Patient Voice and Patient Engagement in Value Assessment Frameworks and HTA Decision-Making for Gene Therapies

Dabbous M[1] MSc, PhD, Raza J[1] PharmD MBA, Connelly B[1] PharmD, Olid Gonzalez A[1] MA, Khemakhem A[2], Sullivan N[1]

[1]Value and Access Consulting, Evidera. MA, Waltham, USA; [2]Value and Access Consulting, Evidera. Paris, France

PCR90

Background

Patient engagement is essential for value assessments

- There is an increasing understanding by industry and health authorities that the patient voice is critical for a comprehensive value assessment.
- In July 2023, ICER established a Patient Council to amplify the patient voice (PV) in value assessments, demonstrating their commitment to soliciting insights from patient groups to inform their assessments.
- The European Patients Academy on Therapeutic Innovation (EUPATI), a multi-stakeholder program training patient advocates launched their 'HTA4Patients' initiative in 2023 educating patient organizations to play a vital role in the HTA process, emphasizing the overall need for PV in market access.
- PV has also had an increasingly important role in Integrated Scientific Advice engagements, with patient lay summaries and PV-specific sections included in briefing document templates.
- PV is specifically important for gene therapies (GTs) as these products are associated with unique, long-term uncertainties. PV can provide valuable insight on unmet needs and a GT's ability to address them.
- We evaluated the utility of PV within HTA appraisals of GTs across seven markets over a 5-year span.

Objectives

- To understand the utility of PV within GT HTA appraisals, our objectives were to:
  - To identify value frameworks that include patient voice.
  - To determine what type of patient engagement has been used for GTs in HTA-decision-making.
  - To assess how patient engagement data for GTs has been received by major HTA bodies.
  - To determine what influence, if any, the PV has had on HTA decisions.

Methods

- In order to assess inclusion of PV, we defined PV as "patient perspective on how the condition impacts the patient's life and the benefits from a therapy, which can be further classified in two broad categories as either patient experience or patient engagement."
- Patient experience is predominantly captured in the form of patient-reported outcomes (PROs) and quality of life (QoL), while patient engagement is considered as any direct input from patients including patient surveys, testimonies, patient expert input, or patient organization feedback.
- We reviewed HTA reports across 7 markets including United States (US), Canada, England, France, Germany, Italy and Spain. This included the ICER patient value frameworks to determine the impact of the PV on GT access.
- We identified HTAs for GTs that had market authorization from 2019-2023 in the countries of interest. A search was conducted in these HTA bodies' websites to identify HTA appraisals: NICE[1], HAS[2], G-BA[3], AIFA[4], AEMPS[5], ICER[6], and CADTH[7].
- Where available, each report was reviewed to assess the inclusion of PV by the Health Technology developer into the submission and the commentary from the HTA body in the report. The context of the PV included and the types of PV and/or patient engagement data reported were also extracted.

Results

Inclusion of PV in HTA decision-making

Overall Findings

- Findings indicate that the mention of PV in HTAs for GTs was prevalent in Germany, England, France, Canada, and the US. However, there was minimal mention of PV across Spain and Italy to support market access (**Table 1**).
  - In the majority of cases we identified, the PV was captured via use of PROs in clinical studies. However, in some cases, the reports reference the PV data during appraisal to explain unmet needs and disease burden. The type of PV utilized varied by country. NICE[1], CADTH[7], and ICER[6] involved patients directly during the appraisal process in the form of input from patient experts and patient organizations.
- When assessing the types of PV involved in the submissions, it was found that there were 4 main types of PVs across the countries (1) Health-related quality of life (HRQoL) data including PROs; (2) direct patient expert/organization involvement in the HTA procedure, (3) patient testimonials of disease and therapy experiences, and (4) quantitative survey data (**Table 2**).
  - While HRQoL data was submitted in each HTA body's GT submission, direct engagements, testimonials, and surveys were included only in NICE[1], CADTH[7], and ICER[6] submissions.

Germany

- In Germany, direct patient engagement is not part of the HTA appraisal process. In Germany, where 13 of the 22 GTs were approved, 11 out of these 13 had PV mentioned in their G-BA[3] benefit-risk reports.
- All 11 of these therapies mentioned PV with reference patient experience as QoL collected via PROs. However, some mentions of PV by the G-BA[3] stated that *"no outcomes in the category 'quality of life' were collected"* as was the case for Libmeldy® or that *"there were no valid outcomes relevant to the benefit assessment in the category"* for Luxturna®; Therefore, without PROs, there was nothing valid for G-BA to look at during their procedure.

Italy

- In Italy, 9 GTs were available and approved. Four of these therapies did not have HTA reports publicly available. For the 5 therapies with publicly available assessments, only 4 GTs had PV mentioned in their appraisals. PV was only mentioned in relation to QoL referring to pharmacoeconomics. However, the patient experience included did not drive the outcomes for recommendations, therefore, it is unclear to what extent the PV influences decision-making in Italy.

