HTA25

Diverging Relative Clinical Benefit Assessment Across HAS and G-BA: A Forecast for EU HTA in Oncology Drugs

Fiona Tolkmitt;[1] Danitza Chávez-Montoya;[2] Ahmad Hecham Alani;[1,2] Matthew Bergsteedt;[1] Mackenzie Mills;[1,2] Panos Kanavos[2]

[1] Hive Health Optimum Ltd. (HTA-Hive), London, United Kingdom

[2] The London School of Economics and Political Science (LSE), London, United Kingdom

Background

- The EU's new JCA regulation aims to unify HTA evaluations, starting with oncology, to improve access to innovative therapies across Europe.
- Standardised clinical benefit assessments streamline access to innovative treatments by reducing redundancies, simplifying processes, and enabling faster, consistent decisions across regions, promoting efficiency and equity in healthcare.
- However, major differences in assessment approaches across countries, particularly among leading HTA bodies like France's HAS and Germany's G-BA, pose significant challenges for national regulatory and reimbursement decisions.

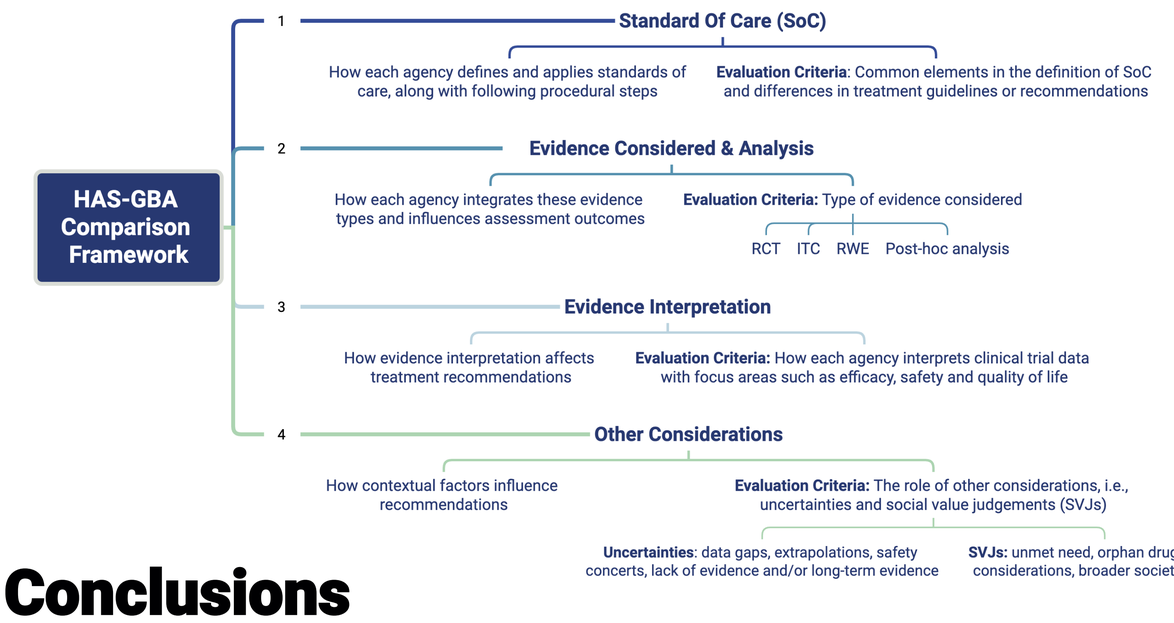
Objectives

- This study examines the alignment (or lack thereof) in clinical benefit ratings for oncology drugs between HAS and G-BA, with implications for future JCA implementation.
- It aims to identify factors driving discrepancies in assessments and forecast challenges and opportunities for harmonisation under the EU JCA regulation.
- Focusing on oncology as the initial therapeutic area, this study contributes insights for streamlining HTA assessments across EU member states.

Methods

- A dataset of initial oncology drug-indication pairs evaluated by both G-BA and HAS was compiled.
- Data extraction included benefit ratings, clinical evidence reviewed, and contextual factors such as unmet need, disease severity and rarity.
- Interagency agreement was assessed using Cohen's kappa statistic (κ) quantify concordance between the agencies.
- Discrepancies were analysed to determine if they arose from differences in the standard of care, the clinical evidence considered, its interpretation or other contributing factors.

HAS Added Benefit	Corresponding Benefit Rating	G-BA Added Benefit
I	I	Major
II	II	Considerable
III		
IV	III	Minor
		Non-Quantifiable
V	IV	No Additional Benefit
No ASMR		Less/Worse



Conclusions

- This study reveals misalignment between HAS and G-BA in assessing the relative clinical benefit of oncology therapies, highlighting potential challenges for the EU JCA process.
- Key areas of divergence include standards of care, evidence considered, evidence interpretation and other factors specific to each agency's methodologies and frameworks.
- Harmonised methodologies and standards across agencies could facilitate greater alignment and support the future success of the JCA.
- Without consensus on best practices, the validity and acceptance of JCA outputs may be limited, potentially impacting the goal of streamlined EU-wide market access for innovative oncology treatments.

