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INFLUENCE OF PATIENT-REPORTED OUTCOMES (PRO) ON MARKET ACCESS DECISIONS IN MARKETS WITH CENTRALIZED HEALTHCARE SYSTEMS

Hogue SL[1], Brogan AP[1], De Muro C[1], D'Alessio D[2], Bal V[2]

[1]RTI Health Solutions, Research Triangle Park, NC, United States; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ United States

BACKGROUND

Patient reported outcomes (PROs) are an accepted and often actively solicited source of evidence used by health authorities and payers in evaluating and approving pharmaceutical interventions in addition to demonstration of the efficacy and safety of the intervention. There is, however, limited information on how payers value PRO data in reimbursement decisions. The clinical evidence section of value dossiers often include PRO data while health related quality of life (HRQoL) data is often incorporated into cost effectiveness analyses of economic models. A multitude of endpoints and variation in how payers in different countries assess evidence makes it difficult to understand the value of PRO data in reimbursement decisions.

An assessment was undertaken to gauge the current and future impact of PRO data on health care decision making in centralized markets, specifically in the oncology therapeutic area.

OBJECTIVE

- To determine the impact of PRO data from clinical trial programs on market access decision making in oncology and other disease areas in centralized markets.

METHODS

- PubMed/MEDLINE, Embase, ISPOR databases, and regulatory and health technology assessment (HTA) websites for the EMA, the UK, France, and Germany were searched to identify PRO data included in regulatory and HTA submissions of four oncology drugs: bevacizumab, pemetrexed, sunitinib, and crizotinib. One-on-one interviews were conducted with 10 payer/decision makers ('payers') from different countries with centralized healthcare systems in 2014. An online assessment was conducted (December 8, 2014, to March 4, 2015) with 5 completed surveys (China, France, Germany, Taiwan, the UK) and 2 partially completed surveys (Australia and South Korea) by payers from the RTI Health Solutions Global Payer Advisory Panel.
- The profiles of the payers and payer advisors interviewed are listed in **Table 1**. All ten respondents were professors of health economics.

Table 1: Payer Profiles

Country	Payer Advisor Profile
Australia	Advisor to Medical Services Advisory Committee (MSAC) and Pharmaceutical Benefits Advisory Committee (PBAC)
France	Advisor to Haute Autorité de Santé (HAS)
Germany	Member of the arbitration board for drug process in the statutory health insurance
Korea	Advisor to Health Insurance Review and Assessment (HIRA)
Netherlands	Advisor to Zorginstituut Nederland (ZINL, formerly CVZ)
Poland	Advisor to Agenca Oceny Technologii Medycznych (AOTM)
Sweden	Advisor to Tandvårds – och läkemedelsförmånsverket (TVL)
Taiwan	HTA advisor
Turkey	Advisor to public and private insurance providers
United Kingdom	Advisor to the National Institute for Health and Care Excellence (NICE)

RESULTS

When asked "what the role of PRO data in market access decision making is", respondents indicated:

"…[it] needs to be patient relevant (e.g., improvements in morbidity, side effects, quality of life [QOL]." — Germany

United Kingdom: "The key role of PROs is getting to the key bit of QALYs [quality of life years] in terms of measurement of utility. They would also like to see symptom or disease specific measures to confirm and support evidence and direction of measures of utility, but they are subsidiary."

"PRO measures have a minor role in overall HTA [Health Technology Assessment] and market decision process - it is additional information that we would like to see for incremental benefit. The most important dimensions are the severity of the condition (for oncology this is not a problem), efficacy, safety and then other dimensions such as unmet needs, mode of administration, mode of action and then QOL. PROs are related to QOL. In the future we expect that PROs will gain some importance." — France

Sweden: "PRO is included in the reimbursement decision. In HE [Health Evaluation] (cost per QALY) - there is willingness to pay more for severe diseases - hence need QOL data for this. In some cases, companies have also used willingness to pay studies for supporting reimbursement."

