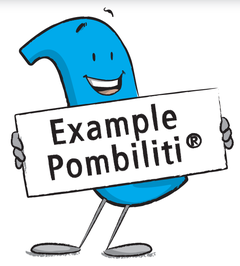
ACCESSUS HEALTH
Your Gateway to Europe
A brand of ECKER ECKER

HTA238

Ecker T., Barz V., Leismann J.



Poster Download

Addressing all PICOs in the JCA dossier – Is it feasible?

Objectives

The PICO framework (Population, Intervention, Comparator, Outcome) provides a standard format for addressing specific research questions and will be used to specify the overall assessment scope for the Joint Clinical Assessment (JCA), reflecting all EU Member States needs. In our PICO exercise, consolidating national PICOs from 16 EU Member States for cipaglucosidase alfa (Pombiliti®) for the treatment of late-onset Pompe disease (LOPD) via an internal scoping process[1] resulted in a total of 13 PICOs, comprising 4 different patient populations and several different comparators. According to Annex I of the first Implementing Act, all identified PICOs should be addressed in the EU HTA dossier and if no results are submitted, the reasons for their omission have to be explained. Therefore, this analysis aims to investigate whether it is feasible to address all identified PICOs in the EU HTA dossier for JCA with the currently available evidence.

Methods

We conducted a systematic literature research to identify relevant randomized controlled trials (RCT) that allow a direct or indirect treatment comparison for cipaglucosidase alfa in LOPD for all consolidated PICOs. For this purpose, the databases MEDLINE and Cochrane as well as the clinical trial registries clinicaltrials.gov, EU-CTR, ICTRP and CTIS were searched for RCTs with adult LOPD-patients (ERT-naïve and ERT-experienced) with alglucosidase alfa, avalglucosidase alfa or Best Supportive Care (e. g. placebo) as comparators.

Results

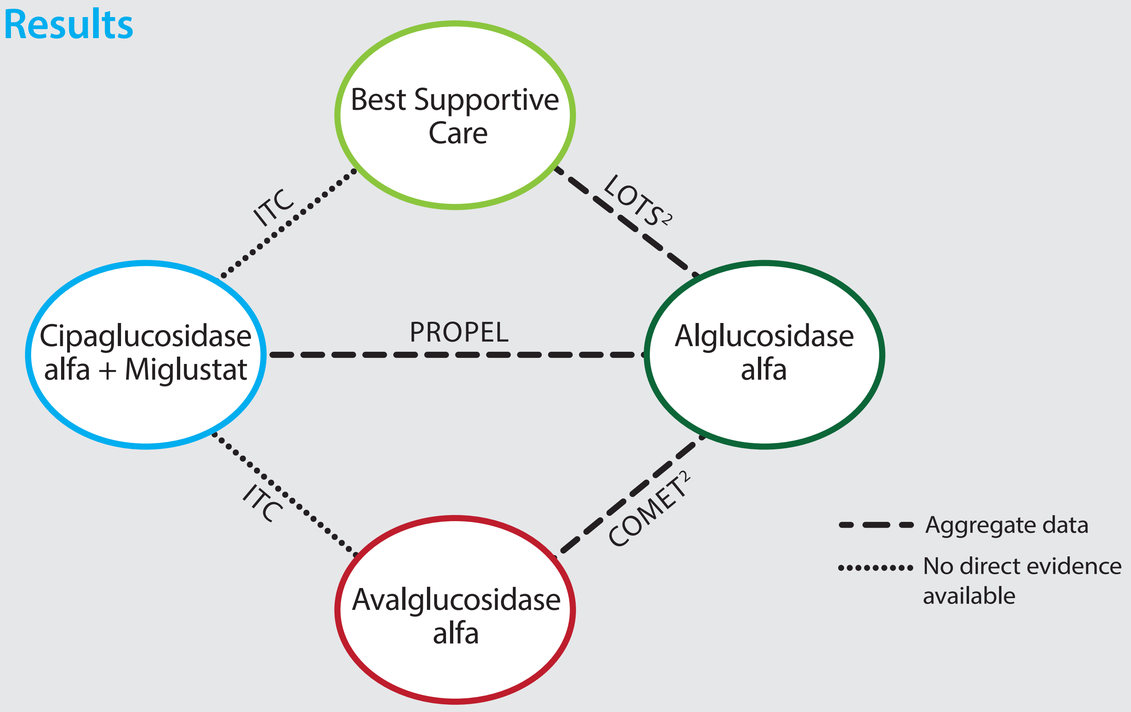


Fig. 1) Network of RCTs allowing a direct or indirect treatment comparison of cipaglucosidase alfa

In the systematic literature research, we identified 3 different RCTs that allow a direct or indirect treatment comparison (ITC) for cipaglucosidase alfa:

- In the pivotal PROPEL study adult patients with LOPD were treated with either cipaglucosidase alfa in combination with miglustat or with alglucosidase alfa and thereby allowing a **direct treatment comparison**.
- However, clinical trials for a direct treatment comparison of cipaglucosidase alfa + miglustat with avalglucosidase alfa or with Best Supportive Care (e.g. placebo as a comparator) were **not identified**.
- Instead, the clinical trials COMET (avalglucosidase alfa vs. alglucosidase alfa) and LOTS (alglucosidase alfa vs. Best Supportive Care) could be used for an **ITC with alglucosidase alfa** as the common comparator.

