EU Joint Clinical Assessment – One for All and All for One?

Anke van Engen  
Managing Principal, Value & Payer Evidence

Anne Willemsen  
Co-Chair, Subgroup for Joint Clinical Assessments

James Ryan  
Director, Global HTA Policy, HTA & Modelling Science

Kim Helleberg Madsen  
Director of Department, Pharmacoeconomics & Availability

This session will include some polling questions – in your app, go to the Q&A/Polling section under Resources in the session page to provide your answers.

The app can be downloaded by scanning the QR code in your programme guide.
The HTA Regulation aims to improve and accelerate patients’ access to new health technologies in the EU

- **Harmonize health technology assessment methodologies across 27 EU member states**
- **Establish predictability of HTA outcomes**
- **Avoid duplication of effort when submitting and reviewing the dossier**
- **Accelerate patients’ access to new medicines**

**Abbreviations**: EU: European Union; HTA: Health technology assessment
The two main elements of the HTAR are scientific advice and assessment of clinical effectiveness & safety on an EU level

**Joint Scientific Consultation (JSC)**

Scientific advice on study design – targeted towards JCA expectations

Can be conducted in parallel with the EMA

Optional and non-binding

Confidential, but deviations from this advice will be publicly visible in JCA report later

**Joint Clinical Assessment (JCA)**

Pan-EU HTA with publicly visible outcome soon after regulatory approval, able to be leveraged by all Member States

Mandatory and in addition to current country-specific processes

No reimbursement or pricing outcome; this continues to be assessed at the country level

Abbreviations: EMA: European Medicines Agency; EU: European Union; HTA: Health technology assessment regulation; JCA: Joint clinical assessment; JSC: Joint scientific consultation
The new EU HTA process introduces an EU-level HTA but will not replace national HTA processes

**DOMAINS OF THE CORE HTA MODEL**

<table>
<thead>
<tr>
<th>Health problem and current use of technology</th>
<th>Description and technical characteristics</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical effectiveness</strong></td>
<td><strong>Cost and economic considerations</strong></td>
<td><strong>Ethical analysis</strong></td>
</tr>
<tr>
<td><strong>Organizational aspects</strong></td>
<td><strong>Patient and social aspects</strong></td>
<td><strong>Legal aspects</strong></td>
</tr>
</tbody>
</table>

The JCA will still require national HTA bodies to assess clinical added value & economic value

No value judgement or conclusions on the overall clinical added value, or economic value

It will evaluate the degree of certainty of the relative effects considering the strengths and limitations of available evidence

JCA subject to requirements of all EU HTA bodies, and “given due consideration”, but content is not binding

JCA should meet requirements of all Member States - “One country, one vote”

Member States cannot request at national level the same information, data, analyses or other evidence that has been already submitted at EU level

Abbreviations: EU: European Union; HTA: Health technology assessment; JCA: Joint clinical assessment

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EUnetHTA 21 has outlined an approach to consolidate the EU PICO based on a survey of the 27 MS

### Conserved PICO

<table>
<thead>
<tr>
<th>PICO</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Full</td>
<td>Full</td>
<td>Full</td>
<td>Subpop A</td>
<td>Subpop B</td>
</tr>
<tr>
<td>Comparator</td>
<td>Drug 1 OR 2</td>
<td>Drug 3</td>
<td>Drug 4</td>
<td>Drug 1</td>
<td>Drug 3</td>
</tr>
<tr>
<td>Outcomes</td>
<td>All</td>
<td>All</td>
<td>All</td>
<td>All</td>
<td>All</td>
</tr>
</tbody>
</table>

Source: Adapted from EUnetHTA 21. Practical Guideline: D4.2 Scoping Process v1.1; August 2023. Abbreviations: CSCQ: Committee for Scientific Consistency & Quality; CTD: Common technical document; EMA: European Medicines Agency; EU: European Union; HTD: health technology developer; MS: Member state(s); PICO: population, intervention, comparator, outcome

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To understand the potential PICO burden, the consolidated EU PICOEs for a hypothetical product in NSCLC were simulated.

