A Patient-Level Simulation to Bridge Data Gaps in Cost-Effectiveness Modelling of B-VEC for Dystrophic Epidermolysis Bullosa

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Poster code: SA2

BACKGROUND

- Dystrophic Epidermolysis Bullosa (DEB) is a rare genetic skin disease caused by a faulty COL7A1 gene. Currently there are no approved curative or recommended targeted and corrective treatments for DEB; standard of care (SoC) consists only of best supportive care (BSC) strategies. BSC measures include dressings and regular bathing to reduce the risk of infection, antibiotics, analgesics and antipruritics, dental care, and enteral feeding.
- B-VEC is a topical gene therapy used to treat Dystrophic Epidermolysis Bullosa (DEB). It works by delivering functional copies of the COL7A1 gene to skin cells using a modified herpes simplex virus type 1 (HSV-1) vector as a carrier.
- B-VEC was assessed in a phase 1/2 (GEM-1) and Phase 3 (GEM-3) trial which wounds were selected and randomized to receive B-VEC or placebo, and each patient was treated with B-VEC for some wounds and with placebo for other wounds (i.e., patients served as their own control).
- A cost-effectiveness model for B-VEC versus BSC was developed and its health states are based on changes in affected body surface area (BSA) over time. Health states are defined as presented in Table 1.

Table 1 Definitions of model health states according to UK clinical experts

Health state	Percentage of BSA open			
	Recurrent wounds	Chronic wounds	Total of recurrent and chronic wounds*	
			Lower bound	Upper bound
Very mild	0% to < 2%	0% to < 0.1%	0.0%	2.1%
Mild	2% to < 4%	0.1% to < 1%	2.1%	5.0%
Moderate	4% to < 15%	1% to < 10%	5.0%	25.0%
Severe	≥15%	≥10%	25.0%	None, except at baseline

*Represents the sum of columns for recurrent and chronic wounds.
BSA=body surface area; UK=United Kingdom.

- **The pivotal Phase 1/2 (GEM-1) and Phase 3 (GEM-3) trials for B-VEC undertook randomization at wound-level, not patient-level, and did not report the number or size of wounds per patient or percentage of BSA covered with wounds. Therefore, data on the effect of B-VEC on percentage of BSA with recurrent or chronic wounds are not available.**

METHODS

- A patient-level simulation was developed using wound-level data from GEM-1, GEM-3, their open-label extension, and published literature.
- Simulated patients were tracked in parallel B-VEC and placebo arms over a 3-year time horizon.
- **The simulation captured wound closure dynamics, duration of closure, reopening size, and risk of chronicity to estimate BSA involvement over time.**
- Data sources that were used in the patient-level simulation to estimate transitions between health states are listed in Table 2.

Table 2 Data sources used in the patient-level simulation to estimate transitions between health states

Model Input	Value			Source
Total BSA per age group	Age subgroup	RDEB	DDEB	Reimer et al. (2020)[1] (RDEB) General population[2] (DDEB)
	0-6	5,129 cm^2	5,607 cm^2	
	6-18	10,097 cm^2	13,408 cm^2	
	18+	13,764 cm^2	17,541 cm^2	
Rate of wound closure per week	Wounds	B-VEC	BSC	GEM-1[3]
	Recurrent	42.54%	14.17%	
	Chronic		0%	
Duration of wound closure in days	B-VEC: 300 BSC: 16.5			GEM-3 and OLE GEM-1
Number of wounds at risk of reopening	Health state	Recurrent	Chronic	Eng et al (2021)[4]
	Very mild	0	0-4	
	Mild	1-2	5-10	
	Moderate	3-4	11-17	
	Severe	≥5	≥18	
Size and increase in size of reopened wounds	3.19cm^2 at reopening B-VEC wounds are treated immediately so they do not grow BSC wounds increase 345% in size			GEM-1[3]
Definition of chronic wounds	Wounds were considered chronic if they remained open for at least 8 weeks			Eng et al. (2021)[4]
Proportion of weeks with treatment (compliance)	90%			GEM-3[5]
B-VEC dosing	Dose per week: For patients 3 years and older, the weekly dose is up to 4.0×10^9 PFU (4 billion) of B-VEC, (i.e., a total of four syringes of 0.5 mL each can be used for those patients). For patients under 3 years of age, the weekly dose is up to 2.5×10^9 PFU (2.5 billion) of B-VEC. To simplify the model and make a conservative assumption, the higher dose was considered for all patients A B-VEC vial can fill 4 syringes with 0.5 mL each. Each syringe could treat 50 cm^2 of open wounds Maximum treatable area per week: 200 cm^2 (maximum of 4 syringes per week) Vial optimization: 80% of patients will participate in vial optimisation, and that it is feasible to share a vial between a maximum of 4 patients.			SmPC [6]

BSA=body surface area; BSC=best supportive care; OLE=open-label extension.

