VALUE CONTRIBUTION OF ETRANACOGENE DEZAPARVOVEC FOR THE TREATMENT OF SEVERE AND MODERATELY SEVERE HEMOPHILIA B IN SPAIN THROUGH MULTICRITERIA DECISION ANALYSIS (MCDA)

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BACKGROUND

- Congenital **Hemophilia B** is a rare bleeding disorder characterized by an increased bleeding tendency due to either a partial or complete deficiency of the essential blood coagulation factor IX (FIX), which may lead to severe comorbidities that reduce patients' quality of life [1,2].
- **Etranacogene dezaparvovec (ED)** is a recombinant adeno-associated virus serotype 5 (AAV5)-based vector gene therapy for the treatment of severe and moderately severe Hemophilia B.
- **Multicriteria decision analysis (MCDA)** methodology has demonstrated usefulness in determining the value contribution of health care interventions, especially in orphan drugs and ATMPs[3-6].

OBJECTIVE

This study assessed the **value contribution of Etranacogene dezaparvovec (ED)** versus current extended half-life recombinant factor IX alternatives (EHL) for the **treatment of severe and moderately severe Hemophilia B (sHB) in Spain using MCDA** and involving a large multidisciplinary panel of stakeholders.

METHODS

- A targeted literature review was conducted to retrieve available evidence for each criterion included in a validated MCDA framework for orphan-drug evaluation and decision-making in Spain[7], which included nine quantitative and four qualitative criteria.
- A multidisciplinary panel of **twenty-eight experts** (haematologists, hospital pharmacists, decision-makers & patients) scored **three evidence matrices** (ED vs Alprolix®, Idelvion® and Refixia®) using an ordinal scale from 0 to +5 (highest value) for non-comparative quantitative criteria and from −5 to +5 for comparative criteria. A qualitative scale with 3 response options was used for qualitative criteria: positive, neutral, or negative impact.
- **Mean and standard deviation** of the scores were calculated for quantitative criteria. For qualitative criteria, the **percentage of experts** who considered that the impact to the current National Health System (NHS) context would be positive, neutral or negative was calculated, respectively.
- **ED's global value contribution vs EHL was calculated** by multiplying the relative weights of the MCDA framework assigned by 98 evaluators and decision-makers in Spain[8] and the value contribution scores assigned by the multistakeholder panel. Global value contribution is expressed in a standardised scale from -1 to +1 (highest value).

Table 1: Adapted MCDA Orphan Drug Framework for the study

DISEASE-RELATED CRITERIA (Quantitative criteria)
Disease severity
Unmet needs
TREATMENT-RELATED CRITERIA (Quantitative criteria)
Efficacy/effectiveness
Safety/tolerability
Patient-reported outcomes (PROs)
Therapeutic impact
Other medical costs
Non-medical/indirect costs
Quality of evidence and Grade of recommendation
CONTEXTUAL CRITERIA
Mandate and scope of healthcare system
Population priorities and access
Common goals and specific interests
System capacity and appropriate use of the intervention

RESULTS

- Scoring results are shown in ***figure 1.*** Hemophilia B is considered a severe disease (mean±SD: 4.3±0,7) that decreases both life expectancy and quality of life, is associated with high morbidity and is perceived to have relevant unmet needs (3,3±0,9) due to the lack of available curative treatments and current limitations in patients' quality of life.
- ED was considered to be more effective than EHL (2.3±1.3), as the percentage of patients who do not return to prophylaxis and have zero bleeding is higher . However, there were uncertainties regarding safety/tolerability (-1.2±1.8) due to potential hepatotoxicity uncertainty relative to the long-term safety of gene therapies.
- Patient reported outcomes were perceived to be better compared to EHL (mean ± SD: 1.8 ± 1.5) due to the single dose administration and the lower bleeding rate.
- ED could result in long-term savings within the health system, in terms of "other medical costs" and "non-medical/indirect costs" criteria (1.6±2.0 and 2.0±1.5, respectively) due to potential reduction of hospitalizations and prophylaxis treatment.
- ED was perceived to provide a high therapeutic impact in relation to the course of the disease (3.9±0.9) supported by high-quality evidence (4.0±1.3).
- The **global value contribution** was 0.45, being consistent with other MCDA studies of innovative orphan drugs

