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Cost-effectiveness analysis of rFVIIIFc, 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

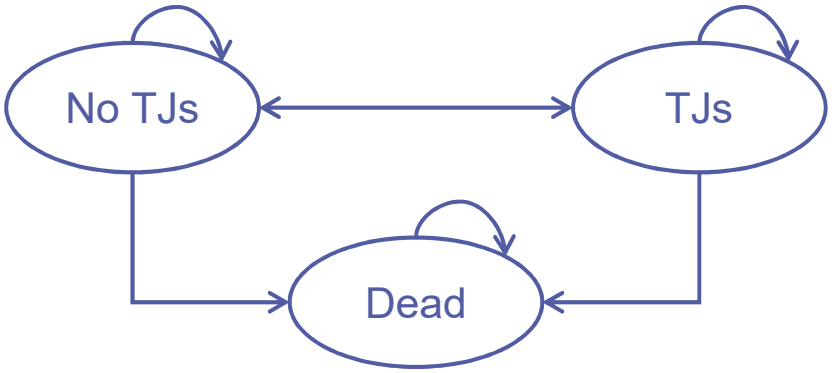
- Hemophilia is an inherited genetic disorder that impairs the body's ability to form blood clots
  - Hemophilia A (HA) is the most common form of the disorder, and is caused by ~~a~~ deficiency of the blood clotting factor VIII (FVIII)
- The hindered ability to form clots leads to an increased risk 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 avoided[1]

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 rates[2-7]
- 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 hemophiliacs[8]
- 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 sources[13-14]

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, rFVIIIFc was associated with improved joint health over time measured by mHJHS[15]; 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 rFVIIIFc were assumed to have a higher utility of approximately 0.012 due to a 4.1-point improvement in mHJHS[15]
  - 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 rFVIIIFc 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)

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

2

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

3

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

Discussion

- rFVIIIFc 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 rFVIIIFc 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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