Patient Experience Information (PEI) and Patient Involvement in Health Technology Assessment (HTA) Processes in 7 European Countries Using Immuno-Oncology Examples:

How Can the Patient Voice Make an Impact?

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Background

Patients can provide unique insights into a disease and treatment (Figure 1). In order to advance the inclusion of the patient perspective in medicine development the European Patients' Academy of Therapeutic Innovation (EUPATI) was formed in 2012 and released guidance for activities to support patient involvement with HTA bodies in 2018.[1] This guidance seeks to improve inclusion of the patient perspective in HTA by:

- Involving patients in the identification and prioritization of health technologies for assessment
- Inviting patient organizations to comment on draft scoping documents
- Including the patient perspective as part of the HTA evaluation
- Describing how the patient perspective was included in the assessment and impacted the decision in final published assessments

Recent HTA appraisals in immuno-oncology (IO) and rare cancers provide an opportunity to gauge the inclusion of the patient perspective in HTA decisions and identify areas of improvement to best meet the guidance outlined by EUPATI.

Figure 1 | Patients provide unique insights

Objective

To describe how the new EUPATI guidance on patient involvement is being implemented practically at the country level and how the patient voice affects HTA recommendations using recent IO and rare cancer examples.

Methods

- Targeted literature review of recently published HTA guidance by IQWiG, HAS, TLV, ZIN, and NICE on IO treatments across different cancer types to describe current implementation of PEI/patient involvement in HTA
- In-depth, qualitative interviews with seasoned HTA advisors in 7 European countries to identify gaps and potential impact of PEI/patient involvement in future HTA decisions (Table 1)

Table 1 | HTA advisor profiles and details about HTA processes in countries examined

Country	HTA Advisor Profile	HTA Archetype	Formal Patient Involvement in HTA	Patient Voting Rights for HTA Decisions
FRANCE	Health economics professor and HAS advisor	Comparative effectiveness	Yes	Yes (Potentially 3 of 21 voting seats at TC)
GERMANY	Health economics professor and member of the arbitration board for drug pricing	Comparative effectiveness	Yes	No
ITALY	Health economics professor and advisor to regional and national health authorities	Budget impact	No (Currently AIFA has to make formal request; expected to change in 3-5 years)	No
NETHERLANDS	Health economics professor and ZIN advisor	Cost effectiveness	Yes	No
SPAIN	Health economics professor and advisor to regional and national health authorities	Budget impact	Yes	No
SWEDEN	Professor and TLV advisor	Cost effectiveness	Yes	Yes (One board member for pricing and reimbursement)
UNITED KINGDOM	Health economics professor, advisor to NICE and SMC	Cost effectiveness	Yes	No

Ways Patients can be Included in HTA processes

Patient involvement

is defined as patients, patient organizations or caregivers engaging with HTA bodies in the evaluation of a new medicine. This could include:

- Participating as part of an HTA review panel
- Fulfilling requests for information from an HTA review committee.

Patient experience information (PEI)

is defined as evidence about the patient experience regarding their experience with the disease or treatment of interest provided. This could include:

- patient-reported outcomes (PRO)
- patient journaling
- patient preferences
- patient interviews
- patient activity tracking

Results: Targeted Literature Review

Patient organizations are made aware of medicine appraisals by two basic mechanisms across all countries examined:

- Public announcement, including social media
- HTA agencies have running lists of accredited organizations that are notified when appraisals in their purview are underway.

At the country level, there is room for more participation from patient associations, however, a likely lack of resources has limited follow-through in HTA participation.

- For example, 19 patient/care groups were invited for comment for the NICE appraisal of atezolizumab for breast cancer, but only two submitted written responses to the NICE appraisal committee.[2,3]
- A recent study by HAS in France found that patient association input was included in only 20% of medicines reviewed (2017-2018).[4]

Among the published HTA documents reviewed (pembrolizumab, nivolumab, cemiplimab, avelumab, atezolizumab, durvalumab), there was a general lack of specificity about how the patient perspective was included in the assessment and the impact on the final decision.

- Published HTA appraisal documents from Germany provided the most detail about how the patient perspective was included in the assessment, with pembrolizumab, nivolumab, and atezolizumab awarded "hints of added benefit" (Hinweis auf Zusatznutzen) for providing evidence regarding health status or health-related quality of life.

In "cost-effectiveness countries" (Netherlands, Sweden, UK), PROs are frequently used as part of cost/ quality-adjusted life years (QALYs) analyses. This analysis only captures a small fraction of the actual patient experience via a generic PRO tool that is often not sensitive to specific diseases. Little additional details are provided in the published HTA about the patient experience and to what extent it is captured in the cost-effectiveness analysis.

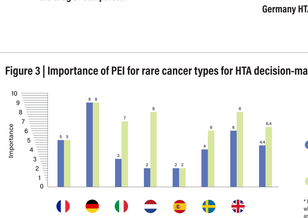
Results: HTA Advisor Interviews

Relative importance of PEI for HTA decisions

PEI has a varied impact across European countries and may become more relevant in the future as the EUPATI guidance and the importance of the patient perspective continues to gain traction (Figure 2).

