

From Theory to Practice in the EU HTA JCA: Early Insights and Lessons Learned

Industry Perspective

27th September 2026





HEADS OF HTA
AGENCIES GROUP

The Heads of HTA Agencies is an independent group of 36 European healthcare agencies working together to advance strategic collaboration on HTA.

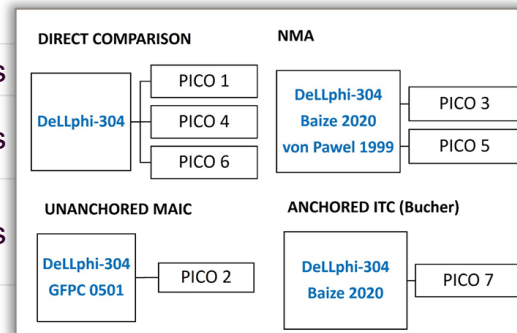
As implementation of the HTAR progresses, the focus will be on learning from practical experience, refining processes, building capacity, and strengthening collaboration.

Statement from Heads of HTA Agencies Group on the publication of the first JCA Report

3 Early JCA Cases in Rare and Specialised Diseases

Overview

	Case 1 – Tovorafenib	Case 2 – Tarlatamab	Case 3 – Lurbinectedin
Indication	Paediatric low-grade glioma (pLGG), WHO Grade 1 & 2	Progressed extensive-stage small-cell lung cancer after 1L treatment	First-line maintenance for extensive-stage small-cell lung cancer
Pivotal Trial	Single-arm trial	RCT	RCT
#PICOs in Scope	8 PICOs (3 Populationen)	7 PICOs	1 PICO
#PICOs submitted	2 PICOs	7 PICOs	1 PICO
#PICOs accepted	1 PICO (Unanchored MAIC, high uncertainty, partially unfavorable)	7 PICOs	1 PICO (RCT)
	The JCA is designed to capture a mature evidence landscape. Increasingly granular molecular segmentation, as well as paediatric and extremely rare subpopulations, result in significant evidence gaps in the JCA - and these gaps can never be fully closed.	Direct comparative data demonstrate a clear survival benefit. However, substantial uncertainty was reported for indirect comparisons, i.e. where no head-to-head comparative data are available. If the standard of care includes therapies for which no modern comparative studies exist, even a highly effective medicine is drawn into a degree of uncertainty.	Compelling efficacy data, particularly for PFS, based on a robust active-controlled RCT - yet several controversial aspects remain, including data cut-offs, hierarchical testing, and certain endpoints. An HTD may conduct a methodologically sound pivotal RCT for a rare disease, yet still see the positive aspects substantially diluted in the JCA.



Quelle: JCA Summary Reports, Kintiga Analysen

The 4th JCA Report – Evidence Gaps versus Statistical Adjustment

	Case 4 – Onasemnogene Abeparvovec (Iltvisma)
Indication	Spinale Muskelatrophie (SMA), ≥ 2 Jahre
Pivotal Trial	Phase III, RCT (52 weeks), Sham-controlled
#PICO in Scope	14 PICO initially, 12 finally due to label change (6 populations initially, 5 finally due to label changes)
#PICO submitted	7 PICO
#PICO accepted	7 PICO (Unanchored MAIC, direct comparative data versus BSC, natural history data set)
	The JCA reveals the limits of statistical adjustment. Despite extensive MAIC analyses, 5 of the 12 final PICO could not be addressed. Evidence gaps arising from a lack of population overlap - particularly between intrathecal and intravenous gene replacement therapy - cannot be closed even through methodologically sophisticated MAICs or network models. For HTDs, the early planning of potential JCA PICO questions therefore becomes a key prerequisite for successful evidence generation.

Quelle: JCA Summary Reports, Kintiga Analysen

Change to the claimed indication

The original claimed indication for this product was “patients 6 months of age and older with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene”. However, the HTD informed the Commission on the 26 February 2026 of a change to the claimed indication to “patients 2 years of age and older with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene”. As a result, the original assessment scope included a subpopulation (Population 3) comprising “patients 6 months to 2 years of age at enrolment with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and with ≤ 4 copies of the SMN2 gene”. Two PICO, PICO 6 and 7, were originally included in the assessment scope for this population. After revision of the claimed indication, however, Population 3 and hence PICO 6 and 7 were deemed no longer relevant and were subsequently removed from the assessment scope.