A **network meta-analysis** combining direct and indirect evidence as shown in figure 1, could therefore be used to gather evidence and analyze the clinical trial outcomes for the EU HTA dossier.

Based on the clinical trials identified, we assessed whether evidence from the possible network meta-analysis of the 3 RCTs (PROPEL, LOTS, COMET) would be sufficient to cover all 13 PICOs. However, as shown below, direct or indirect evidence is only available for 8 out of 13 PICOs. Therefore, 5 PICOs cannot be addressed in the EU HTA dossier with adequate evidence. Overall, if the distinction is made between ERT-naïve and ERT-experienced patients, the number of potential PICOs doubles without the corresponding additional studies being feasible due to the small number of patients with this rare chronic disease.

	Internal Scoping Process[1] (16 Member States – 13 PICOs)	Evidence
Adult patients with LOPD	1. Alglucosidase alfa	✓
	2. Avalglucosidase alfa	✗
	3. Best Supportive Care	✗
Adult patients with LOPD ERT-naive	4. Alglucosidase alfa	✓
	5. Avalglucosidase alfa	✓
	6. Best Supportive Care	✓
Adult patients with LOPD ERT-experienced	7. Alglucosidase alfa	✓
	8. Avalglucosidase alfa	✗
	9. Best Supportive Care	✗
	10. Individualized treatment taking into account previous therapies, selection of – Alglucosidase alfa – Avalglucosidase alfa	✗
Adult patients with LOPD 18-65 years old	11. Total population: Alglucosidase alfa[3]	✓
	12. ERT-naïve: Alglucosidase alfa[3]	✓
	13. ERT-experienced: Alglucosidase alfa[3]	✓

✓ direct or indirect evidence available ✗ direct or indirect evidence not available

Conclusion

- Due to a high number of PICOs, comprising of 4 different patient (sub-)populations and several different comparators, and only a limited number of RCTs, **not all PICOs** can be met with adequate data in the EU HTA dossier.
- Because direct treatment comparisons are not always available, **ITCs and/or NMAs** will play a profound role in preparing the statistical analyses for the EU HTA dossier. Nonetheless, in order to perform an ITC/NMA, the studies must be sufficiently comparable (e.g. study duration, patient population, etc.).
- However, in order to anticipate possible gaps and to address all PICOs, a **timely review of the existing evidence** is essential for preparing the EU HTA dossier.

[1] Please also see Ecker T.et.al."Challenges of the PICO Scoping Process: How does the number of involved member states impact results?", poster, HTA324, ISPOR Europe 2024

[2] ERT-naïve patients only

[3] Requires patient level data

References

- Schoser B et al. "Safety and efficacy of cipaglucosidase alfa plus miglustat versus alglucosidase alfa plus placebo in late-onset Pompe disease (PROPEL): an international, randomised, double-blind, parallel-group, phase 3 trial." Lancet Neurol. 2021
- Diaz-Manera J et al. "Safety and efficacy of avalglucosidase alfa versus alglucosidase alfa in patients with late-onset Pompe disease (COMET): a phase 3, randomised, multicentre trial." Lancet Neurol. 2021
- van der Ploeg AT et al. "A randomized study of alglucosidase alfa in late-onset Pompe's disease." N Engl J Med. 2010
- Ecker T. et al. "Challenges of the PICO Scoping Process: How does the number of involved member states impact results?", poster, HTA324, ISPOR Europe 2024

Abbreviations

ERT: Enzyme-replacement therapy, EU HTA: European Health Technology Assessment, ITC: Indirect treatment comparison, JCA: Joint Clinical Assessment, LOPD: Late-onset Pompe disease, NMA: Network Meta-analysis, RCT: Randomized controlled trial

Accessus Health GmbH · Warburgstr. 50 · 20354 Hamburg · Germany
+49 40 4133081-0 · european-network@accessus-health.eu · www.accessus-health.eu

EUCOPE European Confederation of Pharmaceutical Entrepreneurs AISBL

BIO DEUTSCHLAND