Health Technology Assessment (HTA) Case Studies: Comparing Acceptability of Real-World Evidence (RWE) in Appraisals for Oncology Medicines

Zong JH[1], Pan X[2], Rojubally A[3], Jiao X[1], Bruno A[1], Gdovin Bergeson J[3]

[1]Bayer Healthcare Pharmaceuticals Inc., Whippany NJ, USA; [2]Bayer Healthcare Pharmaceuticals Inc., Boston, MA, USA; [3]Franklin Pharmaceutical Consulting, Cary, NC, USA

BACKGROUND

- Over the past few years real-world evidence (RWE) is increasingly utilized by health technology assessment (HTA) agencies in appraisals and is seen as a high potential asset for decision-making.[1]
- Although different HTA agencies use RWE to different degrees, these agencies each use RWE to better understand the foundation of a products value assessment.[2,3]
- However, clear guidance on RWE to be accepted in HTAs is lacking and is needed to assist HTA decision-makers, as RWE may be able to show long-term benefits or outcomes in patients not well represented in clinical trials.[4]

METHODS

- This review identified oncology medicines with final reports (final appraisal documents) which contained RWE from January to December 2022.
- A search of Technology appraisals published by National Institute for Health and Care Excellence (NICE), Benefit Assessments published by der Gemeinsamer Bundesausschuss (G-BA), and Opinions on Medicinal Products reports published by Haute Autorité de Santé (HAS) was conducted.
- Oncology medicines appraisals referencing RWE were identified using the following key search terms: real-world data, real-world evidence, external, historical, synthetic control; retrospective, observational, non-interventional, pragmatic trials; chart review, claims, registry, electronic medical records (EMR), electronic health records (EHR) and patient reported outcomes including quality of life.
- RWE acceptability was classified as primary evidence, supportive evidence, not adequate, not addressed, or other by reviewer's assessment.
- Oncology medicines reviewed by more than one HTA agency were selected for comparative assessment of RWE acceptability.

OBJECTIVE

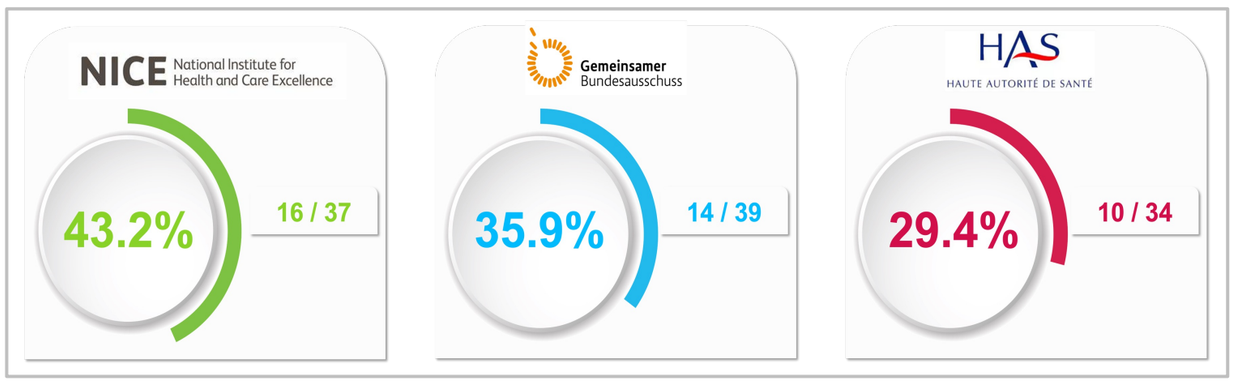
- The objective of this review was to compare RWE acceptability in HTA decision-making in recent appraisals for oncology medicines.

RESULTS

Appraisals with RWE

- In 2022, there were 37 final appraisals for oncology medicines identified from NICE, 39 from G-BA, and 34 from HAS (**Figure 1**).
- From those appraisals, RWE was referenced in 43.2% (16) of appraisals for oncology medicines by NICE, 35.9% (14) by G-BA and 29.4% (10) by HAS.

Figure 1. Extent of RWE Use in Appraisals



CONCLUSIONS

- There is a discrepancy in the assessment of RWE by the 3 HTA agencies in recent oncology appraisals.
- RWE acceptability by NICE as supportive evidence is promising.
- HAS and G-BA's evaluation of RWE suggests emphasis on data quality, selection biases, and confounding factors related to RWE use.
- The study has some limitations as data retrieval may not be standardized across the HTA databases and not all the data from HAS and G-BA has been published in English.
- Demand for quick and uniform access of new oncology therapies warrants harmonization of RWE relevance across HTA agencies.
- Development of comprehensive consensus guidelines with all stakeholders are needed to standardize best practices for RWE studies and assessments.

PLAIN LANGUAGE SUMMARY

- This review demonstrated that each HTA agency used a different approach when assessing the use of RWE in final appraisals.
- If every HTA agency uses a different approach, it is difficult for researchers to know how to best develop RWE studies to inform the HTA agency on the value of a medicine.
- In the absence of uniform guidelines, scientists will continue to generate RWE to support HTA reviews, however the utility in a given country will vary.

