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Cost-effectiveness analysis of rFVIII-Fc, PEGylated rFVIII, and emicizumab for the prophylactic treatment of severe hemophilia A patients without inhibitors in the United States

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Background and Objectives

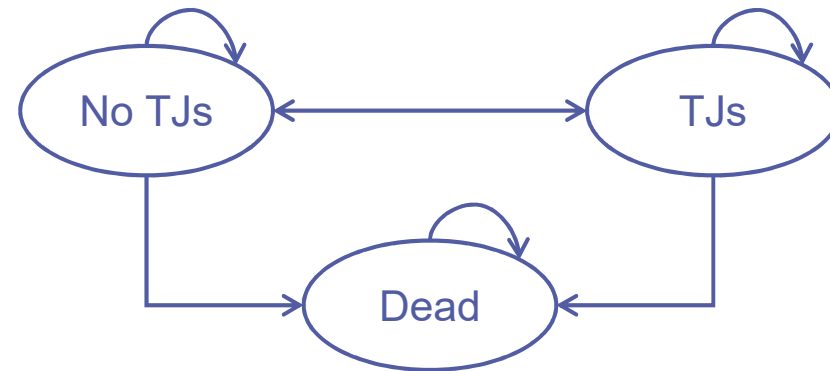
- Hemophilia is an inherited genetic disorder that impairs the body's ability to form blood clots
 - Hemophilia A (HA) is the most common form of the disorder, and is caused by a deficiency of the blood clotting factor VIII (FVIII)
- The hindered ability to form clots leads to an increased risk of spontaneous bleeds, particularly into joints (“hemarthrosis”)
 - While not fatal, repeated hemarthroses are a serious complication of HA and current treatment aims to reduce the risk of bleeding specifically into joints
 - Frequent joint bleeds prevent people with HA from being physically active, taking part in sports and in general, living a full life
- Joints into which frequent bleeds occur are termed “target joints” (TJs), which require urgent and comprehensive treatment if permanent joint damage is to be avoided¹

Background and Objectives

- Until recently, treatment options for patients with HA have largely revolved around the use of FVIII products
- Recombinant FVIII (rFVIII) products may be administered “on-demand” or “prophylactically”, and are considered the cornerstone of severe HA treatment for patients without inhibitors (antibodies against FVIII)
- Standard of care for US patients with severe HA is rFVIII prophylaxis; however recent developments in treatment include:
 - rFVIII products with an extended half-life (EHL) (rFVIII-Fc fusion protein, Eloctate[®] and PEGylated rFVIII, Adynovate[®])
 - Monoclonal antibody (non-factor replacement) emicizumab-kxwh (Hemlibra[®])
- This study aimed to evaluate the cost-effectiveness of these prophylactic treatment options for severe HA patients without inhibitors from a third party US perspective

Methods: Cost-Effectiveness Model

- Owing to the importance of joint health outcomes when attempting to quantify the cost-effectiveness of severe HA treatments, a cost-effectiveness model was constructed with health states based on the absence or presence of TJs, as well as the improvement in the modified hemophilia joint health score (mHJHS)
- Patients were categorized as having at least 1 TJ (“TJs”), or “No TJs”
- The model adopts a Markovian framework and a third-party US payer perspective



- Model outputs were the total costs and total quality-adjusted life years (QALYs) associated with each treatment

Methods: Input Data

- Transitions between health states were determined according to calculated rates of TJ development or resolution based on published literature and background mortality rates²⁻⁷
- Costs relating to the use of on-demand and prophylactic extended half-life rFVIII products and emicizumab were included based on published weight data for US hemophiliacs⁸
- Dosing and efficacy data were obtained from product labels and published literature
 - Clinical outcomes were annualized bleeding rate (ABR) and presence of TJs based on published studies^{2-7, 9-12}
 - A literature review was undertaken to identify evidence regarding joint health improvement
- Utility data were sourced from published literature sources¹³⁻¹⁴

References: 2: Manco-Johnson et al., (2017); 3: Mullins et al., (2017); 4: Mahlangu et al., (2013); 5: Young et al., (2015); 6: Mahlangu et al., (2018); 7: Wang et al., (2016); 8: ICER (2018); 9: Iorio et al., (2017); 10: Nolan et al., (2016); 11: Mahlangu et al., (2018); 12: Adynovi label, (2016); 13: O'Hara et al., (2018); 14: Neufeld et al., (2012). Full list provided at the end of this slide deck.

