GENE THERAPY FOR PEOPLE WITH HAEMOPHILIA B (PWHB): DEVELOPMENT OF A COST-EFFECTIVENESS MODEL FRAMEWORK

Nanxin (Nick) Li[1], Eileen K. Sawyer[1], Konrad Maruszczyk[2], Marta Slomka[2,3], Tom Burke[2], Antony P. Martin[2], Jamie O'Hara[2,4], Matthew Stevenson[5]

[1]uniQure Inc, Lexington, MA, USA, [2]HCD Economics, Daresbury, UK, [3]Medical Research Centre PAS, Department of Neurochemistry, Poland, [4]Faculty of Health and Social Care, University of Chester, Chester, UK, [5]University of Sheffield, UK

Poster No. P154

INTRODUCTION

- Haemophilia B (HB) is a rare congenital blood disorder characterised by deficiency of clotting factor IX (FIX). HB patients with severe and moderately severe disease (IU/dl≤2) experience significant morbidity and require life-long costly treatment with frequent FIX infusions.
- To date, there are relatively few published cost-effectiveness models comparing alternative treatments for HB. Recent developments in the field of gene therapy (GTx) have the potential to bring significant health benefits to HB patients.
- Here, we describe the first phase of research to build a cost-effectiveness model in order to inform healthcare decision makers in terms of incremental cost and health gains of HB gene therapy compared with FIX replacement therapy.

AIM

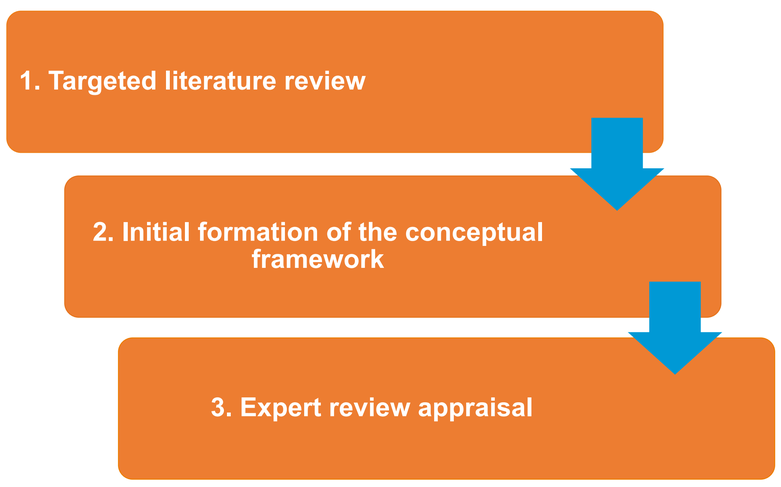
- To reach consensus on an appropriate conceptual framework for economic evaluation of a new GTx in HB.

METHODS

Overview

- An overview of study methods is presented in **Figure 1**.

Figure 1. Study method overview



Targeted literature review

- A targeted literature review (TLR) was conducted to identify published studies of economic modelling in haemophilia.
- Two published systematic literature reviews were identified: Drummond *et al.* 2017 and Thorat *et al.* 2018. Based on these, an update literature search was conducted.
- Searches of relevant economic databases (MEDLINE, Tufts Cost Effectiveness Analysis Registry, National Institute for Health and Care Excellence, National Health Service Evidence) were performed to identify evidence related to the research question.
- Additionally, a manual search for abstracts from relevant conferences was performed (search period: 03/2017-03/2019).
- Studies were included in the review using pre-defined inclusion/exclusion criteria in terms of language (English only), population (haemophilia A [HA] and HB), intervention (factor and non-factor therapy), study type (Cost-utility analysis [CUA], Cost-effectiveness analysis [CEA]), and outcomes (Incremental cost-utility ratio [ICUR], Incremental cost-effectiveness ratio [ICER], Quality adjusted life year [QALY] gained, Life year [LY] gained).

Initial formation of conceptual model framework

- Targeted literature review findings informed the initial formation of the conceptual model framework, based on a PICO (population, intervention, comparators, outcomes) template.

Expert review group appraisal

- An expert panel consisting of clinicians, Health Technology Assessment (HTA) specialists, and patient advocacy representatives evaluated the conceptual model framework.

RESULTS

Targeted literature review

- The TLR identified 26 economic evaluations (EE) in haemophilia, published 2002-2019 **(Figure 2).**
- The majority of studies focused on treatments for severe HA patients. Two studies investigated both HA and HB. One study included HB population only.
- A total of 21 out of 26 models were structured as Markov cohort models, 2 employed patient-level simulation, 2 utilised decision trees, and 1 study was trial-based EE (no modelling).
- Six studies performed both CEA and CUA. Two studies performed CEA only and 18 studies performed CUA only.
- In recently published economic models, there is a greater emphasis on considering the full spectrum of haemophilia complications within the model framework, including factor activity levels, types of bleeds, exogenous factor use, joint deterioration in addition to quality-of-life.

Conceptual model framework

Conceptual model framework is summarized in **Table 1**.

