Medi-Qualité omega

EU Joint Clinical Assessment

FIRST LESSONS AND STRATEGIC INSIGHTS

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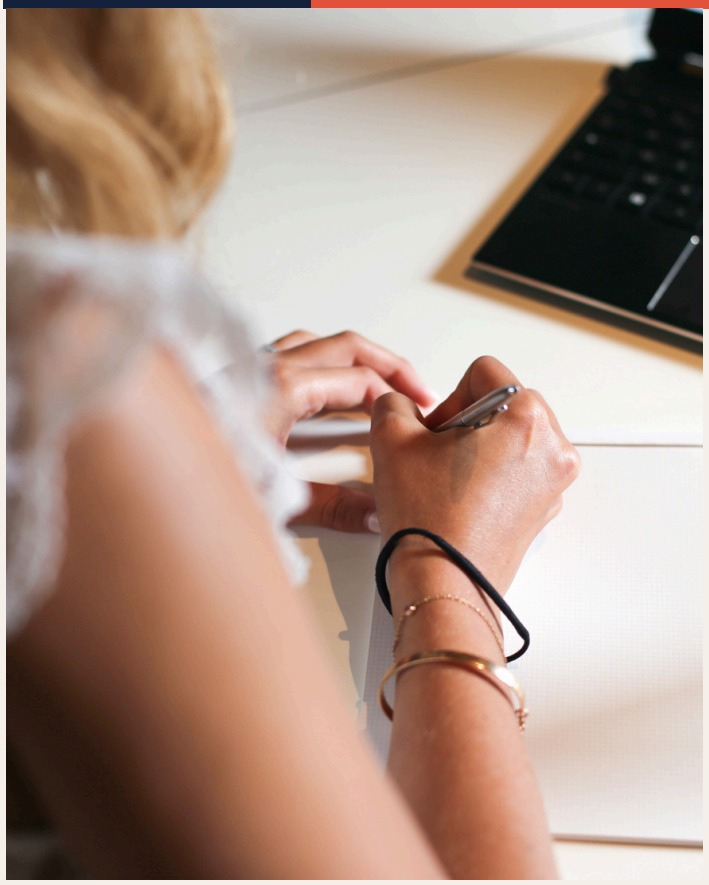
Navigating the JCA

Since January 2025, the **EU Joint Clinical Assessment (JCA)** is officially live for oncology and ATMPs, marking a **transformative shift in HTA processes across Europe** by creating a **single EU-level clinical assessment** to support national HTA decisions. The first lessons from the PICO exercises are starting to emerge and could help highlight both the opportunities and operational challenges that the life science industry must address.

This report provides key insights and reflections on how to navigate this new joint HTA process effectively.

1. PICO Complexity: A Challenge for the Industry



The first **JCA Subgroup PICO exercises**, conducted on three medicinal products (Durvalumab, Adagrasib & Etranacogene dezaparvovec), revealed a **range of 7 to 13 PICOs per product**. [1] While these do not represent the final endorsed guidelines, they provide valuable insights into the reasoning behind PICO scoping, helping manufacturers refine their approach to JCA assessment.

[1] PICO exercises - European Commission

A key driver of the high number of PICOs is the **diversity in sub-populations and comparators** observed. The exercice for Durvalumab included 6 sub-populations and 7 comparators, Adagrasib 8 sub-populations and 10 comparators, and Etranacogene dezaparvovec 2 sub-populations and 7 comparators. [1]

In oncology, for instance, such complexity is often due to factors like treatment line, histology, and sequencing. Additionally, national differences in standards of care and local guidelines across EU member states result in a broader range of comparators. These divergences can be explained by **national sovereignty in healthcare policy**, where **economic disparities impact drug availability** across countries (e.g., Western and Eastern Europe), and **cultural factors shape public health priorities and treatment practices**, further reinforcing variations.

