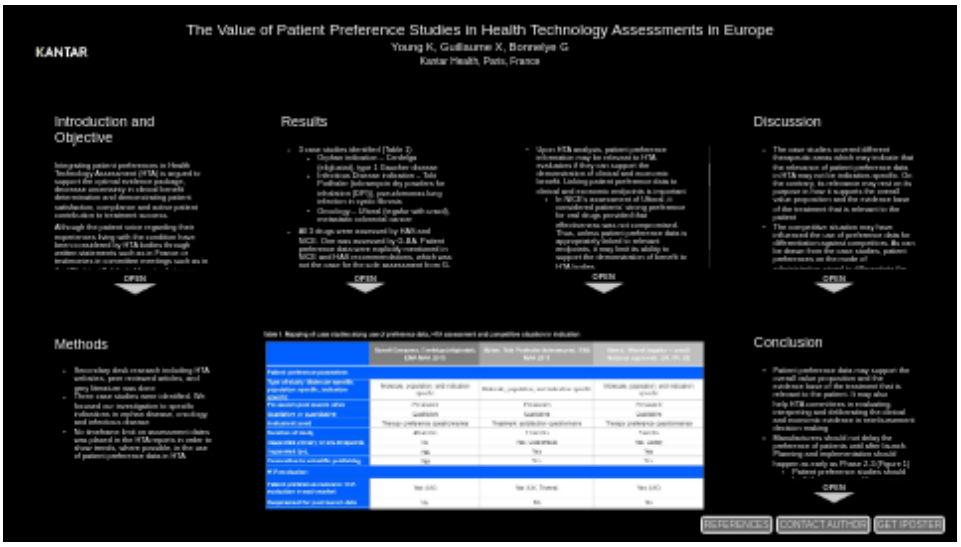
The Value of Patient Preference Studies in Health Technology Assessments in Europe



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INTRODUCTION AND OBJECTIVE

Integrating patient preferences in Health Technology Assessment (HTA) is argued to support the optimal evidence package, decrease uncertainty in clinical benefit determination and demonstrating patient satisfaction, compliance and active patient contribution to treatment success.

Although the patient voice regarding their experiences living with the condition have been considered by HTA bodies through written statements such as in France or testimonies in committee meetings such as in the UK, it is still debated how to derive any potential evidence from preferences that allow optimized evidence demonstration and incorporate these in HTA in a systematic, standardised and quantitative manner. Until further scientific systematisation of such evidence, best practice may be the best guide on the strategic use of patient preference in HTA decision making and evidence uncertainty management. Depending on markets, each setting may face different decision makers and different value drivers in the use of patient preference information.

Due to the lack of guidance on how to optimize evidence demonstration and systematically incorporate quantitative patient preference studies in HTA, the study aimed to investigate patient preference data's relevance in HTA. The development of case studies has been done with the aim of identifying across indications differences in the type and use of patient preference data, how preference data is developed, for which purpose, and how it has been valued in UK, France and Germany.

RESULTS

- 3 case studies identified (Table 1)
  - Orphan indication – Cerdelga (eliglustat), type 1 Gaucher disease
  - Infectious Disease indication – Tobi Podhaler (tobramycin dry powders for inhalation (DPI)), pseudomonas lung infection in cystic fibrosis
  - Oncology – Uftoral (tegafur with uracil), metastatic colorectal cancer
- All 3 drugs were assessed by HAS and NICE. One was assessed by G-BA. Patient preference data were explicitly mentioned in NICE and HAS recommendations, which was not the case for the sole assessment from G-BA
- Patient preference studies were incorporated in phase 3 trials for all 3 cases. Qualitative methods were used by means of treatment preference or treatment satisfaction questionnaires. The attributes assessed included efficacy, side effects, mode of administration, convenience, and overall satisfaction. All patient preference data supported the primary or secondary endpoints, and QoL data. All 3 drugs had relevant competitors at launch (Table 2)

- Upon HTA analysis, patient preference information may be relevant to HTA evaluators if they can support the demonstration of clinical and economic benefit. Linking patient preference data to clinical and economic endpoints is important
  - In NICE's assessment of Uftoral, it considered patients' strong preference for oral drugs provided that effectiveness was not compromised. Thus, unless patient preference data is appropriately linked to relevant endpoints, it may limit its ability to support the demonstration of benefit to HTA bodies
  - HAS' final assessment of Cerdelga states that 'although the provision of an oral form releasing bimonthly infusions of enzyme therapy is likely to have an impact on the organization of care, this impact was not shown.' Again, identifying this missing link designates the inherent value of presenting how patient preference data relates to clinical and economic benefits

- Patient preference data may also be considered alongside health economic evidence. No indication exists that patient preference data may substitute validated QoL questionnaires nor can it replace QALY which uses general population preferences to generate utility scores in cost-utility analysis

  - In NICE's assessment of Tobi Podhaler, the Committee acknowledged that 'the small QALY gain for tobramycin dry powders for inhalation (DPI) was uncertain because QoL data were not collected… it agreed it was reasonable to assume that there would be some QALY gain for tobramycin DPI over nebulised tobramycin in view of the reported benefits in terms of ease of use and convenience although it acknowledged that the number of withdrawals from the EAGER trial did not indicate this relationship.'