"Companies submit the analysis of PROs as part of clinical data. [There are] no standard criteria for assessment of PROs submitted by the manufacturer…" — Poland

Turkey: "[PRO data has] minimal use [as] supplementary information, but in terms of the decision making, it's quite low."

"We evaluate that evidence pretty much on the same basis as other evidence…. So if it's a relatively low level of evidence, for example a case series, then that would be regarded as a fairly low level of evidence, and that would be true whether it's a PRO measure or a clinical input." — Australia

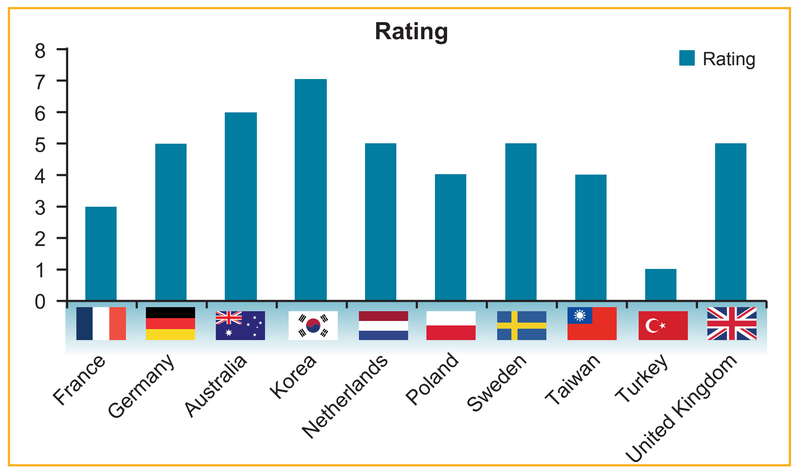
South Korea: "From the perspective of clinicians in Korea, I'm not sure what extent PROs are considered as important clinical endpoints BUT the PROs can very much influence decisions with HIRA (Health Insurance Review and Assessment)."

"PRO is new for Taiwan. There is not a strong requirement from the government for PRO data… if included in HE then it is a plus for the review process…" — Taiwan

When asked "to rate the level of importance given to PRO data for market access of new oncology treatments"

- on a scale of 1 to 7 where 1 means 'not important' and 7 means 'extremely important', the average rating was 4.5 (**Figure 1**).

Figure 1: Rating of the level of importance given to PRO data



Rated on a scale of 1 to 7 where 1 means "not at all useful" and 7 means "extremely useful"

South Korea: "PRO can move the needle. Really need to publish and educate payers about PROs outside of QALYs."

Sweden: "…there is a willingness to pay more for severe diseases…[we] need QoL data for this."

Turkey: "Cancer is a special area of concern in the Turkish healthcare system, because it's really sensitive to say no to a cancer drug…That's why PRO data is not that important…."

When asked to describe the specific characteristics that a PRO endpoint for treatment in oncology should have, respondents listed the following:

- Validated, objective, reliable measurements that encompass a broad range of effects and symptoms and are relevant to all patients receiving treatment
- Statistical significance and clinical relevance; should produce QALY weights and translate to utilities

Australia: "[evaluate] cancer indications…that [are] unrelated to survival… the extent to which the oncology product improves even progression-free survival in the absence of any impact on overall survival is important."

Germany: "PRO data needs to be patient relevant (improvement sin morbidity, side effects, QoL)…compliance and convenience are not considered."