The health technology developer (HTD) provides evidence informing PICO 1, 2, 3, 8, 9, 10 and 11. However, the evidence for Population 1 (in the full claimed indication), informing PICO 1, 2 and 3, is the same evidence as that submitted for PICO 8, 9, 10 and 11. This is because the available evidence in the full claimed indication is limited to a subpopulation which also matches those defined for PICO 8-11. There is no comparative evidence available in patients who cannot sit, or patients who can walk independently. Consequently, no such evidence is included in the JCA report.

For PICO 4 and 5, the HTD carried out a quantitative indirect treatment comparison feasibility assessment (ITC FA) of available individual patient data (IPD) and summary level data (SLD) from trials and patient registries, the results of which have been included in the dossier and appendices. The HTD concluded there was insufficient overlap between the populations of the intervention clinical trials and those of the available comparator data, precluding the possibility of performing a valid comparison of OA IT with OA IV. Therefore, no comparative evidence is presented in the dossier for PICO 4 and 5, and consequently no comparative results are included in the JCA report. The assessors agree with the HTD’s assessment that there is insufficient overlap.

Early JCAs: A High Bar for Evidence, Not a Simplified Pathway

- └ The JCA was intended to create a common European clinical evidence foundation.
- └ In practice, it can translate one regulatory indication into numerous national decision problems and PICOs.
- └ The resulting evidence requirements may exceed what a single global development programme can realistically address.
- └ Particularly in rare diseases, paediatric settings and highly segmented populations, evidence gaps are often structural - not a consequence of insufficient analytical effort.
- └ A feasible and proportionate JCA should not only assess methodological certainty but also reflect outcomes that matter to patients and the clinical realities of rare and severe diseases.
- └ The final PICO scope is defined late in the process, while evidence generation decisions are often locked in years earlier. This creates a structural mismatch between development timelines and HTA evidence expectations.
- └ **Industry perspective:**
The JCA risks adding a new layer of evidentiary complexity unless scope-setting and evidence expectations become more focused, feasible and predictable.

Scope-Setting: The Root Cause of the Evidence Challenge

- └ The final JCA scope defines the evidence questions that an HTD must address.
- └ Diverging national treatment pathways can result in multiple populations, comparators and outcomes within one European assessment.
- └ Yet pivotal-study designs and evidence-generation decisions are often fixed years before the final JCA scope is known.
- └ This creates a structural tension between European evidence expectations and feasible clinical development programmes.
- └ **Industry perspective:**
A focused, clinically meaningful and feasible PICO scope is the prerequisite for an assessable and decision-useful JCA.

Joint Scientific Consultations: From Late Evidence Gaps to Early Evidence Planning

- └ Joint Scientific Consultations (JSCs) offer an opportunity to discuss likely European evidence needs during clinical-development planning.
- └ They can support earlier consideration of likely comparators, endpoints, subgroups and treatment pathways.
- └ However, early advice cannot fully eliminate uncertainty where future national PICOs remain diverse or where direct evidence is not feasible.
- └ For rare diseases, paediatric indications and highly segmented populations, advice must be timely, scalable and proportionate.
- └ **Industry perspective:**
JSCs should become a practical planning tool for all HTD - not a limited procedural opportunity for few.

Statistical Sophistication Cannot Replace Missing Evidence

- └ Indirect comparisons, MAICs and network meta-analyses can support decision-making - but they cannot compensate for missing population overlap or absent comparative data.
- └ In the first JCAs, methodological sophistication did not always translate into evidence considered sufficiently robust for all PICOs.
- └ Requiring evidence for every national treatment pathway can create an unrealistic standard, particularly where comparators are outdated, unavailable or not supported by modern trials.
- └ The consequence may be that clinically meaningful evidence is overshadowed by uncertainty in comparisons that are not feasible to generate directly.
- └ **Industry perspective:**
Methodological limitations should be assessed proportionately and in the context of disease rarity, unmet need and the practical feasibility of evidence generation.