As the JCA framework evolves, we can only hope that the final guidance will account for these complexities and strike a balance between harmonization and the reality of national healthcare diversity across Europe, especially now that the process is underway. The published list of ongoing JCA currently includes two products: tovorafenib (pediatric low-grade glioma) and lifileucel (ATMP cell therapy for metastatic melanoma). [2]

➡️ **Even within an EU consolidated approach, national nuances influence PICO definitions**

[2] Data extracted on 16 April 2025

2. Not an Early Scientific Advice: Strategy Must Be Finalized Upfront

JCA is a final joint clinical assessment, not a joint scientific advice. This means that manufacturers should not be surprised by the number or complexity of PICOs. By the time the JCA starts, **trial design, endpoints, comparators, and subgroups must already be locked.** There is **no room for dialogue, negotiation, or iteration at this stage,** making it critical for manufacturers to anticipate PICO diversity well in advance.

Given the diversity of treatment landscapes across Europe, **PICO scoping must happen upstream**, integrating **early simulations** (both base-case & worst-case scenarios) to account for potential variations. Mapping out EU-wide guidelines, standards of care, and comparator landscapes **before pivotal Phase III** will help avoid surprises and ensure alignment with JCA expectations.

Having proactively anticipated PICO variability, **manufacturers must develop the IT and HR infrastructure to extract dynamic PICOs and subgroups on demand,** and adapt their evidence-generation strategies accordingly.

For indirect treatment comparisons (ITCs), a strategic approach is essential. **Manufacturers should distinguish between clear comparators** (e.g., those recommended in clinical guidelines like ESMO), for which indirect comparisons may be expected **and requests where an ITC may not be feasible due to a lack of external data.** In such cases, it is **acceptable to justify why a PICO is not feasible** using a literature review to support arguments. Submitting a low-quality ITC simply to fulfill a request can be counterproductive.

💡 **Key Takeaways:**
✅ **PICO scoping should be completed early (as early as phase 3 design), the industry must anticipate complexity through strategic simulations**
✅ **Trial designs, endpoints & comparators must align with expected PICOs before pivotal Phase III**
✅ **Cross-functional collaboration (Regulatory, Market Access, Biostats, Clinical) is essential to optimize JCA readiness**

3. Extremely tight deadlines: A True Operational Challenge

JCA operates on a strict and ambitious timeline [3], requiring rapid, in-depth submissions:

Step	Day
Start of JCA (submission of the regulatory dossier to the EMA)	D1
PICO scoping process	D43
Disclosure of the PICO schemes	D126
Dossier submission by pharmaceutical company	D215

➡️ From PICO validation to dossier: **only 89 days**

💡**Key Takeaways:**
✅**~3 months to submit a compliant dossier once PICOs are validated, no room for late-stage adjustments**
✅ **Companies must prepare national dossiers in parallel to PICO discussions**
✅ **These timelines strengthen the positioning outlined above for the need to finalize evidence generation plans as early as phase 3 design stage**

[3] Procedural guidance for JCA medicinal products; JCA procedure; standard procedure

4. Impact of JCA on Countries: National Decisions Still Matter

While the JCA introduces a centralized clinical assessment, **its impact will vary significantly across member states, as pricing and reimbursement decisions remain firmly at the national level**. While the JCA seeks to standardize clinical value assessment, its effect on local HTA outcomes will depend on how each country incorporates its conclusions into existing frameworks. Member states will consider the JCA results by including the report in their national HTA documentation, but they are not required to adopt its findings and may request additional analyses. This could lead to potential for variation between member states in terms of how the JCA is used and the extent to which complementary analyses will be requested.

One key challenge is the **diversity in national HTA methodologies**. Some countries, like Germany and France, rely heavily on added clinical value through national frameworks. Other markets, like the Netherlands and Sweden, place greater emphasis on cost-effectiveness. This means that despite a shared EU-level clinical report, national agencies may still interpret and weigh the findings differently, leading to **varying reimbursement outcomes and access timelines across markets.**

Ratings for clinical benefit remain at the national level. Countries like France (via SMR/ASMR), Germany (via Zusatznutzen), Italy, and Spain apply distinct rating systems, scales, and decision-making doctrines, which are not harmonized across the EU. Furthermore, some countries integrate unique national considerations, such as France's evaluation of public health impact (ISP).

