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

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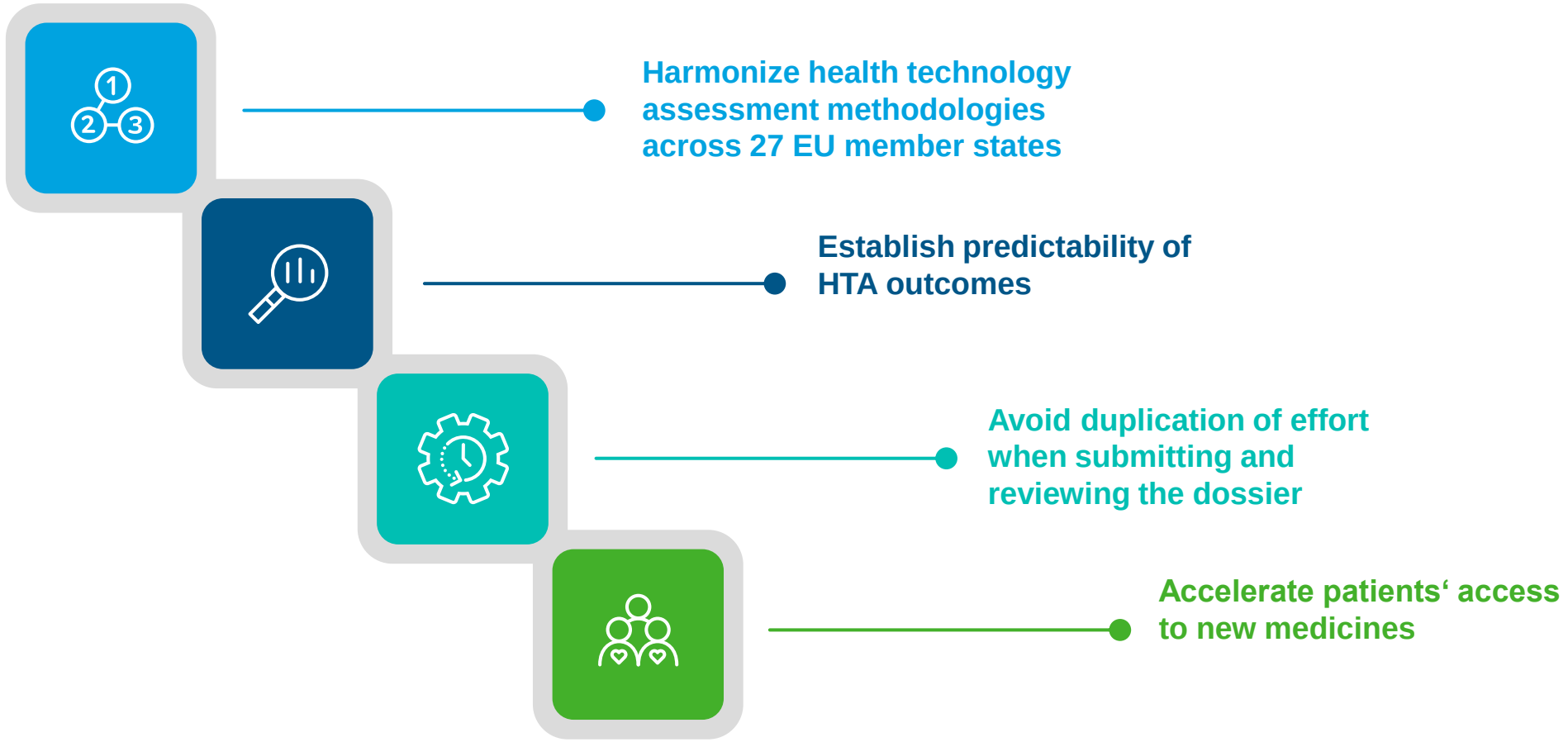
*This session will include some polling questions – in your app, go to the **Q&A/Polling section under Resources** in the session page to provide your answers*