Patient Relevance Requires Focus — Not PICO Proliferation

- └ Patient and clinician involvement is a core element of the EU HTA framework.
- └ Their input can help ensure that outcomes and comparators reflect real-world clinical practice and patient priorities.
- └ However, more PICOs do not automatically mean more patient relevance.
- └ Excessively granular evidence questions may fragment small populations and reduce the interpretability of the overall evidence base.
- └ **Industry perspective:**
Patient-centred HTA requires clinically meaningful questions, proportionate evidence expectations and transparent prioritisation - not the accumulation of every possible national decision problem.

A Common Assessment Does Not Yet Mean a Common Access Pathway

- └ The JCA produces a common European assessment of clinical evidence.
- └ However, national HTA bodies retain their own methodological standards, timelines and decision criteria.
- └ Limitations identified at EU level may be carried into national procedures - potentially before national agencies have considered additional data or country-specific clinical context.
- └ The first German AMNOG experience with tovorafenib shows that JCA and national assessment can rely on different data cuts and reach different views on the relevance of comparative evidence.
- └ **Industry perspective:**
Without practical alignment between EU and national processes, the JCA may create parallel evidence assessments rather than reduce duplication and accelerate patient access.

What Industry Needs from the Next Phase of Implementation

- └ Focused PICO scopes that concentrate on clinically meaningful and feasible evidence questions.
- └ Early, structured and meaningful developer involvement during scoping.
- └ Proportionate methodological standards for rare diseases, paediatric populations and innovative therapies.
- └ Transparent and predictable processes that allow evidence generation to be planned in time.
- └ Real EU–national alignment to prevent the JCA from becoming an additional, rather than a simplifying, evidentiary layer.

- └ **Key message:**
The success of the JCA should be measured by whether it improves predictability, reduces unnecessary duplication and supports faster patient access - not by the number of PICOs assessed.
- └ **A practical route forward:**
Joint Scientific Consultations should become a scalable and accessible tool for early alignment on feasible European evidence strategies.

The first JCA entered the AMNOG process, but AMNOG is not JCA: different question, different answer.

└ The Disappearance of comparative Evidence

- Tovorafenib underwent a European JCA based on **eight PICOs** in the assessment scope.
- Evidence was submitted by company for **two PICOs**.
- **Only one PICO** was assessed in the JCA, an unanchored Matching-Adjusted Indirect Comparison (MAIC), yet assessors expressed substantial reservations with considerable statistical uncertainty.
- In the AMNOG, this MAIC was **excluded entirely** – unsurprisingly in view of G-BA's decision-making in the past. In addition, several endpoints were highlighted as not patient-relevant.
- Company presented the MAIC only supportively:

2) Der pU weist in Modul 4 des Dossiers auf einen indirekten Vergleich von Tovorafenib mit der Kombination aus Dabrafenib und Trametinib hin, der im JCA-Dossier des pU dargestellt wurde. Jedoch zieht der pU den indirekten Vergleich nicht zur Ableitung eines Zusatznutzens heran, sondern betrachtet diesen lediglich als einordnend und informativ für den deutschen Versorgungskontext.

└ „Timing Issues“ between Europe and Germany

- The JCA primarily relied on the two-year data cut from the FIREFLY-1 study. For the German benefit assessment, company submitted a more mature three-year data cut, which the G-BA accepted because of the longer follow-up period.
- When the German procedure commenced in May 2026, the final JCA report had not yet been formally published. As a result, the G-BA could not directly rely on the published JCA and instead assessed the dossier using the JCA submission package, the German AMNOG dossier, regulatory documents, and the FIREFLY-1 study data.

Berücksichtigung des JCA-Reports

Der JCA-Report zu Tovorafenib (JCA-MP-2024-06) war zu Beginn des Nutzenbewertungsverfahrens am 15.05.2026 noch nicht veröffentlicht und konnte daher entsprechend § 7 Absatz 1 Nr. 2 Arzneimittel-Nutzenbewertungsverordnung (AM-NutzenV) für die vorliegende Nutzenbewertung nicht berücksichtigt werden.