- The first step of the patient-level simulation was to simulate a cohort of 1,000 individual patients who were subsequently tracked while being hypothetically treated with B-VEC or placebo. The following characteristics at baseline were sampled:
  - Age group
  - Total BSA
  - Health state
  - BSA with open chronic wounds
  - BSA with open recurrent wounds
- Once baseline patient characteristics were sampled, the next step was to track each patient in the hypothetical B-VEC and placebo arms for up to 3 years.
- The following were tracked on a weekly basis:
  - BSA covered in chronic and recurrent wounds
  - total BSA open
  - health state
  - B-VEC vials consumed
- The period of three years was selected because, in the patient-level simulation, it was observed that the per-cycle consumption of B-VEC vials had stabilised after approximately 2–3 years. The transitions between health states are tracked for only two years, as those stabilise earlier than the consumption of B-VEC.
- The simulation was repeated until the estimated outputs achieved convergence and their outcomes were recorded.
- This record of simulated patients was then used to calculate transition probabilities and Markov model inputs on the consumption of B-VEC.

RESULTS

- The simulation successfully generated plausible patient trajectories consistent with disease natural history reported by clinical expert expectations, although there is no long-term patient-level evidence to validate outcomes against.
- Figure 1 and Figure 2 present the health-state distribution of the model cohort in the first 24 months in the B-VEC and BSC arms, respectively, for the overall cohort (i.e., paediatrics, adolescents and adults).