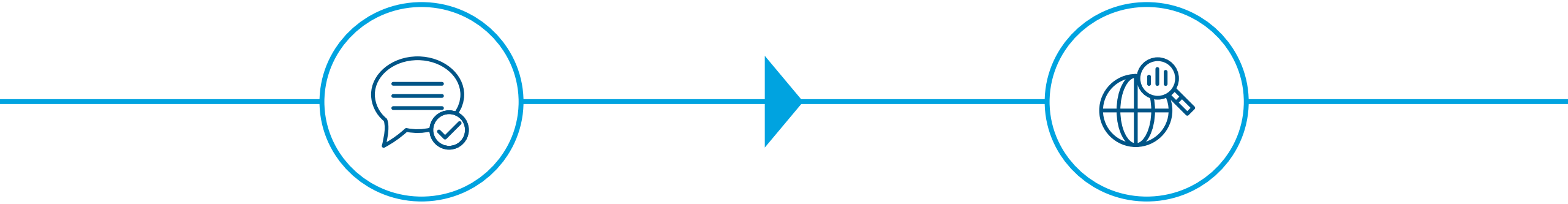
The app can be downloaded by scanning the QR code in your programme guide

The HTA Regulation aims to improve and accelerate patients' access to new health technologies in the EU



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

Health problem and current use of technology	**Description and technical characteristics**	**Safety**
Clinical effectiveness	Cost and economic considerations	Ethical analysis
Organizational aspects	Patient and social aspects	Legal aspects

In JCA scope *In scope of national HTA bodies*

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

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

1. Submission of CTD to EMA
2. Creation of PICO survey by JCA secretariat
3. PICO survey filled in by all 27 MS

Plus 23 responses. MS encouraged to involve local patient and clinical experts

Country 1

Population	Full
Comparator	Drug 1 *OR* Drug 2

Country 2

Population	Full	Subpop A	Subpop B
Comparator	Drug 1 *OR* Drug 2 *OR* Drug 3	Drug 1 *OR* Drug 3	Drug 3

Country 3

Population	Subpop A	Subpop B
Comparator	Drug 1 *OR* Drug 2	Drug 2 *OR* Drug 3

Country 4

Population	Full
Comparator	Drug 3 *AND* Drug 4

…

4. PICO consolidation by assessors
5. PICO validation during JCA CSCQ meeting

Consolidated PICOs

PICO	1	2	3	4	5
Population	Full	Full	Full	Subpop A	Subpop B
Comparator	Drug 1 **OR** 2	Drug 3	Drug 4	Drug 1	Drug 3
Outcomes	All	All	All	All	All

Each PICO will contain only 1 population & 1 comparator. PICO consolidated as much as possible but must meet needs of all MS. ***No involvement of HTD***

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

To understand the potential PICO burden, the consolidated EU PICOs 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

PICO	1	2	3	4
Population	Non-squamous or squamous histology; PD-L1 expression ≥ 50%	Non-squamous histology; PD-L1 expression < 50%	Squamous histology; PD-L1 expression ≥ 1% to < 50%	Squamous histology; PD-L1 expression < 1%
Comparator	Pembrolizumab monotherapy	Pembrolizumab in combination with carboplatin and pemetrexed	Pembrolizumab in combination with carboplatin and a taxane	Carboplatin in combination with vinorelbine or gemcitabine or paclitaxel
Outcomes	1. Overall survival 2. Progression-free survival 3. Objective response rate 4. Duration of response 5. Serious adverse events 6. Discontinuation due to adverse events 7. Deaths related to adverse events	1. Overall survival 2. Progression-free survival 3. Objective response rate 4. Duration of response 5. Serious adverse events 6. Discontinuation due to adverse events 7. Deaths related to adverse events	1. Overall survival 2. Progression-free survival 3. Objective response rate 4. Duration of response 5. Serious adverse events 6. Discontinuation due to adverse events 7. Deaths related to adverse events	1. Overall survival 2. Progression-free survival 3. Objective response rate 4. Duration of response 5. Quality of life (assessed by EQ-5D-3L and LCSS) 6. Serious adverse events 7. Discontinuation due to adverse events 8. Deaths related to adverse events

Source: Medicinrådets. Nivolumab (Opdivo) in combination with ipilimumab (Yervoy) and 2 cycles of platinum-based chemotherapy for the first-line treatment of metastatic non-small cell lung cancer in adults; 2022. Abbreviations: EQ-5D-3L: European Quality of Life 5 Dimensions 3 Level Version; LCSS: Lung cancer symptom scale; NSCLC: Non-small cell lung cancer; PICO: Population, intervention, comparator, outcome

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

HYPOTHETICAL SCENARIOS	1L NSCLC	
	EU HTA reports	EU + NICE report[1]
Populations	EMA label + 8 subpopulations	EMA label + 10 subpopulations
Comparators	9	9
Number of PICOs	10	14
Number of PICOs requested by single MS (%)	5 (50%)	7 (50%)
PICOs requiring ITC (%)	5 (50%)	8 (57%)
Outcomes	28	28

[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