Table 1. Conceptual model framework

Population

- Severe or moderately severe (≤2% of normal circulating FIX) adult HB non-inhibitor patient population.

Intervention

- Long term safety and long-term efficacy of GTx should be reflected in the model.

Comparators

- HB GTx should be compared with the current standard of care (FIX prophylaxis).

Outcomes

- QALY, LY, bleeds.

Additional analytical details

Type of analysis

- CUA and CEA.

GTx outcome

- Complete response (no bleeds), partial response (remission to the mild form of HB), and no response (patients continue with FIX prophylaxis).

Model structure

- A Markov model structure incorporating bleeding, joint damage, and QoL should be used to assess the clinical and economic value of HB GTx.
- Different types of value-based payment plans for GTx should be reflected in the model with respect to treatment effects.

Perspective

- Payer perspective in the base-case.

Time horizon

- Lifetime in the base-case.

Sensitivity analysis

- Durability of the GTx should be tested, consistent with recent guidelines.[1]

Expert review group appraisal

- The expert review group appraised the proposed modelling framework **(Table 1)** and determined it was appropriate for evaluating the cost-effectiveness of HB GTx.
- For model structure **(Figure 3),** there are three Markov sub-models representing joint deterioration of HB patients as measured by number of problem joints[2]. A "problem joint" exhibits symptoms of chronic joint pain and/or limited range of movement due to compromised joint integrity (i.e. chronic synovitis and/or haemophilic arthropathy).
- Each sub-model consists of three mutually exclusive health states: No bleed; Bleed (not joint); Bleed (joint). Death was the absorbing state for all three sub-models.

Figure 3. Proposed model structure

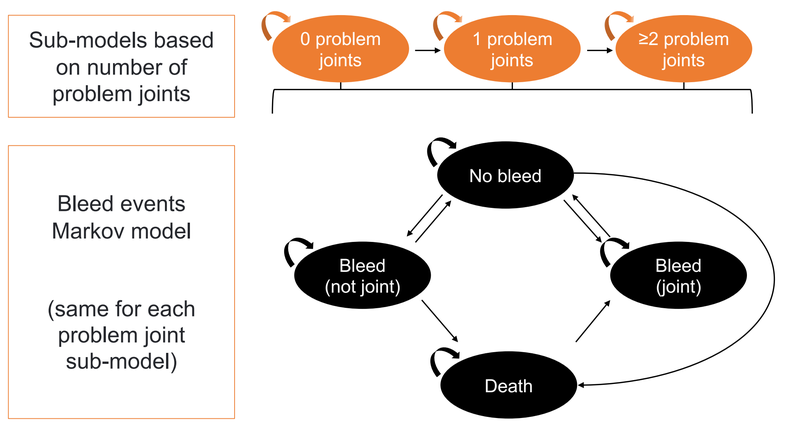
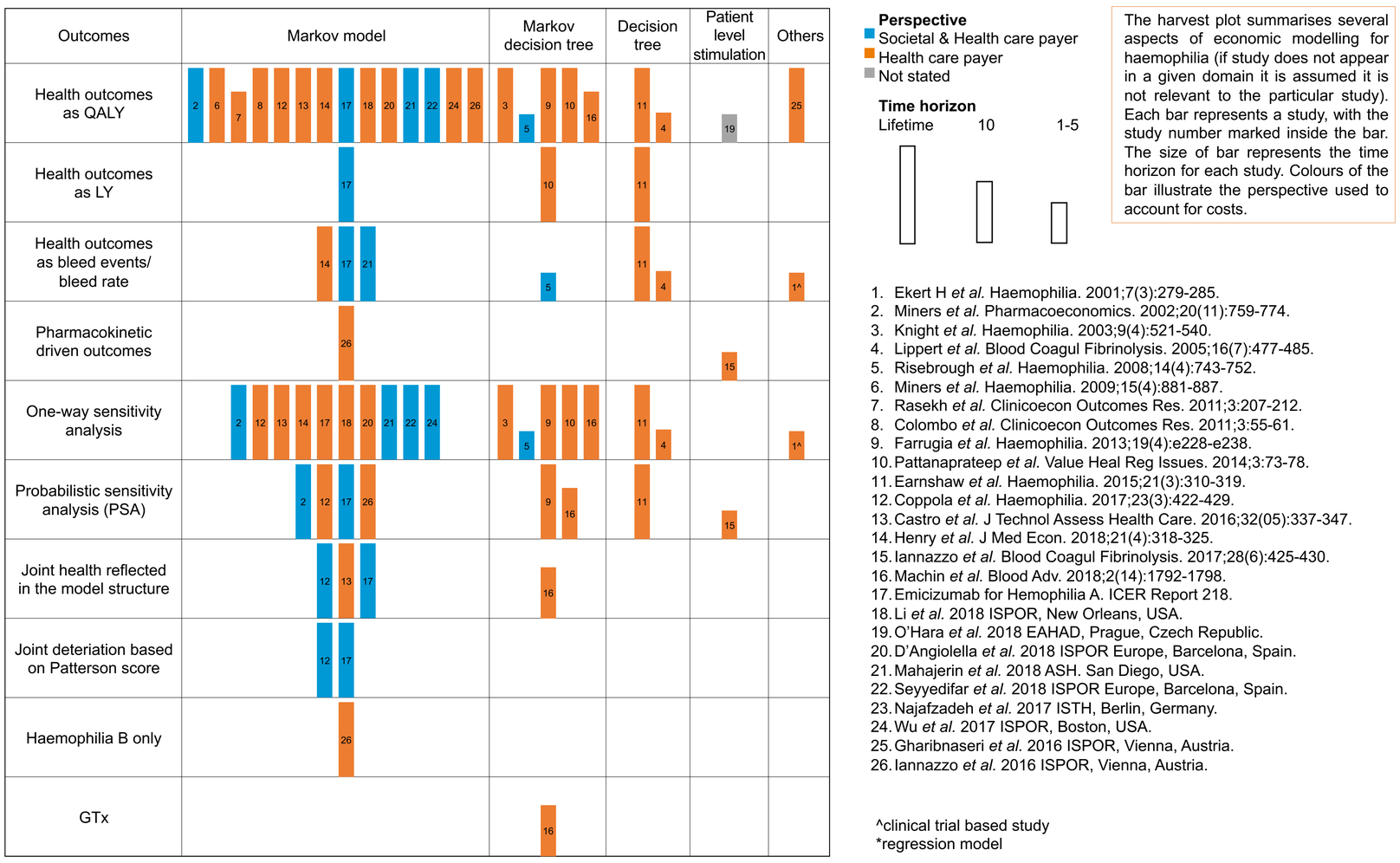