- Through providing complementary data that only a patient who suffers the disease knows, patient preference data may help HTA committees in evaluating, interpreting and deliberating the clinical and economic evidence in reimbursement decision making[18-21]

DISCUSSION

- The case studies covered different therapeutic areas which may indicate that the relevance of patient preference data in HTA may not be indication-specific. On the contrary, its relevance may rest on its purpose in how it supports the overall value proposition and the evidence base of the treatment that is relevant to the patient
- The competitive situation may have influenced the use of preference data for differentiation against competitors. As can be drawn from the case studies, patient preferences on the mode of administration aimed to differentiate the offering against multiple treatment options where no clearly superior option for patients exists. This trend has been sustained throughout the earliest and latest assessments
- Patient preference studies were not assessed to replace neither clinical nor economic evidence and thus would not be used to recommend products that are not clinically effective or cost-effective. In contrary, it provided complementary insight on the relevance of the clinical outcomes in the daily life of a patient who suffers from the disease

- In 2020, NICE shared their perspective regarding the use of Patient Preference Studies in HTA Decision Making where they have identified its role to inform reimbursement decisions.[4] The organisation has stated that although the NICE methods guide does not specifically cite patient preference studies, these may be deemed relevant and accepted alongside core evidences when the need is justified. Although they do not see discrete choice experiment (DCE) data being directly incorporated into health economic modelling as this is not in line with the reference case in their Guides to Methods for Technology Appraisals where health-state valuation needs to reflect societal rather than patient values, they see it being submitted alongside it. They have also identified its role in guiding the selection of appropriate endpoints in the early phases of development and, although beyond the scope of this article, to inform benefit-risk assessments carried out by regulatory bodies.

METHODS

- Secondary desk research including HTA websites, peer reviewed articles, and grey literature was done
- Three case studies were identified. We focused our investigation to specific indications in orphan disease, oncology, and infectious disease
- No timeframe limit on assessment dates was placed in the HTA reports in order to show trends, where possible, in the use of patient preference data in HTA

CONCLUSION

- Patient preference data may support the overall value proposition and the evidence base of the treatment that is relevant to the patient. It may also help HTA committees in evaluating, interpreting and deliberating the clinical and economic evidence in reimbursement decision making
- Manufacturers should not delay the preference of patients until after launch. Planning and implementation should happen as early as Phase 2-3 (Figure 1)
  - Patient preference studies should be fit for purpose and by no means required for all drugs in development. Planning entails questions like: What is the aim of the patient preference study? Can it address a gap or uncertainty which may support the determination of the drug's value by HTA bodies? Is information unavailable from other sources and only can be achieved by patient insights?
- Manufacturers should identify and use appropriate and robust methodologies for measuring patient preference data and linking them to validated clinical and economic outcomes. Validation with key stakeholders should always be sought
  - Multiple qualitative and quantitative methods are available in the exploration and elicitation of patient preference. It is not confined to qualitative research exemplified in the sampled case studies. Both types of preference researches must be held to scientific standards and robust in their methods as qualitative research has been shown to be a necessary step to achieving more rigorous quantitative evidence.[1]As the method must be appropriated to the research question, it must also be acceptable to HTA evaluators. Alignment with HTA bodies' requirements and expectations are imperative. The HTA bodies must be familiar and have confidence on the methods used for preference elicitation. Should requirements remain unclear, early scientific advice and payer insights are tools that can be used to achieve alignment which benefits all stakeholders
- Once the results are available, a critical analysis of the data should include understanding how the results relate to the overall value proposition of the offering
  - The significance of the results and any heterogeneity in patient preferences should be contextualised in terms of how this supports the positioning of the treatment in the patient pathway, and ultimately how it provides insight on the overall value of the drug. Thereafter, value should be communicated effectively to HTA bodies at submission thus supporting committees in evaluating and interpreting the clinical and economic evidence in reimbursement decision making and allowing them to make decisions that are oriented to a greater patient focus

REFERENCES

1. Hollin IL, Craig BM et al. Reporting Formative Qualitative Research to Support the Development of Quantitative Preference Study Protocols and Corresponding Survey Instruments: Guidelines for Authors and Reviewers. Patient. 2020 Feb;13(1):121-136. doi: 10.1007/s40271-019-00401-x. https://www.ncbi.nlm.nih.gov/pubmed/31840215

