Cost-effectiveness of Treatment Strategies for Severe Hemophilia A Patients in the United States

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BACKGROUND

Hemophilia A is a rare genetic bleeding disorder associated with high morbidity and significant financial burden. For bleed prevention, about 80% of patients use prophylaxis, 20% on-demand infusions of either standard half-life factor VIII products (SHL-FVIII) or the newer extended half-life products (EHL–FVIII). Adeno-associated virus (AAV)-derived gene delivery by a single intravenous infusion can lead to sustained factor level for years. Introduction of gene therapy is further adding heterogeneity to the treatment paradigm.

OBJECTIVES

To compare the cost-effectiveness of eight treatment strategies:

1) On-demand treatment using SHL-FVIII
2) On-demand treatment using EHL-FVIII
3) Prophylaxis using SHL-FVIII
4) Prophylaxis using EHL-FVIII
5) Gene therapy with on-demand SHL-FVIII administered before injection and after factor level waning.
6) Gene therapy with on-demand EHL-FVIII administered before injection and after factor level waning.
7) Gene therapy with prophylaxis SHL-FVIII administered before injection and after factor level waning.
8) Gene therapy with prophylaxis EHL-FVIII administered before injection and after factor level waning.

And to determine the price at which gene therapy would be cost-effective compared to each of the alternatives.

METHODS

Model type: Microsimulation Markov model

Time horizon: Lifetime horizon (birth to death)

Perspective: Societal perspective in the United States

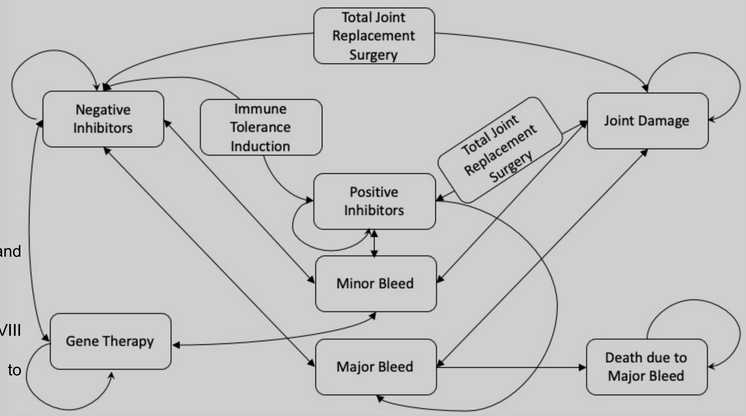
Annual discounting rate: 3%

Gene therapy administration age: 18 years

Gene therapy price: $2,000,000/patient.

Gene therapy effectiveness: Restart prophylaxis/on-demand treatment after 6 years (based on clinical trial data).

Inclusion criteria: Model is inclusive of patients who developed FVIII inhibitors and/or AAV antibodies although they were not eligible to receive gene therapy.



RESULTS

- Gene therapy priced at $2,000,000 and effective for 6 years, is not cost-effective compared to on-demand treatment, assuming a 150,000/QALY threshold.
- At a gene therapy price of $625,000, gene therapy preceded and followed by on-demand SHL–FVIII, is cost-effective compared to on-demand treatment using SHL–FVIII.
- At a gene therapy price of $1,925,000, gene therapy preceded and followed by on-demand SHL–FVIII, is cost-effective compared to on-demand treatment using EHL–FVIII.
- Gene therapy priced at $2,000,000 and effective for 6 years, is dominant compared to prophylaxis with SHL-FVIII or EHL-FVIII.

	On-demand treatment using SHL-FVIII	On-demand treatment using EHL-FVIII	Prophylaxis using SHL-FVIII	Prophylaxis using EHL-FVIII
Costs	$8,234,037	$8,764,330	$20,144,062	$24,147,829
Effects in QALYs	14.34	14.67	23.18	23.73
Cost/QALY	$574,201	$597,432	$869,028	$1,017,608
ICER/QALY	$649,858	$620,023	Gene Therapy is Dominant	Gene Therapy is Dominant
	Gene therapy preceded and followed by on-demand using SHL-FVIII	Gene therapy preceded and followed by on-demand using EHL-FVIII	Gene therapy preceded and followed by prophylaxis using SHL-FVIII	Gene therapy preceded and followed by prophylaxis using EHL-FVIII
Costs	$8,896,892	$9,378,153	$19,703,755	$23,383,234
Effects in QALYs	15.36	15.66	24.12	24.57
Cost/QALY	$579,225	$598,860	$816,905	$951,699

ICER: Incremental Cost-Effectiveness Ratio
QALY: Quality Adjusted Life Year

CONCLUSIONS

This is the first model to assess benefits for the whole hemophilia population rather than only the gene therapy-eligible group. Distributing the gains yielded by introducing gene therapy to the eligible group on the whole patient population offers a more realistic understanding to decision makers. Our model reveals cost-effectiveness of AAV-mediated hemophilia A gene therapy at different price points ranging between $625,000 to $2,000,000. The results are influenced by the costs and effects of the alternative treatment approach which are based on the clinical protocol (on-demand treatment versus prophylaxis) and the clotting factor used (SHL-FVIII versus EHL-FVIII).