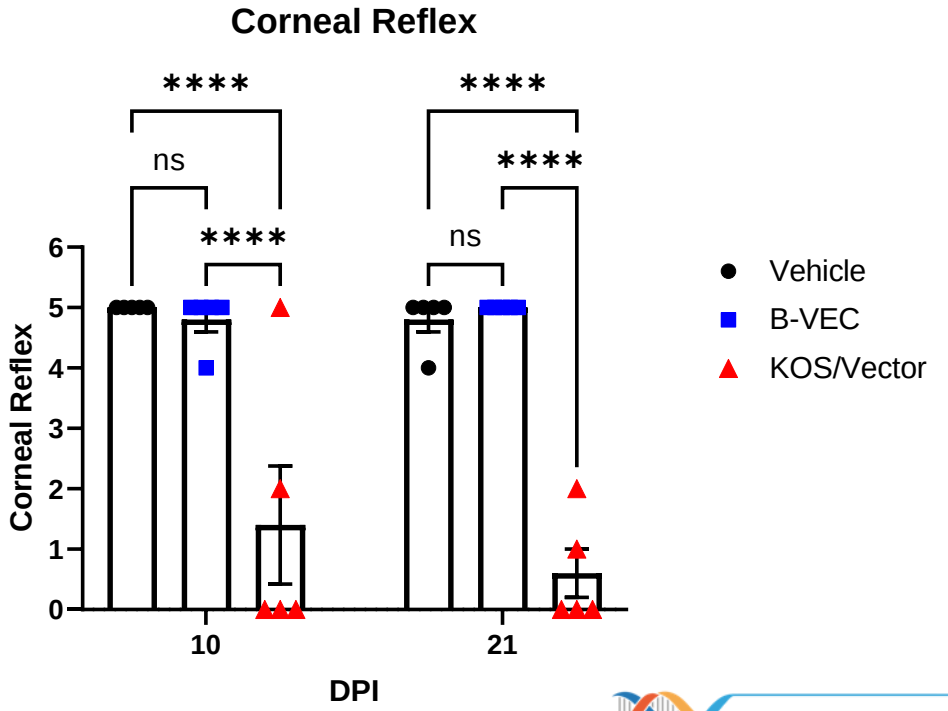


Topical B-VEC application to the wounded murine cornea does not cause pathology





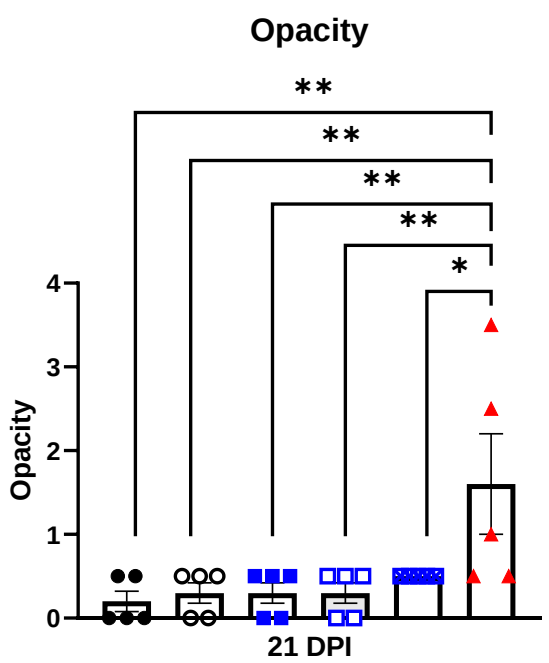


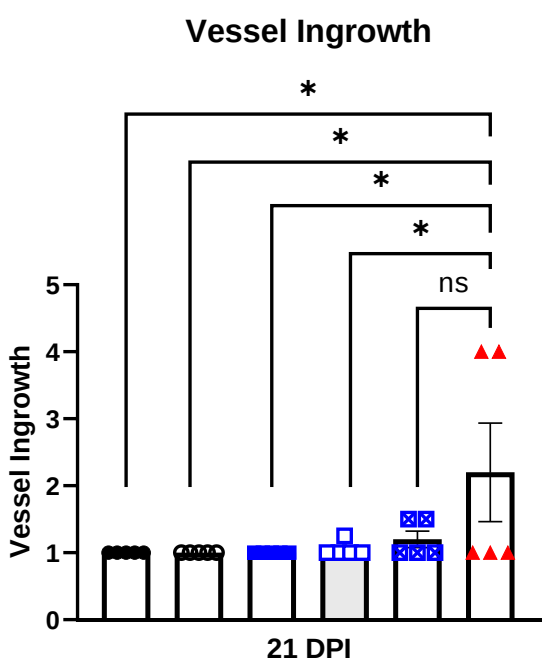


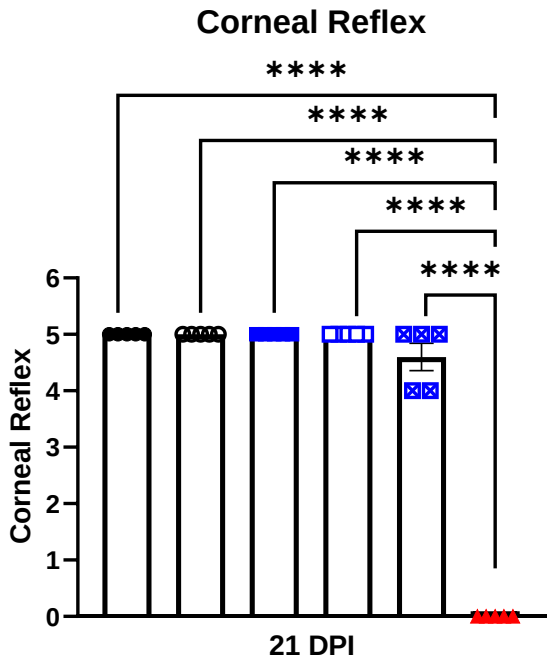
Data analyzed with repeated measures 2-way ANOVAs with Tukey's post tests. **p<0.01; ****p<0.0001, ns: not significant.

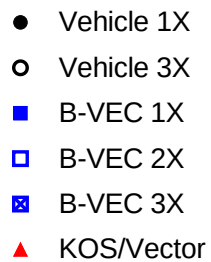
Repeated topical B-VEC application to the wounded murine cornea is safe

	DPI 0	2	4	10	21
	Corneal wound + Treatment			Blinded HSK clinical scoring*	Blinded HSK clinical scoring
● Vehicle 1X	X			X	X
○ Vehicle 3X	X	X	X	X	X
■ B-VEC 1X	X			X	X
□ B-VEC 2X	X		X	X	X
⊠ B-VEC 3X	X	X	X	X	X
▲ KOS/Vector	X			X	X









*10dpi data not shown as B-VEC did not separate from vehicle control at 10 dpi, as shown in previous results

Data analyzed with repeated measures 2-way ANOVAs with Tukey's post tests. *p<0.05; **p<0.01; ****p<0.0001, ns: not significant.

Summary

Efficacy

- Human COL7A1 was expressed in B-VEC treated corneas, but not the underlying sensory nerves

Safety

- B-VEC treated corneas developed little or no pathology
- B-VEC HSK clinical scores were not statistically different from vehicle treated corneas in either single and repeat dose experiments
- KOS/Vector treated corneas developed moderate to severe HSK after a single dose with 190-fold less virus than the B-VEC dose used

Conclusion

- B-VEC may be safe for repeated, topical treatment of human DEB corneal manifestations