HTA200

Understanding Joint Clinical Assessment scoping requirements in oncology: Results of a rapid PICO prediction exercise via an in-house expert network

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Background

- Starting 12 January 2025, all cancer medicines and advanced therapy medicinal products (ATMPs) with new active substances, for which an application for marketing authorization is submitted to the European Medicines Agency, will undergo a Joint Clinical Assessment (JCA), involving all 27 European Union (EU) Member States[1].
- The scoping process is a fundamental part of the JCA, defining the PICO (population, intervention, comparator, outcome) requirements to be addressed by Health Technology Developers (HTDs) in the HTD submission dossier[1].
- In 2023, the European Network for Health Technology Assessment (EunetHTA) 21 conducted PICO exercises to provide insights on the likely extent of the data to be presented in the HTD submission dossier[2].

Objectives

- To simulate the PICO scoping process by assessing a hypothetical new drug (Cenpicomab) for adults with metastatic castration-resistant prostate cancer across 16 EU Member States.
- To extend the scope of EUnetHTA 21's PICO exercise for Pluvicto (Lutetium [^{177}Lu] vipivotide tetraxetan)[3], considering requirements from 8 additional countries and the most recently launched comparators.

Methods

- A targeted review of European and national guidelines and past HTAs from 16 EU countries was conducted in May 2024.
- PICOs were collected through an online survey with Cencora in-house market access experts located throughout the region and consolidated based on the EUnetHTA 21 scoping process practical guideline[4].

Results

- **Country-specific PICOs** were obtained in a **3-week timeframe**, including a 1-week clarification phase.
- **Four subpopulations** were identified in addition to the full population defined in the hypothetical target product profile. **Subpopulations were requested by 11 out of 16 countries**. France, Greece, Poland, Portugal, and Spain did not state any subgroups. The Czech Republic was the only country in which the full population was not considered relevant (**Table 1**).
- In total, **11 comparators were identified** for the assessment scope. The number of relevant comparators for the national assessments ranged from 1 in Greece to 10 in Ireland.
- While for most countries, evidence on at least 1 of the comparators was likely sufficient, **5 out of 16 countries** (Germany, Ireland, Italy, Portugal, and Spain) **would request data against each of the identified comparators,** ranging from 2 comparators in Italy to 7 comparators in Portugal.
- Differences in national PICO requirements resulted in **18 consolidated PICOs; of which, 9 were for the full population** (**Table 2**), 3 were for **Subpopulation 1 and 2** each, 2 were for **Subpopulation 3,** and 1 for **Subpopulation 4**. Two locally identified comparators for the full population were not considered in the consolidated PICOs (Flutamide, Belgium; platinum-based chemotherapy, Finland).
- In total, **20 relevant clinical outcomes** for the assessment scope were identified. The number and type of relevant outcomes differed between countries and ranged from 2 in the Netherlands to 19 in Ireland. **Overall survival was the only outcome that was considered relevant by all assessed countries**, followed by grade ≥3 adverse events (n=14) and radiological progression-free survival (n=13) (**Figure 1**).

Table 1. Relevant populations identified for the JCA scope of Cenpicomab (hypothetical drug)

Population		Countries	
Full population	Adult patients with progressive PSMA-positive mCRPC who have been treated with androgen receptor pathway inhibition and taxane-based chemotherapy	**15/16**	BE, DE, DK, ES, FI, FR, GR, IE, IT, LU, NL, NO, PO, PT, SE
Subpopulation 1	Full population + symptomatic bone metastases and no known visceral metastasis	**9/16**	BE, CZ, DK, IE, IT, LU, NL, NO, SE
Subpopulation 2	Full population + BRCA1/2 mutation	**8/16**	DE, DK, FI, IE, IT, NL, NO, SE
Subpopulation 3	Full population + contraindication for chemotherapy and HRR mutation	**4/16**	DE, FI, NO, SE
Subpopulation 4	Full population differentiated by performance score (cut-off value 2) and/or presence of visceral metastases	**1/16**	DK

Key: BE: Belgium; BRCA1/2: BReast CAncer gene 1/2; CZ: Czech Republic; DE: Germany; DK: Denmark; ES: Spain, FI: Finland; FR: France; GR: Greece; HRR: homologous recombination repair; IE: Ireland; IT: Italy; JCA: Joint Clinical Assessment; LU: Luxembourg; mCRPC: metastatic castration-resistant prostate cancer; NL: Netherlands; NO: Norway; PO: Poland; PSMA: prostate-specific membrane antigen; PT: Portugal; SE: Sweden.