References

European Federation of Pharmaceutical Industries and Associations (EFPIA), 2024. Guidance Needed to Ensure EU Joint Clinical Assessment Improves Patient Access to Innovative Cancer Treatments. *EFPIA*. Available at: https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/guidance-needed-to-ensure-eu-joint-clinical-assessment-improves-patient-access-to-innovative-cancer-treatments/

European Commission, 2024. Commission Facilitates Faster Access to Medicines with Clear Rules for Joint Clinical Assessments. *European Commission*. Available at: https://health.ec.europa.eu/latest-updates/commission-facilitates-faster-access-medicines-clear-rules-joint-clinical-assessments-2024-05-23_en

Giuliani, G., et al., 2018. Leveraging EUnetHTA's conceptual framework to compare HTA decision drivers in France, Italy, and Germany from a manufacturer's point of view. *Health Economics Review*, 8(24). Available at: https://healtheconomicsreview.biomedcentral.com/articles/10.1186/s13561-018-0201-y

Kisser, A., et al., 2022. Towards Compatibility of EUnetHTA JCA Methodology and German HTA: A Systematic Comparison and Recommendations from an Industry Perspective. *The European Journal of Health Economics*, 23, pp. 863–878. Available at: https://link.springer.com/article/10.1007/s10198-021-01400-2

Results

- Analysis of 146 matched first oncology drug-indication pairs revealed poor agreement between HAS and G-BA (κ = 0.29), indicating substantial divergence in added clinical benefit assessments
- G-BA Added Benefit: Among the matched drug-indication pairs, the ratings were distributed as follows: Major: 4 (3%), Considerable: 23 (16%), Minor: 14 (10%), Non-quantifiable: 26 (18%), No additional benefit: 77 (53%), and Less/Worse: 2 (1%).
- HAS Ratings: The HAS evaluations for the same pairs were categorised as follows: ASMR I/II: 0 (0%), ASMR III: 34 (23%), ASMR IV: 39 (27%), ASMR V: 47 (32%), and No AMSR: 26 (18%).

Case Study 1: Standard of Care

Apalutamide + Androgen Deprivation Therapy (ADT) – Erleada®
For metastatic Hormone-Sensitive Prostate Cancer (mHSPC)

ASMR III
01.07.2020*

No Additional Benefit Proven
20.08.2020*

Different comparators accepted by agencies
- **HAS:** ADT alone.
- **G-BA:** ADT in combination with either docetaxel (with or without prednisone or prednisolone) or in combination with abiraterone acetate and prednisone or prednisolone.

Case Study 2: Evidence Considered & Analysis

Trastuzumab-Deruxtecan – Enhertu®
As a third line HER2-positive Breast Cancer

ASMR V
16.06.2021*

Considerable Added Benefit
02.02.2023*

Different main trials considered
- **HAS:** Based on a non-comparative Phase II study, DESTINY-BREAST 01.
- **G-BA**: Based on an ongoing, open-label, randomised, Phase III study, DESTINY-Breast02 (data cut-off from 30 June 2022).

Case Study 3: Evidence Interpretation

Sacituzumab Govitecan – Trodelvy®
As a third line for Unresectable or metastatic Triple-Negative Breast Cancer

ASMR III
06.04.2022*

Major Additional Benefit
19.05.2022*

Different opinion of safety profile and generalisability
- **HAS:** Highlighted specific AEs, particularly gastrointestinal and haematological effects and raisd concerns about the generalisability of the trial results.
- **G-BA:** viewed the overall safety profile favourably and does not express concerns regarding the generalizability of the trial results.

Case Study 4: Other Considerations

Avapritinib – Ayvakyt®
For Unresectable or metastatic Gastrointestinal Stromal Tumors (GIST)

ASMR V
10.03.2021*

Non-quantifiable Added Benefit
15.04.2021*

Different pathway for orphan drugs
- **HAS:** does not automatically confer a benefit based on orphan status, and determined there was insufficient data to give an added benefit rating.
- **G-BA:** Considers added benefit to be proven for orphan drugs by default, evaluating only the extent of this benefit.

*Outcome date

Abbreviations

Adverse Events, AEs; Amélioration du Service Médical Rendu (Improvement of the Medical Benefit), ASMR; Androgen Deprivation Therapy, ADT; Gemeinsamer Bundesausschuss (Federal Joint Committee), G-BA, Haute Autorité de Santé (French National Authority for Health), HAS; Health Technology Assessment, HTA; Human Epidermal Growth Factor Receptor 2, HER2; Indirect Treatment Comparisons, ITCs; Joint Clinical Assessment, JCA; Randomised Controlled Trial, RCT; Real-world Evidence, RWE; Standard of Care, SoC

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For further information, please contact f.tolkmitt@hiveoptimum.com