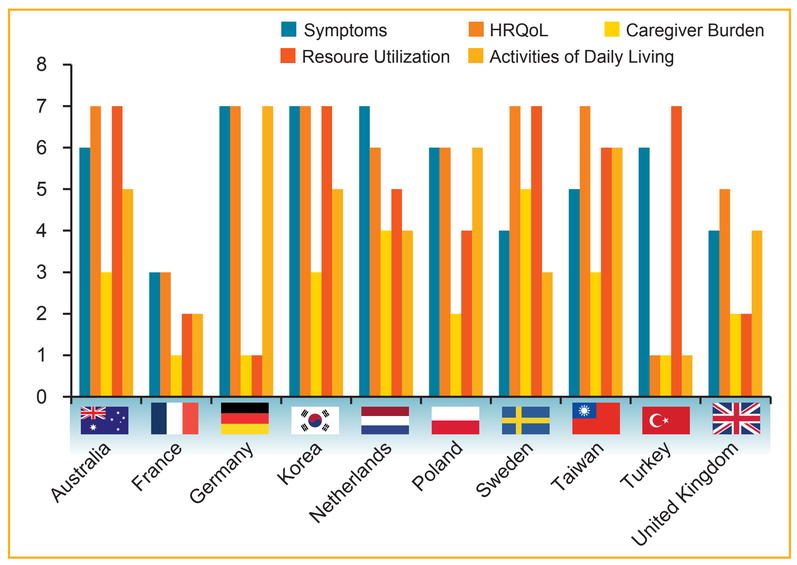
Netherlands: "[There is a] new separate process for evaluating drugs…. Oral drugs - PRO is only accepted from registration trials. For hospital or clinic intravenous administered drugs PRO data is accepted from registration and postmarketing trials."

Poland: "Companies submit the analysis of PROs as part of clinical data – there are no standards criteria for assessment of PROs submitted…"

Respondents indicated that PRO data is more useful in the evaluation of chronic or palliative therapy options and that overall the importance of PRO data will increase in the future.

- Overall, the respondents indicated that PRO measures had value in clinical trials of oncology therapies.
- PRO data should optimally be collected in Phase 3 and post-marketing trial data with emphasis on comparator trial data and real world clinical experience.
- PRO data are very important, especially in the advanced metastatic stage of cancer
- There were minimal differences in the usefulness of PRO measures by cancer indication.
- Assessment of symptoms and health-related QoL were consistently ranked as the PRO measures with greatest value (**Figure 2**)
- PRO data has the greatest impact at the local level where positive data could impact uptake, reimbursement, and market share.

Figure 2: Rating of the Value of PRO data by Type



Rated on a scale of 1 to 7 with 1 being unimportant to 7 being very important

Payer's advice for pharmaceutical manufacturers with respect to communicating PRO evidence to decision makers:

Integrate

France: "PRO data should be only used to support and to translate (as viewed from the patients) the clinical benefits of the treatment. If you don't have an effective drug, forget PROs."

"…[provide] more information to key opinion leaders – they can have a big impact on decision makers…." — Poland

Turkey: "…if the PRO analysis is made in a different culture, you cannot translate the results to another culture easily….if you are talking about caregiver burden, it's quite different in different cultures."

Validate

United Kingdom: "- analyze data with care and use high quality measures that are valid…early modeling of where the utility gain is going to come from enables you to see at which stage in the disease the main utility gain is going to come from. Publications of the key date are useful…"

"provide the data in a way that's convincing with respect to its rigor and [that] is representative of the patient's journey…show that it has been collected in a way that is rigorous and provides true insight into that experience." — Australia

Taiwan: "Adoption by the US and Europe is key…if information is available from FDA or EMA then we trust it more…"

Educate

Netherlands: "show [PRO data] to clinicians. This is the flow of information: manufacturer → clinicians → reimbursement authority"

"the prescribers are not used to PRO data and they need to be educated…" — Sweden

Korea: "…inform clinicians of the PRO and other clinical data. They are the ones who will be called upon…as consultants. This is an important avenue for reimbursement."

CONCLUSIONS

- **Currently, inclusion of PRO data in reimbursement decision making varies by country and within country by payer type: national, regional, local decision-maker**
- **There are minimal requirements or guidelines currently available addressing whether and how health care decision makers use PRO evidence**
- **There is a growing recognition that the patient perspective is important to decisions regarding market access in centralized markets and may be a key differentiator among therapeutic options**
- **Effective PRO data should be collected using validated methods that emulate real world clinical experience and published in peer-reviewed journals**

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