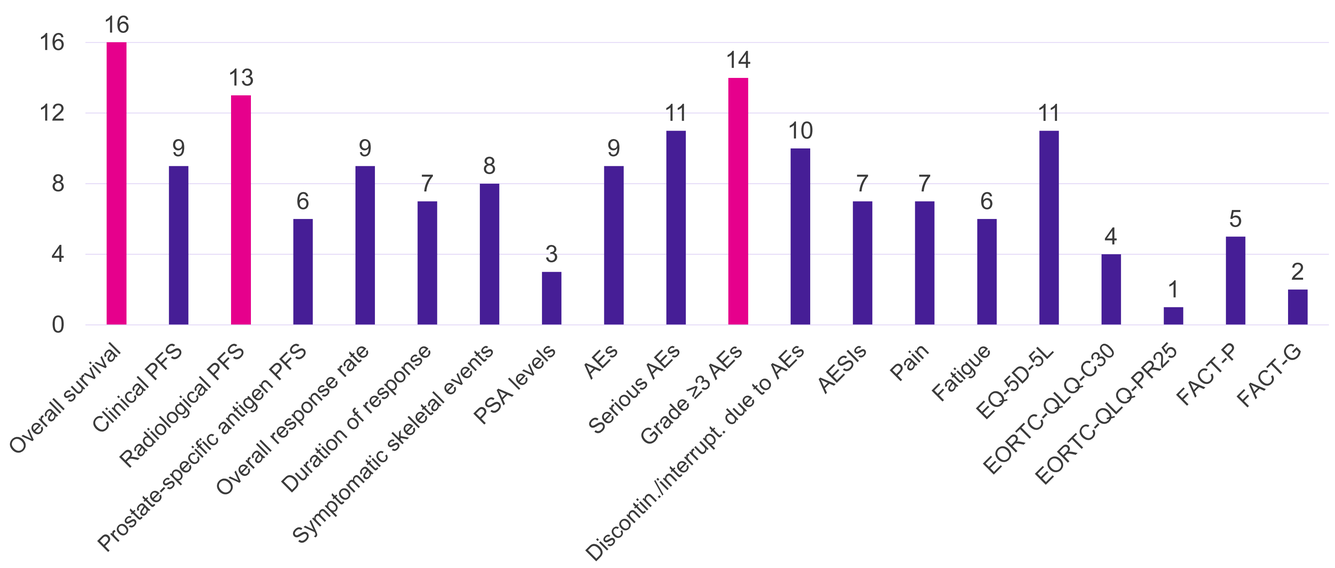
Table 2. Consolidated PICOs for the full population for Cenpicomab (hypothetical drug)

	PICO 1	PICO 2	PICO 3	PICO 4	PICO 5	PICO 6	PICO 7	PICO 8	PICO 9
Population	**Full population**								
Intervention	*Cenpicomab (hypothetical drug)*								
Comparator	Abiraterone+ prednisone/ prednisolone	Best supportive care*	Cabazitaxel+ prednisone/ prednisolone*	Docetaxel+ prednisone/ prednisolone*	Enzalutamide	Lutetium (177Lu) vipivotide tetraxetan+ androgen deprivation therapy*	Olaparib*	Radium-223*	Radium-223+ luteinizing hormone-releasing hormone analogue*
Outcomes	*See Figure 1*								
Countries	BE, **DE**, FI, FR, **IE**, LU, NL, NO, **PT**, SE	**DE**, DK, **ES**, FI, **IE**, NL, NO, SE	BE, **DE**, DK, **ES**, FI, **IE**, **IT**, LU, NL, NO, **PT**, SE	BE, DK, FI, **IE**, LU, NL, NO, **PT**, SE	BE, **DE**, DK, FI, FR, **IE**, LU, NL, NO, **PT**, SE	BE, **DE**, FI, GR, **IE**, **IT**, NL, PO, **PT**	DK, **PT**	**ES**, FI, PO	PO, **PT**

Note: Countries in **bold** represent the countries the PICO was derived from due to the request for data against all identified comparators.
*Comparators also considered in PICOs for subpopulations (not presented here).

Key: BE: Belgium; CZ: Czech Republic; DE: Germany; DK: Denmark; ES: Spain, FI: Finland; FR: France; GR: Greece; IE: Ireland; IT: Italy; LU: Luxembourg; NL: Netherlands; NO: Norway; PICO: population, intervention, comparator, outcome; PO: Poland; PT: Portugal; SE: Sweden.

Figure 1. Number of countries requesting data against specified clinical outcomes



Note: Pink columns indicate top 3 outcomes requested by countries.

Key: AE: adverse event; AESI: AE of special interest; EORTC-QLQ(-PR25): European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (-Prostate); EQ-5D-5L: EuroQol-5 Dimension-5 Level; FACT-G: Functional Assessment of Cancer Therapy-General; FACT-P: Functional Assessment of Cancer Therapy-Prostate; PFS: progression-free survival; PSA: prostate-specific antigen.

Conclusions

- Our analysis indicates that a **2- to 3-week timeframe would be sufficient to collect comprehensive country PICOs** via an online survey with local market access experts.
- Comparing our results to the outcomes from EUnetHTA 21's PICO exercise for Pluvicto, where 6 consolidated PICOs across 8 countries were defined[3], we confirmed that **considering variations in clinical guidelines and treatment standards across <u>all</u> EU Member States** at the time of the scoping may **lead to numerous consolidated PICOs in oncology indications.**
- These **findings are in line with a recent simulation by the European Federation of Pharmaceutical Industries and Associations (EFPIA)** for 3 authorized oncology treatments, including orphan and ATMP, which resulted in a large number of potential PICOs across only 7 countries, ranging from 7 to 23 PICOs after consolidation[5].

- While PICO simulations allow HTDs to gain insights into country-specific responses, the **PICO scope defined within the JCA framework will not assign countries to specific PICOs, nor will it reveal the number of countries to which the PICO requirements apply.**
- With the final guidance for the scoping process by the Member State Coordination Group on Health Technology Assessment (HTA CG) still outstanding (as of 1 November 2024)[6], **details on the scoping procedure and implications for the JCA scope remain uncertain only 2 months before the start of the JCA.**

References

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