Figure 1: Scoring results of the quantitative criteria of ED vs EHL

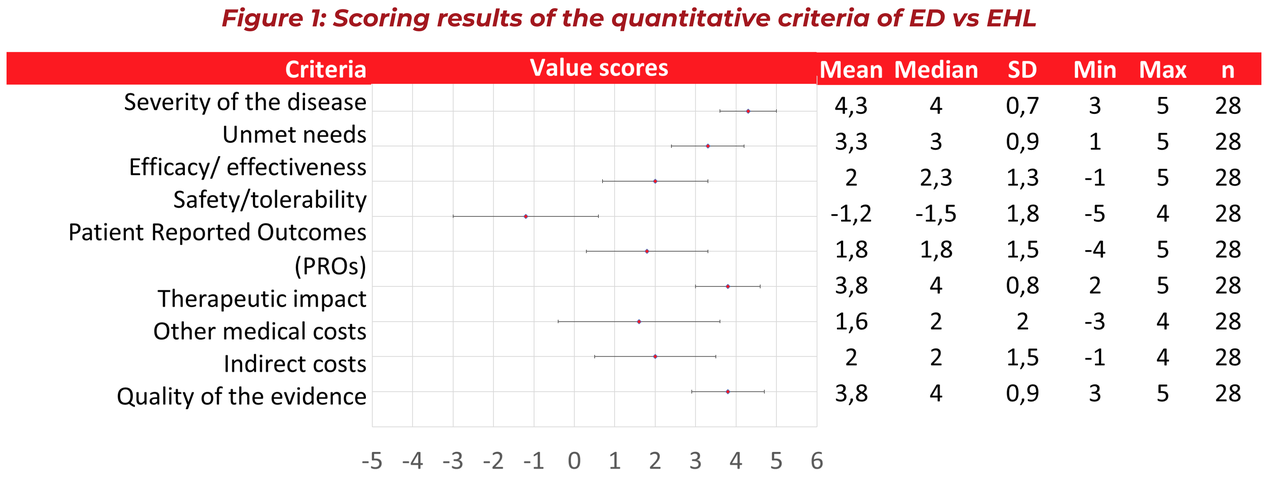


Figure 2: Value contribution of ED vs EHL

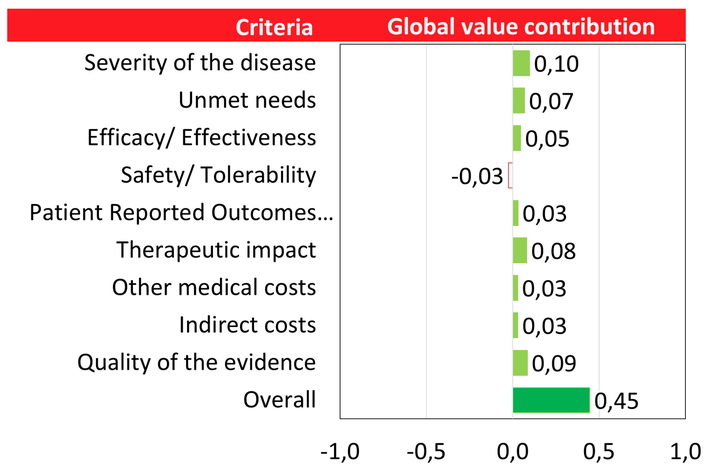
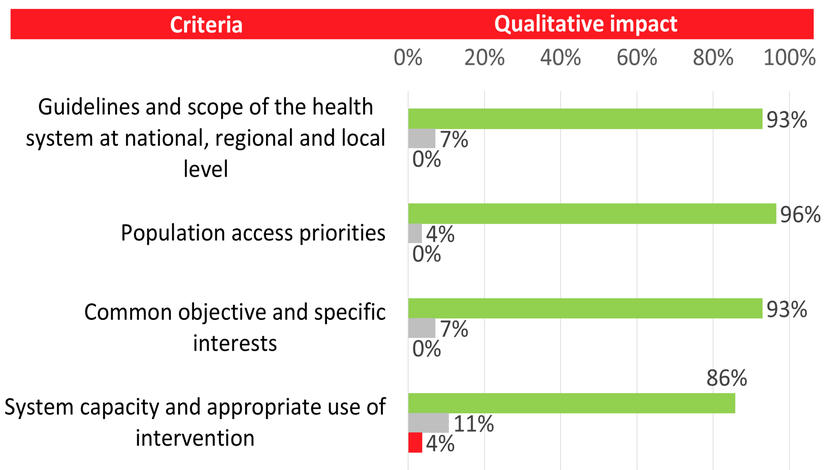


Figure 3: Scoring results of the qualitative criteria



- Experts perceived that the **incorporation of ED** for the treatment of sHB would have a positive impact on all qualitative criteria (***figure 3***) as it is aligned with the priorities of the NHS and the rare diseases strategy. Experts perceived a positive impact on the specific interests of patients, mainly because of its single dose, which allows patients to discontinue prophylaxis, as well as being effective in controlling bleeding. Experts considered that the health system is ready to implement and ensure the proper use of ED although some experts perceived potential financial barriers which are associated with the potential pricing of the treatment. ED adoption is expected to generate savings for the NHS compared to the expenses linked with chronically administered long half-life clotting factors.

CONCLUSIONS

- **Etranacogene dezaparvovec (ED)** has shown a higher value contribution compared to current extended half-life factor IX alternatives in the treatment of severe and moderately severe Hemophilia B. ED was considered as more effective than EHL and with a positive therapeutic impact in relation to the course of sHB, although there is perceived uncertainty on its long-term safety.
- **MCDA methodology** has proven to be a valuable tool in highlighting the holistic value contribution of a new gene therapy.

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