RESULTS CONT.

Table 1. RWE Approach, Acceptability and Methodology Bias

Drug Name/ Disease Indication	HTA	RWE Approach	RWE Acceptability	Study Design Bias	Data Quality Bias	Selection Bias	Outcome Bias	Analysis Bias	HTA Outcome
amivantamab	NICE	Indirect comparison	Not adequate	✓		✓	✓	✓	Not recommended
non-small cell lung cancer	G-BA	Indirect comparison	Not adequate			✓	✓	✓	Additional benefit not proven
sotorasib	NICE	Indirect comparison	Supportive					✓	Recommended to Cancer Drug Fund (CDF)
non-small cell lung cancer	G-BA	Descriptive comparison	Not adequate			✓	✓	✓	Additional benefit not proven
tepotinib	NICE	Indirect comparison	Supportive			✓		✓	Recommended with Commercial Arrangement (CA)
non-small cell lung cancer	G-BA	Descriptive comparison	Not adequate		✓			✓	Additional benefit not proven
avapritinib	HAS	Indirect comparison	Supportive					✓	Minor clinical added value
systemic mastocytosis	G-BA	Indirect comparison	Not adequate			✓	✓	✓	Not-quantifiable additional benefit
axicabtagene-ciloleucel	HAS	Indirect comparison	Not adequate	✓	✓		✓	✓	No clinical added value
follicular and diffused large B-cell lymphoma	G-BA	Indirect comparison	Not adequate		✓	✓		✓	Non-quantifiable additional benefit
tisagenlecleucel	HAS	Indirect comparison	Not adequate		✓		✓	✓	No clinical added value
follicular lymphoma	G-BA	Indirect comparison	Not adequate		✓	✓		✓	Non-quantifiable additional benefit

Acceptability of RWE

- Six oncology medicines reviewed by more than one HTA agency were selected as case studies for comparative assessment of RWE acceptability: amivantamab, sotorasib and tepotinib (NICE and G-BA); avapritinib, axicabtagene-ciloleucel and tisagenlecleucel (HAS and G-BA) (**Table 1**).
- Acceptability of RWE by NICE was in alignment with G-BA for amivantamab (RWE not adequate) and divergent for tepotinib and sotorasib (NICE: RWE as supportive and G-BA: RWE not adequate).
- HAS and G-BA were in alignment for tisagenlecleucel and axicabtagene-ciloleucel (RWE not adequate) and divergent for avapritinib (HAS: RWE as supportive and G-BA: RWE not adequate).

RWE Use and Methodology Bias

- RWE was mainly leveraged as an external control for indirect treatment comparison to support clinical trials results in NICE, G-BA and HAS appraisals (**Table 1**).
- RWE methodology biases identified from HTA reviewers' comments were related to study design, data quality, population selection, outcome and analysis.
- Analysis limitations due to confounders was prevalent across all 3 HTA agencies, followed by selection bias, outcome bias and data quality bias.
- In the case of amivantamab, NICE cited several RWE methodology biases, which inherently influenced RWE acceptability in the appraisal and impacted the HTA outcome.
- In the case of avapritinib reviewed by HAS, RWE was noted as supporting the appraisal despite some uncertainties in the analysis.
- There is greater scrutiny of RWE methodology by HAS and G-BA and lowest RWE acceptance by G-BA compared to HAS and NICE.

REFERENCES

1. Akehurst R, Murphy L, Oriol Solà-Morales, Cunningham D, J. Mestre-Ferrandiz, Gérard de Pouvourville. Using Real-World Data in the Health Technology Assessment of Pharmaceuticals: Strengths, Difficulties, and a Pragmatic Way Forward. *Value in Health*. 2023;26(4):11-19. doi: https://doi.org/10.1016/j.jval.2023.01.010
2. National Institute for Health and Care Excellence, NICE real-world evidence framework
3. Haute Autorité de Santé, H.A.S., Études en vie réelle pour l'évaluation des médicaments et dispositifs médicaux. 2021: Saint-Denis La Plaine.
4. Tara Cowling, Ransi Nayakarathna, Allison L. Wills, Dipti Tankala, Nancy Paul Roc & Stephane Barakat (2023) Early access for innovative oncology medicines: a different story in each nation, Journal of Medical Economics, 26:1, 944-953, DOI: 10.1080/13696998.2023.2237336

DISCLOSURES

- This study was funded by Bayer Healthcare Pharmaceuticals. Editorial support was provided by Franklin Pharmaceutical Consulting and funded by Bayer Healthcare Pharmaceuticals.
- At the time of this study Zong JH, Pan X, Jiao X, and Bruno A were employed by Bayer Healthcare Pharmaceuticals. Jiao X and Bruno A are no longer employed by Bayer.
- Rojubally A, and Gdovin Bergeson J conducted this study with Franklin Pharmaceutical Consulting and were compensated for their services