Method in the madness – Acceptance of indirect evidence in Joint Clinical Assessments

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Background

- From 2025, select pharmaceuticals will be mandated to undergo a joint clinical assessment (JCA) at the European level. In preparation, EUnetHTA21 (2021-2023) is developing methodological guidelines for JCAs
- This research evaluates indirect treatment comparison (ITC) acceptance in JCAs and assesses how the corresponding ITCs faired during national assessments

Methods/description

- Publicly available information on EUnetHTA JCAs from JA3 (2016-2021) for individual drugs were identified alongside the associated appraisals by national HTA agencies from Germany (G-BA), France (HAS), Sweden (TLV)

Results

- Twenty JCAs were identified, of which 16 achieved marketing authorisation (MA). 10/16 JCAs contained an ITC. The ITC methodology varied between submissions: 4/10 Bucher; 1/10 Matching Adjusted Indirect Comparison (MAIC); 5/10 Bayesian, and 1/10 propensity score weighting (PSW). Out of the ten JCA submissions containing an ITC, only two ITCs were considered appropriate for use from the JCAs, using Bucher and Bayesian methodology
- Of the ten products with a JCA which contained an ITC: eight were submitted to the G-BA, with only 1/8 containing an ITC (unknown method); which was not accepted. Eight were submitted to HAS with 3/8 containing an ITC (MAIC, Bayesian, PSW), one achieved ASMR≤3; however, the ITC (PSW) was not accepted. Six were submitted to the TLV with 2/6 containing an ITC (MAIC) of which one ITC was accepted. In all identified cases, manufacturers submitted the same ITCs for JCA and HTA agencies. Critiques of ITCs across both JCA and national assessments were generally driven by the heterogeneity of the included studies

JCAs/ITCs identified

- 20 Joint clinical assessments
- 16 Marketing authorization
- 10 Indirect treatment comparisons

Methodology of the 10 ITC submitted for JCA*

- 50% Bayesian
- 40% Bucher
- 10% Matched-adjusted treatment comparison
- 10% Propensity score weighting

→ 20% Accepted for use by JCA (Bayesian and Bucher)

HTA assessment of the 10 products with ITC

	Products assessed	ITCs submitted	ITCs accepted
G-BA	8	1	0
HAS	8	3	0
TLV	6	2	1

Topline HTA critiques of ITCs by the GBA, HAS, TLV

- Heterogeneity in follow-up, patient and disease characteristics
- Variability in endpoint definitions
- Insufficient/uncertain if all essential effect modifiers and prognostic factors had been adjusted
- Methodology resulting in small sample (MAIC)

Note: *ITCs may have used multiple methodology

Conclusions

- Despite the majority of JCA submissions containing ITCs, acceptance of the methodology by the G-BA, HAS, and TLV during evaluation was low
- Furthermore, in the corresponding national submissions, ITCs were often excluded, and acceptance was also unlikely
- With the new HTA regulation, there is an opportunity to increase uptake of ITCs at European and national level; however, there is a risk that without strong direction from the EC, the use of ITCs may delay access to new pharmaceuticals in Europe

Abbreviations

AMD: Age-related macular degeneration; AML: Acute myeloid leukemia; DLBCL: Diffuse large B-cell lymphoma; EC: European Commission; ECOG: Eastern Cooperative Oncology Group; EUnetHTA: European Network for Health Technology Assessment; G-BA: Gemeinsamer Bundesausschuss; HAS: Haute Autorite de Sante; HTA: Health technology assessment; ITC: Indirect treatment comparison; JA3: Joint Action 3; JCA: Joint Clinical Assessment; LOT: Line of therapy; MA: Marketing authorization; MAIC: Matching-adjusted indirect comparison; NSCLC: Non-small cell lung cancer; PSW: Propensity score weighting; R/R: Relapsed or refractory; SCT: Stem cell transplant; SPMS: Secondary progressive multiple sclerosis; T1DM: Type 1 diabetes mellitus; TLV: Tandvards-Och lakemedelsformansverket; UC: Ulcerative colitis

References

[1] eunethta 2022. Assessment archive JA3(2016-2021). Available at: https://www.eunethta.eu/rapid-reas/
[2] G-BA 2022. Available at: https://www.g-ba.de/
[3] HAS 2022. Available at: https://www.has-sante.fr/jcms/pprd_2986129/en/home
[4] TLV 2022. Available at: https://www.tlv.se/