England

- In England, 10 GTs were approved, out of which 9 had HTA reports published by NICE[1]. Of these 9 appraisals, 6 included PV. Patient organizations submitted their patient engagement data based off survey results, testimonials, and interviews. In the reports, NICE[1] briefly mention patient expert opinions on disease burden, unmet need, and available therapies.

France

- In France, 12 GTs were available and approved. Of these 12 appraisals, 8 included the PV. PV was only mentioned in relation patient experience via QoL using generic and/or specific questionnaires. Less than half of the appraisal including PV (3 out of 8) were considered to have a source of bias in the assessment of QoL.

Spain

- In Spain, 10 GTs were approved at the time of our analysis. Of these 10 appraisals, 6 included the PV. PV was only mentioned in relation to QoL collected using generic and/or specific questionnaires. In 2 out of those 6 appraisals, the low completion rate of the QoL questionnaires did not allow reliable conclusions.

Table 1. PV in HTA Decision-Making and PV Role

Gene Therapy*	PV in HTA Decision-Making for GTs						
	NICE *England*	HAS *France*	G-BA *Germany*	AIFA *Italy*	AEMPS *Spain*	ICER *US*	CADTH *Canada*
Hemgenix® (2022)	○	●	●	○	●	●	●
Adstiladrin® (2022)	○	○	○	○	○	●	○
Roctavian® (2022)	○	●	●	○	●	●	○
Carvykti® (2022)	○	●	●	○	●	○	●
Skysona® (2022)	○	●	●	●	●	○	○
Abecma® (2021)	○	●	●	○	●	●	●
Breyanzi® (2021)	○	●	●	○	○	○	●
Delytact® (2021)	○	○	○	○	○	○	○
Libmeldy® (2020)	●	●	●	●	●	●	○
Tecartus® (2020)	●	●	●	●	○	○	●
Zynteglo® (2022)	●	●	●	●	○	●	○

● PV mentioned in HTA report ● PV not mentioned in HTA report ● GT assessed; no official report available
○ GT not assessed by HTA body ○ GT not approved by regulator ● GT MA withdrawn

Abbreviations: AEMPS = Spanish Agency of Medicines and Medical Devices; AIFA = Italian Medicines Agency; CADTH = Canadian Agency for Drugs and Technologies in Health; G-BA = Federal Joint Committee; GT = gene therapy; HAS = Haute Autorité de santé; HTA = health technology assessment; ICER = Institute for Clinical and Economic Review; MA = market authorization; NICE = National Institute for Health and Care Excellence

Table 1. PV in HTA Decision-Making and PV Role (Cotd.)

Gene Therapy*	PV in HTA Decision-Making for GTs						
	NICE *England*	HAS *France*	G-BA *Germany*	AIFA *Italy*	AEMPS *Spain*	ICER *US*	CADTH *Canada*
Zolgensma® (2019)	●	●	●	●	●	●	●
Collategene® (2019)	○	○	○	○	○	○	○
Luxturna® (2017)	●	●	●	●	●	●	●
Yescarta® (2017)	●	●	●	●	●	●	●
Kymriah® (2017)	●	●	●	●	●	●	●
Strimvelis® (2016)	●	○	●	●	○	○	○
Imlygic® (2015)	●	○	●	○	●	○	○
Casgevy® (2024)	●	●	●	○	○	●	●
Elevidys® (2023)	○	○	○	○	○	○	○
Lyfgenia® (2023)	○	○	○	○	○	●	○
VyJuvek® (2023)	○	○	○	○	○	○	○

● PV mentioned in HTA report ● PV not mentioned in HTA report ● GT assessed; no official report available
○ GT not assessed by HTA body ○ GT not approved by regulator ● GT MA withdrawn

Abbreviations: AEMPS = Spanish Agency of Medicines and Medical Devices; AIFA = Italian Medicines Agency; CADTH = Canadian Agency for Drugs and Technologies in Health; G-BA = Federal Joint Committee; GT = gene therapy; HAS = Haute Autorité de santé; HTA = health technology assessment; ICER = Institute for Clinical and Economic Review; MA = market authorization; NICE = National Institute for Health and Care Excellence

United States

- In the US, 19 of 22 GTs evaluated were approved by the FDA10. In the US there is no formal HTA body. For the purpose of HTA related insights, ICER6 Final Evidence Reports were used to identify the use of PV within the US. Across ICER6 evaluations, there was a significant amount of PV mentioned, predominantly patient engagement in the form of patient focus groups, patient or disease foundation input, and patient experience was mentioned in the form of PROs. A total of 12 evaluations related to these products were identified with 75% including both patient engagement and patient experience, 8% including only patient experience, and 17% including no patient input.