Figure 1 Health-state distribution of the model cohort over time in the B-VEC

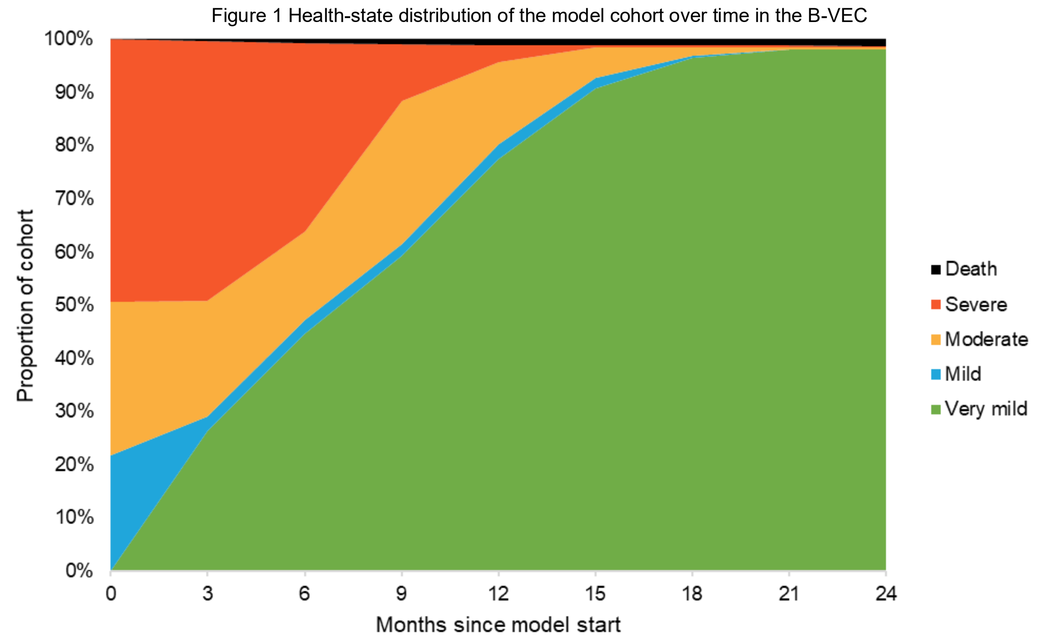
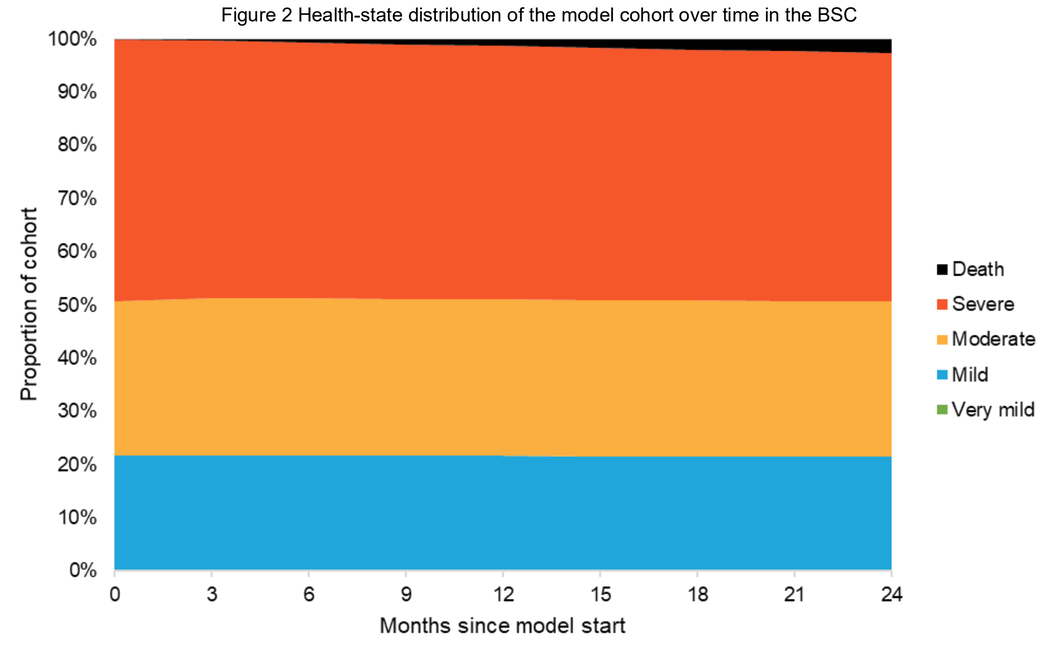


Figure 2 Health-state distribution of the model cohort over time in the BSC



- **The model predicts that one year of treatment with B-VEC is enough to bring approximately 80% of patients into the very mild health state (<2.1% BSA with open wounds). In contrast, BSC patients are stable according to the initial health states distribution while they are alive.**
- The model predicts that the average number of vials consumed across the cohort declines over time (Table 3). This is because patients reach a stable state where they have very few wounds reopening occasionally, which means they do not need treatment every week.

Table 3 Number of B-VEC vials used per cycle by health state, by year and by age subgroup according to the patient-level simulation

Age subgroups	Year	Very mild	Mild	Moderate	Severe
0 to <6 years	1	0.79	5.03	9.10	11.5
	2	0.40	5.03	9.10	11.5
	3+	0.38	5.03	9.10	11.5
6 to <18 years	1	1.13	6.88	10.62	11.8
	2	0.51	5.70	8.46	11.8
	3+	0.40	5.70	8.46	11.8
≥18 years	1	1.76	7.59	11.34	11.8
	2	0.63	6.35	10.76	11.6
	3+	0.36	6.35	10.76	11.6

- Over a lifetime horizon, due to the accumulated gains that B-VEC offers, and the consequent improvement in health condition which is translated into greater disposition of patients in better health states, it is expected that B-VEC provides a longer life expectancy with better quality of life in patients with DEB compared to both comparators in the analysis.

CONCLUSION

The patient-level simulation offers a viable solution for modelling treatment impact and resource use in the absence of patient-level trial data. This approach may be particularly valuable in rare diseases like DEB, where traditional data sources are limited.

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ABBREVIATIONS

DEB: dystrophic epidermolysis bullosa; BSA: body surface area; BSC: best supportive care; DDEB: dominant dystrophic epidermolysis bullosa; RDEB: recessive dystrophic epidermolysis bullosa; SoC: standard of care

DISCLOSURE

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