- The importance of PEI (as perceived by interviewees) did not change if specific to the oncology therapeutic area or more specifically immuno-oncology, except for France. The HTA advisor from France noted that PEI can be more important for end stage or metastatic cancer. Lower ratings for PEI for IO medicines in France and Spain were attributed to the lack of familiarity with IO.
- PEI can have a significant impact in Germany, particularly if there are saftety/tolerability issues associated with the medicine under assessment or the comparator.
- In order to maximize impact, PEI must be translated into country-specific outcomes that resonate with the respective payers and HTA archetypes (e.g. cost-effectiveness, comparative effectiveness or budget impact).

Figure 2 | Importance of PEI for HTA decision-making*



* Rated on a scale of 0 to 10, where 0 is not important at all and 10 is extremely important

"Spain is not a QALY country, but a budget impact country. Side effects have high costs to the healthcare system. If manufacturer can translate how adverse events lower costs to the system that would be helpful. Show QoL/PRO data has impact to budget impact and that would be powerful!"

Spain HTA Advisor

"PEI is critically important if there are safety/tolerability issues associated with the drug or comparator"

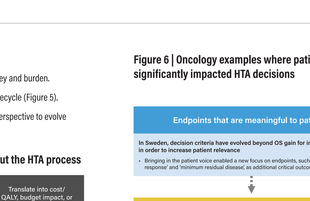
Germany HTA Advisor

Importance of PEI for rare cancers

Including patient information and input in HTA decisions for rare cancers is particularly relevant. (Figure 3).

- Lack of information for rare cancers make PEI more important than oncology in general.
- There is a need for more information for rare cancers and the number of affected patients are lower; therefore, the patient voice can play more important role in HTA decision-making.

Figure 3 | Importance of PEI for rare cancer types for HTA decision-making*



* Rated on a scale of 0 to 10, where 0 is not important at all and 10 is extremely important

"PEI is more important in rare or less common cancers because need more information about the disease and patient voice can play more important role!"

Italy HTA Advisor

Importance of post-progression PEI for oncology HTA decision-making in (immuno)-oncology

Post-progression PEI provides additional insight into the patient perspective and can impact HTA decisions, particularly in "cost-effectiveness" countries (Figure 4). Further, HTA advisors indicated that post-progression PEI is most important for rare cancer types that are the least understood (data not shown).

- Post-progression PEI has been perceived as a missed opportunity in cost/QALY countries, particularly cost/QALY evaluations with extended time horizons.
- Historically, post-progression PRO data has not been captured due to trial designs and definitions. HTA evaluators in cost-effectiveness markets are keen to understand the level of QALY decrease from pre- to post-progression as this will impact the cost/QALY analysis.

Figure 4 | Importance of Post-progression PEI for HTA decision-making*

* Rated on a scale of 0 to 10, where 0 is not important at all and 10 is extremely important

"Patient is in 3 health states - pre-progression, post-progression, and dead... [Post-progression PRO] is very important, but poorly done because when patients progress - they stop collecting data. But we want to know in cost/QALY model what is the drop in progression based on QoL or symptoms - continue PRO follow-up during progression phase."

UK HTA Advisor

"If additional efficacy is still being seen. Post-progression PEI is important if patient continues to benefit in some way."

Germany HTA Advisor

Manufacturers can play a critical role in bringing the patient perspective into the HTA process (Figure 5).

- Manufacturers can bring in the patient voice during the HTA appraisal process, e.g. by showing the patient journey and burden.
- The holistic view on patients' experiences should start uclinical trial design and continue throughout the drug lifecycle (Figure 5).
- Patient involvement and PEI can impact and in rare instances even reverse HTA decisions by using the patient perspective to evolve inputs into HTA submissions beyond overall survival gain (Figure 6).

Figure 5 | Patient input should start early in clinical development and continue throughout the HTA process

Figure 6 | Oncology examples where patient input significantly impacted HTA decisions

Conclusions

- Most HTA processes in European countries do not meet EUPATI guidelines regarding the level of patient involvement.
- There are opportunities for PEI to provide differentiation among treatment options and affect HTA decisions, particularly for the treatment of rare cancers. PEI collected post-progression can be useful, especially in "cost-effectiveness countries".
- Manufacturers should collect PEI in clinical trials and real-world evidence studies, analyze these data with scientific rigor and translate this evidence into country-specific outcomes (e.g., cost/QALYs, budget impact, comparative effectiveness) to maximize the influence of the patient voice on HTA decisions.
- The results of this study might be limited by the a small sample size of experts participating.
- Increased patient involvement and use of PEI will drive better informed and better targeted HTA decisions.

"Target patient experience as part of the trial. Has to be tied to the impact of the drug."

France HTA Advisor

"With IO therapies, there is little patient experience information. A competitive opportunity exists in certain therapy areas because clinical data is similar and then the patient perspective and PEI can differentiate among treatment options."

Italy HTA Advisor

References

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To be determined