HIGHLY SPECIALISED TRIALS: HAS ELIGIBILITY FOR NICE HIGHLY SPECIALISED TECHNOLOGY APPRAISALS BECOME MORE STRICT?

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BACKGROUND/INTRODUCTION

- Since its introduction, the National Institute of Health and Care Excellence's (NICE) Highly Specialised Technology (HST) appraisal pathway has been used to successfully appraise 15 technologies for rare conditions
- Selection for HST requires technologies to meet seven criteria, two of which relate to the size of the population:
  - "The target patient group for the technology in its licensed indication is so small that treatment will usually be concentrated in very few centres in the NHS"
  - "The technology is expected to be used exclusively in the context of a highly specialised service"
- There have been examples of manufacturers of orphan designated drugs advocating for appraisal via HST, but being routed via standard single technology appraisal (STA) processes instead
- As more orphan products demanding high prices are approved, we explore whether application of HST criteria relating to population size have become more stringently applied

OBJECTIVE(S)

- To observe trends in the strictness of application of HST criterion with regards to the acceptable clinical evidence base.

METHODS

- This study compared number of patients included in pivotal clinical trials and assessed in NICE HST (scheduled prior to June 2021) over time
- The number of patients from whom data was considered during the HST was extracted, alongside number of patients in the "pivotal" trial. These figures were analysed as a proportion of the estimated number of UK patients, to observe any trends in the rarity of indications being assessed over time.
- Data for the next 5 HSTs "in development" were also extracted and compared against the first 5 HST appraisals to observe any differences in future versus early appraisals.

RESULTS

- Data from 14 published and 5 "in development" HSTs were extracted (**Table 1**)
- There was no trend over time in average number of patients (in the UK) that were potentially eligible for technologies undergoing HST. All treatments recommended via HST related to conditions estimated to affect ≤400 patients in the UK (**Figure 1**)

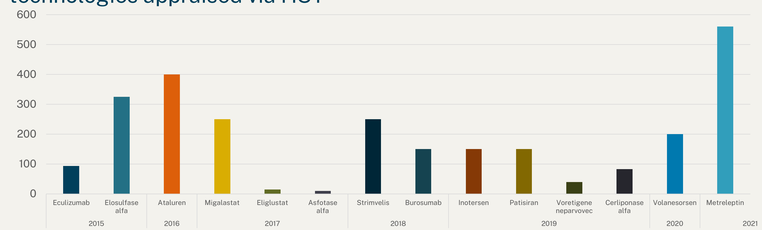
RESULTS

Table 1 Extracted HSTs

Publication date / other	Generic name	Status
28/01/2015	Eculizumab	Complete
16/12/2015	Elosulfase alfa	Complete
20/07/2016	Ataluren	Complete
22/02/2017	Migalastat	Complete
18/06/2017	Eliglustat	Complete
02/08/2017	Asfotase alfa	Complete
07/02/2018	Strimvelis	Complete
10/10/2018	Burosumab	Complete
22/05/2019	Inotersen	Complete
14/08/2019	Patisiran	Complete
09/10/2019	Voretigene neparvovec	Complete
27/11/2019	Cerliponase alfa	Complete
21/10/2020	Volanesorsen	Complete
24/02/2021	Metreleptin	Complete
Final scope: 30/09/20	Givosiran	In development
Draft scope: 19/08/20	Arimoclomol	In development
Draft scope: 24/11/20	Lenti-D	In development
Proposed	Lonafarnib	In development
Draft scope for comments: 08/01/21	Maralixibat	In development

Onasemnogene abeparvovex was not initially included as it was not published but did not appear as "in development". It was later analysed as part of poster development

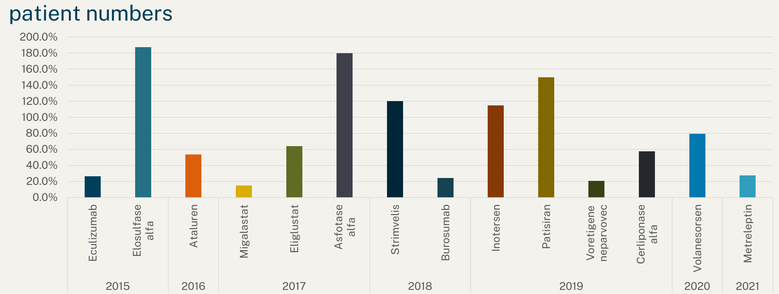
Figure 1 Estimated number of patients in the UK in conditions treated by technologies appraised via HST



Where available, estimated number of patients was extracted from the final scope published by NICE

- When considering the evidence base supporting HST submissions in proportion to estimated number of patients in the UK, results varied from 26% to 187.2%.
  - The recent recommendation of Onasemnogene abeparvovec (Zolgensma) by NICE represents an even lower result (7.1%), although this is likely an underestimate as it does not account for restrictions applied to the recommendation (genetic subtypes and age)
- When using pivotal trial size, proportions ranged from 15% to 187.2% (including Zolgensma drops the lower end to just 2.3% (**Figure 2**)

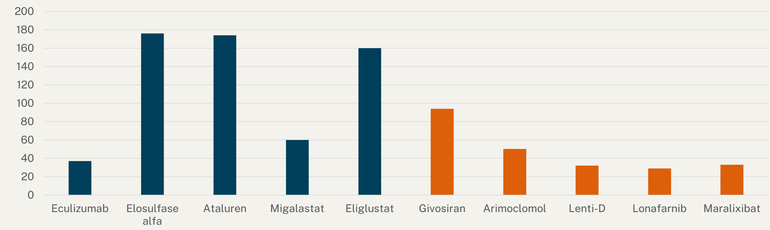
Figure 2 Number of patients in pivotal trial as a proportion of estimated UK patient numbers



Proportions calculated as [total number of patients in pivotal trial(s)/estimated number of patients in the UK]

- Although there was no clear trend in this output, when the first 5 HSTs were compared with 5 proposed HSTs, there was a trend towards a reduced number of patients in the pivotal trial for HSTs proposed (**Figure 3**)

Figure 3 Number of patients in pivotal trial: first 5 HSTs vs 5 proposed HSTs



DISCUSSION

- Since initial data analyses were conducted, some products (e.g., lonafamib and maralixibat) have moved further down the pipeline whilst others have moved up (e.g., odevixibat, setmelanotide and Selumetinib)
- There does not appear to be a change in the application of the population size criterion over time.
- However, some products achieving reimbursement via HST do so using a restricted population, which could impact on the relevance of these results.
- NICE is currently undertaking a methods review, which may change the goalposts for manufacturers hoping to see their products assessed via HST.

CONCLUSIONS

- This analysis suggests that eligibility for HST based on number of patients enrolled in clinical trials as a proxy for target patient group size has been consistently applied for HST, with no obvious trend observed.
- However, when we consider pivotal trial population for the first 5 HST's vs 5 HSTs currently proposed, there is a clear trend towards reduced pivotal trial population.
- This may suggest that as the HST process develops, eligibility via size of addressable population will become more stringent.
- It will be interesting to follow the effect the NICE topic selection proposal has on this trend, particularly with relation to the routing of gene therapies, where a further restriction to a prevalence of 50 patients and incidence of no more than 40/year is proposed .

REFERENCES

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