Results

- Based on the literature review, rFVIII Fc was associated with improved joint health over time measured by mHJHS¹⁵; no data regarding mHJHS were identified for PEGylated rFVIII or emicizumab
- An improvement in mHJHS of 1 point was assumed to be associated with a utility benefit of 0.003, and so patients receiving rFVIII Fc were assumed to have a higher utility of approximately 0.012 due to a 4.1-point improvement in mHJHS¹⁵
 - Patients receiving PEGylated rFVIII, and emicizumab were assumed to have a 0-point improvement in mHJHS (based on a lack of data identified)

Results

- The base-case analysis (Table 1) showed that rFVIII Fc was associated with the most QALYs (26.15) and lowest overall cost (\$15.64m)
- A sensitivity analysis in which a 1-point improvement in mHJHS was associated with a utility increment of 0.001 showed comparable results (Table 2)
- A further sensitivity analysis wherein on-demand rFVIII costs were removed for emicizumab patients also demonstrated similar results (Table 3)

1

Treatment	Costs	QALYs
rFVIII Fc	\$15.64m	26.15
PEGylated rFVIII	\$17.07m	25.80
Emicizumab	\$16.10m	25.83

2

Treatment	Costs	QALYs
rFVIII Fc	\$15.64m	25.85
PEGylated rFVIII	\$17.07m	25.80
Emicizumab	\$16.10m	25.83

3

Treatment	Costs	QALYs
rFVIII Fc	\$15.64m	26.15
PEGylated rFVIII	\$17.07m	25.80
Emicizumab	\$15.92m	25.83

Discussion

- rFVIII Fc is the only EHL rFVIII treatment with published evidence demonstrating improved joint health through the mHJHS
- This cost-effectiveness analysis, which includes the impact of treatment on joint health, indicates that rFVIII Fc is associated with lower costs and more QALYs compared to PEGylated rFVIII and emicizumab
- Further data collection is required to establish the longer-term impacts of treatment on joint health outcomes, and consequently the cost effectiveness of alternative treatment options
 - In particular, the lack of available data to capture changes in joint health for comparator treatments is a key limitation in the analysis presented
 - This study also assumed a 1 point improvement in the mHJHS is associated with a utility benefit of 0.003 – further validation of this assumption is required

Thank you

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References

1. Mulder et al., (2004) <https://www.ncbi.nlm.nih.gov/pubmed/15479389>
2. Manco-Johnson et al., (2017) <https://www.ncbi.nlm.nih.gov/pubmed/28836341>
3. Mullins et al., (2017) <https://www.ncbi.nlm.nih.gov/pubmed/27891721>
4. Mahlangu et al., (2013) <https://www.ncbi.nlm.nih.gov/pubmed/24227821>
5. Young et al., (2015) <https://www.ncbi.nlm.nih.gov/pubmed/25912075>
6. Mahlangu et al., (2018) <https://www.ncbi.nlm.nih.gov/pubmed/30157389>
7. Wang et al., (2016) <http://www.bloodjournal.org/content/128/22/3791?sso-checked=true>
8. ICER (2018) [https://icer-review.org/wp-content/uploads/2017/08/ICER Hemophilia Final Evidence Report 041618.pdf](https://icer-review.org/wp-content/uploads/2017/08/ICER_Hemophilia_Final_Evidence_Report_041618.pdf)
9. Iorio et al., (2017) <https://www.ncbi.nlm.nih.gov/pubmed/28233383>
10. Nolan et al., (2016) <https://www.ncbi.nlm.nih.gov/pubmed/26218032>
11. Mahlangu et al., (2018) <https://www.ncbi.nlm.nih.gov/pubmed/30157389>
12. Adynovi label, (2016) <https://www.fda.gov/> (search 'Adynovi')
13. O'Hara et al., (2018) <https://www.ncbi.nlm.nih.gov/pubmed/29720192>
14. Neufeld et al., (2012) <https://www.ncbi.nlm.nih.gov/pubmed/22999142>
15. Oldenburg et al., (2018) <https://www.ncbi.nlm.nih.gov/pubmed/29082639>