Figure 2. TLR summary



^clinical trial based study
*regression model

CONCLUSIONS

- Based on TLR and expert inputs, a consensus about the model framework was achieved for a cost-effectiveness model of HB GTx.
- Experts agreed that the model should reflect the natural history of the disease incorporating bleeding events, progressing joint deterioration, and impact on QoL.
- This model should directly reflect the natural history of the disease. It will also help to capture how the advent of GTx could transform HB management.

1. Ekert H *et al.* Haemophilia. 2001;7(3):279-285.
2. Miners *et al.* Pharmacoeconomics. 2002;20(11):759-774.
3. Knight *et al.* Haemophilia. 2003;9(4):521-540.
4. Lippert *et al.* Blood Coagul Fibrinolysis. 2005;16(7):477-485.
5. Risebrough *et al.* Haemophilia. 2008;14(4):743-752.
6. Miners *et al.* Haemophilia. 2009;15(4):881-887.
7. Rasekh *et al.* Clinicoecon Outcomes Res. 2011;3:207-212.
8. Colombo *et al.* Clinicoecon Outcomes Res. 2011;3:55-61.
9. Farrugia *et al.* Haemophilia. 2013;19(4):e228-e238.
10. Pattanaprateep *et al.* Value Heal Reg Issues. 2014;3:73-78.
11. Earnshaw *et al.* Haemophilia. 2015;21(3):310-319.
12. Coppola *et al.* Haemophilia. 2017;23(3):422-429.
13. Castro *et al.* J Technol Assess Health Care. 2016;32(05):337-347.
14. Henry *et al.* J Med Econ. 2018;21(4):318-325.
15. Iannazzo *et al.* Blood Coagul Fibrinolysis. 2017;28(6):425-430.
16. Machin *et al.* Blood Adv. 2018;2(14):1792-1798.
17. Emicizumab for Hemophilia A. ICER Report 218.
18. Li *et al.* 2018 ISPOR, New Orleans, USA.
19. O'Hara *et al.* 2018 EAHAD, Prague, Czech Republic.
20. D'Angiolella *et al.* 2018 ISPOR Europe, Barcelona, Spain.
21. Mahajerin *et al.* 2018 ASH. San Diego, USA.
22. Seyyedifar *et al.* 2018 ISPOR Europe, Barcelona, Spain.
23. Najafzadeh *et al.* 2017 ISTH, Berlin, Germany.
24. Wu *et al.* 2017 ISPOR, Boston, USA.
25. Gharibnaseri *et al.* 2016 ISPOR, Vienna, Austria.
26. Iannazzo *et al.* 2016 ISPOR, Vienna, Austria.

ADDITIONAL REFERENCES

1. Pearson S. Early Experience with Health Technology Assessment of Gene Therapies in the United States: Pricing and Paying for Cures. In: OHE Seminar Briefing 25.; 2019.
2. O'Hara J, Khair K, McLaughlin P, *et al.* "Problem Joint" a more patient relevant definition for joint morbidity in haemophilia. Eur Assoc Haemoph Allied Disord (EAHAD) 6-8th Feb 2019, Prague, Czech Republic. 2019.

ACKNOWLEDGEMENT

This work was supported by uniQure Inc.

Presented at The 13th Annual Congress of the European Association for Haemophilia and Allied Disorders, EAHAD 2020, The Hague, 5-7 February 2020