Quelle: JCA Summary Reports, Kintiga Analysen

EU HTA and AMNOG: A Test for Europe's Innovation Framework

- └ EU HTA can reduce duplicated clinical assessments and support more coherent evidence evaluation across Europe.
- └ However, different national comparators, endpoints and dossier requirements continue to complicate clinical development and market-access planning.
- └ If EU and national processes remain fragmented, Europe risks adding complexity rather than reducing it.
- └ Efficient HTA processes are therefore not only an administrative issue - they are relevant for investment, clinical research and launch decisions.
- └ **Industry perspective:**
EU HTA must strengthen Europe's attractiveness as a location for pharmaceutical innovation - not create a further barrier to patient access.

The Implementation Risk: Parallel Assessment Instead of Reduced Duplication

- └ EU HTA and AMNOG operate in closely connected, but not fully aligned, timelines.
- └ JCA reports may become available only after the national AMNOG process has already started.
- └ European and national dossier requirements are not yet fully harmonised.
- └ The practical consequence can be parallel evidence preparation and parallel assessment, rather than a genuine reduction in workload.
- └ **Industry perspective:**
A common European clinical assessment only creates efficiency if national systems can use it in a timely and meaningful way.

What Industry Needs: An EU–National Interface That Works

└ Flexible timelines

- National processes must be able to integrate JCA reports once they are available.
- Rigid timelines should not prevent meaningful use of EU-level assessment outputs.

└ Harmonised requirements

- National dossier requirements should align with EU requirements wherever scientifically possible.
- Additional national analyses should be limited to clearly justified cases.

└ Consistent methods

- EU and national HTA should better align on endpoints and methodological expectations.
- Patient-relevant outcomes should be recognised consistently across assessment levels.

└ Systematic and transparent use

- National HTA bodies should use JCA outputs systematically and transparently, while retaining the ability to consider justified country-specific evidence needs.

└ Key message:

The objective should be interoperability, predictability and less duplication - not an additional assessment layer.

The Measure of Success: Better Access, Not More Process

- └ The JCA does not replace national decisions on added benefit, pricing or reimbursement.
- └ Its success should therefore not be measured by the number of PICOs, reports or procedural steps.

The relevant test is whether EU HTA:

- └ reduces repeated evidence reviews;
- └ improves predictability for developers and HTA bodies;
- └ preserves proportionate evidence standards for innovation;
- └ supports faster national reimbursement decisions and patient access.

└ Industry perspective:

The test of EU HTA is not whether Europe produces one more report. The test is whether it reduces duplication, improves predictability and enables faster access to innovation.

EU JCA and US MFN: A New Global Pricing Risk

Forward-looking risk scenario

- └ The JCA does not set prices - but it can shape the clinical evidence narrative used in national pricing and reimbursement negotiations.
- └ An unfavourable or uncertain JCA may increase pressure for restrictions, rebates or managed-entry agreements across European markets.
- └ National price outcomes may then be amplified through international reference pricing.
- └ If US MFN mechanisms increasingly use international prices as benchmarks, European HTA outcomes may gain direct relevance for US pricing exposure.
- └ **Industry perspective:**
Clinical evidence uncertainty in Europe may no longer remain a national market-access issue - it can become a global pricing risk.

The Industry Response: Integrate Evidence and Global Pricing Strategy

- └ JCA preparation can no longer be managed independently from global pricing and launch strategy.
- └ Evidence risks should be stress-tested early against:
 - national P&R consequences,
 - international reference-pricing exposure,
 - potential US MFN scenarios.
- └ Comparator choice, endpoint maturity, subgroup evidence and indirect-comparison credibility must be addressed during Phase II/III planning.
- └ Launch sequencing must balance early patient access with price visibility and potential global reference effects.
- └ **Industry perspective:**
The response cannot be to deprioritise Europe - but Europe must avoid creating evidence and pricing disincentives that delay launches and restrict patient access.

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