Additionally, the **absence of an economic component in JCA** means that, in countries that rely on cost-effectiveness analysis (CEA) and budget impact (BI), national HTA bodies will continue conducting their own economic assessments, which could **lead to divergent conclusions on pricing and reimbursement eligibility.**

The risk? Potential delays if national bodies request additional clinical data beyond what was submitted for JCA. **However, JCA may provide substantial benefits for EU countries with limited HTA infrastructure, offering them a standardized, high-quality clinical evidence report that can serve as a reliable foundation for national decisions.** This could help accelerate assessments, improve consistency, and reduce duplication of effort across the EU, while more established HTA bodies are likely to maintain complementary national requirements.

🎯 In simple terms, **JCA provides a joint clinical evidence report on relative clinical value** (efficacy, safety, patient-relevant outcomes, comparators), **but excludes all economic, ethical, societal, or country-specific appraisal aspects. National bodies remain fully responsible for pricing, reimbursement, and local evaluations.**

➡️ Companies must still **plan beyond JCA, on a country by country level,** to ensure smooth market access across Europe

💡 **Key Takeaways:**

✅ **JCA does not replace national HTA assessments, it informs but does not dictate local reimbursement outcomes**

✅ **Variability in how countries integrate JCA conclusions may lead to differences in pricing, reimbursement, and market access timelines**

France's Position : National Sovereignty Maintained [4]

- **HTA remains national:** JCA reports will serve as supportive evidence but do not replace HAS assessments. Full reimbursement dossiers still required
- **Supplementary analyses:** HAS may request additional data (e.g. French comparators, population specifics, real-world practice)
- **No legal overhaul:** Only procedural adjustments via ministerial decrees (e.g. dossier structure), not new laws
- **Scientific advice shift:** EU Joint Scientific Consultation (JSC) takes priority; Medicines that have undergone or plan to undergo JSC will not be eligible for early scientific advice at the national level. National early scientific advice remains available but is now exclusively provided in written format
- **Data rules:** JCA data accepted; any post-JCA data or additional evidence may still be requested

👉 **In short:** France is embracing JCA as a collaborative tool, not a replacement. They are refining processes to integrate JCA outputs more efficiently while preserving their autonomy and rigor in HTA decision-making.

[4] Haute Autorité de Santé

Strategic Recommendations: How to Prepare for JCA

The EU Joint Clinical Assessment is not just an additional hurdle, it is a fundamental shift in how clinical evidence will be assessed across Europe.

Early insights confirm that **high PICO volumes** could be expected, **especially in complex areas like oncology and ATMPs**, where fragmented treatment landscapes and multiple guidelines drive PICO granularity. At the same time, **compressed timelines leave no room for late adjustments**.

To successfully navigate JCA, manufacturers must **shift from a reactive to a proactive** strategy, embedding JCA readiness into their development and evidence-generation plans as early as Phase II and while designing phase III protocol. Key steps include:

✅ **Integrate JCA strategy into clinical development planning early,** align trial designs, endpoints, and comparators with expected EU-wide PICOs

✅ **Conduct internal PICO simulations** to stress-test evidence generation and anticipate worst-case high-PICO scenarios

✅ **Ensure early cross-functional collaboration** across Regulatory, Clinical, RWE, Market Access, and Biostatistics to avoid late-stage gaps

✅ **Monitor national HTA adaptations** to understand how JCA will be incorporated at the country level

Importantly, JCA is not a joint early dialogue, it is a binding joint assessment that sets the tone for national HTA discussions. However, while JCA is reshaping the evaluation of clinical evidence at the EU level, it does not replace national HTA processes. Pricing, reimbursement, and economic assessments remain firmly under the jurisdiction of individual member states, meaning that market access challenges will still vary across countries.

🧪 **The ongoing assessments of tovorafenib (pediatric low-grade glioma) and lifileucel (ATMP for metastatic melanoma), the first products to enter the full JCA process, will serve as real-world test cases, offering the first concrete insights into how the JCA operates in practice beyond the earlier PICO pilot exercises.**

🔑 **Ultimately, success in JCA will depend on early preparation, robust evidence generation, and a coordinated strategy, not just for JCA itself but for navigating national HTA landscapes to secure patient access across Europe.**

💬 ***How is your company preparing for JCA?***

Let's exchange insights!

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