Canada

- In Canada, 9 GTs were approved, out of which 8 had HTA reports published by CADTH7 and 1 currently under review. All 8 appraisals included the PV. Patient groups submitted their patient engagement data mainly based off survey results. CADTH7 highly values patient input, highlighted by the inclusion of a 'Summary of Patient Input' section in their appraisals. They rely on patient input for describing disease burden, unmet need, current treatments, and outcomes of interest.

Table 2. PV Types submitted to each HTA body

NICE	HAS	G-BA	AIFA	AEMPS	ICER	CADTH
●	●	●	●	●	●	●
●					●	●
●					●	●
●						

● HRQoL (PROs) ● Testimonial ● Survey ● Direct patient engagement

Abbreviations: AEMPS = Spanish Agency of Medicines and Medical Devices; AIFA = Italian Medicines Agency; CADTH = Canadian Agency for Drugs and Technologies in Health; G-BA = Federal Joint Committee; HAS = Haute Autorité de santé; HRQoL = health-related quality of life; HTA = health technology assessment; ICER = Institute for Clinical and Economic Review; NICE = National Institute for Health and Care Excellence

Discussion

Patient Voice trends across the countries of scope

- Overall, all countries mentioned PV in some capacity in HTA appraisals of GTs.
- However, the type of PV and the extent to which it may have influenced final HTA outcomes varies greatly.
- For the majority of countries, PV was mentioned as patient experience, specifically via PROs. In the case of the HAS[2], G-BA, AIFA[4], and AEMPS[5], PV was only mentioned in HTA appraisals captured via PROs. In France, Germany, Italy, and Spain, PV may be considered important, but patient engagement is largely ignored.
- Patient engagement, at least directly, is currently not included in the value frameworks in France, Germany, Italy, and Spain.
- In the case of NICE[1], ICER[6], and CADTH[7], PV has been mentioned captured via patient experience data and patient engagement data, including direct patient engagement, testimonials, and surveys. In the UK, US, and Canada, value frameworks specifically include and incorporate direct patient engagement which can lead to a more comprehensive assessment framework allowing for patient to influence HTA appraisal outcomes.
- With the establishment of the Patient Council, it is clear that PV is important to ICER[6] in the US. However, as ICER is an independent HTA body, it is unclear how important PV will actually be to other US payers and proxies acting as HTA bodies.
- As two of the objectives of the ICER[6] Patient Council are to "evaluate [the] current process of patient engagement to identify gaps and opportunities for improved communication and participation and [to] ensure that the HTA process is inclusive of a diversity of experiences," ICER[6] may influence an increase in the adoption of PV in value frameworks in the US.
- However, how influential ICER[6] will be in propelling forward PV inclusion inHTA appraisals across the US is yet to be determined as the independent HTA body increasingly gains popularity in the US.
- Across Europe, the new EU HTA regulation provides an opportunity to strengthen the involvement of patient communities in HTA processes. The HTA4Patients project aims to empower patients and patient organizations to vital role in the implementation of new patient frameworks. EUCAPA trainings equip patients and patient representatives with the skills, tools, insights, and expertise they need to engage in joint clinical assessments and scientific consultations within the EU HTA regulation.
- As GTs are increasingly approved with uncertainties concerning to both HTA bodies and payers, PV can provide critical insight in the value of these therapies via direct patient engagement and patient experience.
- GT developers should consider comprehensive PV strategies to ensure PV is captured not only in the clinical trial via PROs but via multiple routes to ensure various HTA needs are met and that PV is amplified, with patients being able to play an increasingly important role in their own health decision-making.
- GT developers have an opportunity to shape how these therapies are valuated by major health authorities by pushing PV forward and proposing new policies to influence the evolution of value frameworks to adopt and include PV.

Conclusions

- The patient voice is increasingly important to support market access decisions. Yet, there remains room for improvement and harmonization as various frameworks in place can lead to heterogeneous HTA outcomes. Understanding the full potential of the PV will be critical for US developers heading to the EU, where the new EU HTA Joint Clinical Assessment has yet to detail guidance on how patients will be engaged in assessments.

References

1. https://www.nice.org.uk/
2. https://www.has-sante.fr/
3. https://www.g-ba.de/
4. https://www.aifa.gov.it/
5. https://www.aemps.gob.es/
6. https://icer.org/
7. https://www.cadth.ca/
8. https://icer.org/who-we-are/people/icer-patient-council/
9. https://www.ema.europa.eu/en/homepage
10. https://www.fda.gov/
11. https://www.canada.ca/en/health-canada.html

Presented at ISPOR—The Professional Society for Health Economics and Outcomes Research ● 5–8 May 2024 ● Atlanta, GA, USA

Funding provided by Evidera Inc., a business unit of PPD, part of Thermo Fisher Scientific