Topical Application Of Beremagene Gaeperpavec, 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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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\(^3\)

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

- Corneal wound + Treatment
- Harvest TGs and corneas for gene expression
- Blinded HSK clinical scoring + Histology

Days post infection (DPI)

<table>
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<tr>
<th>Days</th>
<th>Human COL7A1 Transcripts</th>
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<tr>
<td>0</td>
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<tr>
<td>1</td>
<td>1×10^3</td>
</tr>
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<td>4×10^3</td>
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<td>21</td>
<td>5×10^3</td>
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</tbody>
</table>

- Ophthalmic Branch (V1)
- Mandibular Branch (V3)
- Maxillary Branch (V2)
- Trigeminal Ganglion (TG)

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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

<table>
<thead>
<tr>
<th>DPI</th>
<th>Corneal wound + Treatment</th>
<th>Blinded HSK clinical scoring*</th>
<th>Blinded HSK clinical scoring</th>
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<td>21</td>
<td>○ B-VEC 3X</td>
<td>X</td>
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</tr>
<tr>
<td></td>
<td>△ KOS/Vector</td>
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</tr>
</tbody>
</table>

### Data Analysis

*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