2. Soekhai, V. et al. Methods for exploring and eliciting patient preferences in the medical product lifecycle: a literature review. Drug Discov. Today 24, 1324-1331

3. Sarri G, Kenny J, Freitag A, Mountian I, Szegvari B, Maniadakis N, et al. How frequently is patient experience formally assessed in health technology assessments? Results from a systematic literature review. In: Value in Health. Barcelona (2018). p. PHP315. Available online at: https://tools.ispor.org/ScientificPresentationsDatabase/Presentation/84225?pdfid=57776 accessed December 10, 2018

4. Bouvy JC, Cowie L, et al. Use of Patient Preference Studies in HTA Decision Making: A NICE Perspective. Patient. 2020 Apr;13(2):145-149. doi: 10.1007/s40271-019-00408-4. https://www.ncbi.nlm.nih.gov/pubmed/31942698

5. EMA. Cerdelga EPAR. 2014. https://www.ema.europa.eu/en/documents/assessment-report/Cerdelga-epar-public-assessment-report_en.pdf

6. NICE. Eliglustat for treating type 1 Gaucher disease. 2017. https://www.nice.org.uk/guidance/hst5

7. G-BA. Benefit Assessment for Eliglustat. 2015 https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/166/#nutzenbewertung

8. HAS. Cerdelga assessment. 2015. https://www.has-sante.fr/jcms/c_2572136/fr/Cerdelga-eliglustat-medicament-du-metabolisme

9. EMA. Tobramycin nebuliser solution: list of nationally authorised medicinal products. 2015. https://www.ema.europa.eu/en/documents/psusa/tobramycin-nebuliser-solution-list-nationally-authorised-medicinal-products-psusa/00009316/201412_en.pdf

10. EMA. Tobi Podhaler EPAR. 2011. https://www.ema.europa.eu/en/documents/assessment-report/tobi-podhaler-epar-public-assessment-report_en.pdf

11. NICE. Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis. 2013 https://www.nice.org.uk/guidance/ta276/chapter/4-Evidence-and-interpretation

12. HAS. Tobi Podhaler Assessment. 2011 https://www.has-sante.fr/jcms/c_1172458/fr/tobi-podhaler

13. NICE. Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer. 2003. https://www.nice.org.uk/guidance/ta61/chapter/4-Evidence-and-interpretation

14. Douillard JY et al. Multicenter phase III study of uracil/tegafur and oral leucovorin versus fluorouracil and leucovorin in patients with previously untreated metastatic colorectal cancer. J Clin Oncol. 2002 Sep 1;20(17):3605-16. https://www.ncbi.nlm.nih.gov/pubmed/12202661

15. Carmichael J et al. Randomized comparative study of tegafur/uracil and oral leucovorin versus parenteral fluorouracil and leucovorin in patients with previously untreated metastatic colorectal cancer. J Clin Oncol. 2002 Sep 1;20(17):3617-27. https://www.ncbi.nlm.nih.gov/pubmed/12202662

16. Borner M et al. Patient preference and pharmacokinetics of oral modulated UFT versus intravenous fluorouracil and leucovorin: a randomised crossover trial in advanced colorectal cancer. European Journal of Cancer. Volume 38, Issue 3, 2002, Pages 349-358. https://www.sciencedirect.com/science/article/pii/S0959804901003719

17. HAS. Uft Assessment. 2006. https://www.has-sante.fr/jcms/pprd_2985027/fr/uft

18. Facey K, Bedlington N et al. Putting Patients at the Centre of Healthcare: Progress and Challenges for Health Technology Assessments. The Patient - Patient-Centered Outcomes Research. December 2018, Volume 11, Issue 6, pp 581–589

19. Berglas S, Jutai L et al. Patients' perspectives can be integrated in health technology assessments: an exploratory analysis of CADTH Common Drug Review. 2016. Research Involvement and Engagement 2:21

20. Staley K, Doherty C. It's not evidence, it's insight: bringing patients' perspectives into health technology appraisal at NICE. Research Involvement and Engagement 2: 4 (2016)

21. Rozmovitz, L, Mai, H, Chambers, A, et al. What does meaningful look like? A qualitative study of patient engagement at the pan-Canadian. 2018. Oncology Drug Review: Perspectives of reviewers and payers. J Health Serv Res Policy 23, 72–79

22. NICE. NICE provides first scientific advice on patient preference study design. https://www.nice.org.uk/news/article/nice-provides-first-scientific-advice-on-patient-preference-study-design. Accessed April 4 2020

23. EMA. Tobramycin nebuliser solution: list of nationally authorised medicinal products. 2015. https://www.ema.europa.eu/en/documents/psusa/tobramycin-nebuliser-solution-list-nationally-authorised-medicinal-products-psusa/00009316/201412_en.pdf

24. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden. Version 5.0. 2017.