**Product X trial design**

**P**

1L metastatic non-small cell lung cancer, no sensitizing EGFR mutation or ALK translocation
Stratification factors: gender, PD-L1 status, squamous vs non-squamous histology

**I**

Hypothetical product X

**C**

Platinum-based chemotherapy

**O**

Primary endpoint: OS
Secondary endpoints: PFS; ORR; DoR; TTR; ORR, PFS & OS by PD-L1
Safety: Serious AEs; Discontinuation/deaths due to AEs
QoL: EQ-5D; LCSS

**Treatment landscape**

11 EMA approved regimens for 1L NSCLC without actionable mutations.

Latest regimen approved by EMA was **nivolumab in combination with ipilimumab** and 2 cycles of platinum-based chemotherapy.

Six of the 27 MS had a published HTA report for this regimen.

ESMO guidelines recommended pembrolizumab or atezolizumab combination therapies as standard options for patients with non-squamous and squamous disease (regardless of PD-L1 expression) and pembrolizumab monotherapy for patients with PD-L1 ≥50%.

Abbreviations: AE: Adverse event; BICR: Blinded, independent, central review; DOR: Duration of treatment; EGFR: Epidermal growth factor receptor; EQ-5D-3L: European Quality of Life 5 Dimensions 3 Level Version; ESMO: European Society for Medical Oncology; LCSS: Lung cancer symptom scale; NSCLC: Non-small cell lung cancer; ORR: Overall response rate; OS: Overall survival; PFS: Progression-free survival; PICO: Population, intervention, comparator, outcome; TTR: Time to treatment.
As an example, the Danish PICO for nivolumab included 4 PICOs, varying based on population & comparator

<table>
<thead>
<tr>
<th>PICO</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Non-squamous or squamous histology; PD-L1 expression ≥ 50%</td>
<td>Non-squamous histology; PD-L1 expression &lt; 50%</td>
<td>Squamous histology; PD-L1 expression ≥ 1% to &lt; 50%</td>
<td>Squamous histology; PD-L1 expression &lt; 1%</td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>Pembrolizumab monotherapy</td>
<td>Pembrolizumab in combination with carboplatin and pemetrexed</td>
<td>Pembrolizumab in combination with carboplatin and a taxane</td>
<td>Carboplatin in combination with vinorelbine or gemcitabine or paclitaxel</td>
</tr>
</tbody>
</table>


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Based on the assessments by 6 countries the anticipated number of PICOs for Product X would be 10

1-4
PICO per country
Inclusion of NICE increased the number of PICOs for the JCA to 14

50%
Based on an RCT
For 5 out of the 10 PICOs head-to-head RCT data would be available (of the 14 with NICE, 6 would have H2H evidence)

50%
Requested by one country
Inclusion of NICE increased the number to 7

1L NSCLC

<table>
<thead>
<tr>
<th>HYPOTHETICAL SCENARIOS</th>
<th>EU HTA reports</th>
<th>EU + NICE report¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Populations</td>
<td>EMA label + 8 subpopulations</td>
<td>EMA label + 10 subpopulations</td>
</tr>
<tr>
<td>Comparators</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Number of PICOs</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Number of PICOs requested by single MS (%)</td>
<td>5 (50%)</td>
<td>7 (50%)</td>
</tr>
<tr>
<td>PICOs requiring ITC (%)</td>
<td>5 (50%)</td>
<td>8 (57%)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>28</td>
<td>28</td>
</tr>
</tbody>
</table>

¹ Includes NICE, as a proxy of remaining MS

Abbreviations: H2H: Head-to-head; MS: Member state(s); NICE: National Institute for Health and Care Excellence; NSCLC: Non-small cell lung cancer; PICO: Population, intervention, comparator, outcome; RCT: Randomized controlled trial