Navigating Prospective PICO Consolidation in Oncology: Insights from Retrospective Simulations for Crowded and Non-Crowded EU Treatment Landscapes

HTA216

Online version and linked evidence requirements analysis

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Objective

To simulate the EU JCA scoping process for a single oncology therapy in two indications, to explore how different treatment comparator landscapes impact the number of PICOs generated.

Background

- Joint Clinical Assessment (JCA) will become mandatory for first-indication oncology drugs in 2025 and orphan medicines in 2028.
- Manufacturers remain concerned around the potentially large number of populations, interventions, comparators and outcomes (PICOs) to be addressed in manufacturer dossiers, to be submitted within 100 days of scope determination.[1]
- Predicting PICOs will be crucial for manufacturers to proactively plan evidence strategies and allocate internal resource ahead of dossier development.

Methods

- Scoping was simulated for the anti-PD-L1 inhibitor avelumab in:[2]
  - The densely populated **first-line advanced renal cell carcinoma (RCC)** treatment landscape;
  - The sparsely populated **metastatic Merkel cell carcinoma (MCC)** treatment landscape, where avelumab launched as a **first-to-market, orphan drug**.
- Targeted searches of HTA bodies in the 27 EU member states identified publicly available appraisals, from which PICOs were consolidated per EUnetHTA21 scoping guidance.[3] Outcomes presented in published HTA records were also explored.
- A conservative approach was taken to consolidation, due to limited information available in published HTA documents and limited EUnetHTA21 scoping guidance:
  - It was assumed that all listed comparators were required, unless otherwise specified.
  - Physician's choice was considered a separate comparator, although it likely is a combination of other available comparators.
- National and European guidelines for RCC and MCC were also sourced through targeted searches and reviewed to identify additional PICOs. Searches were limited to guidelines published ahead of avelumab's marketing authorisation in each indication, to reflect the treatment landscape at the time of HTA. In this poster, a PICO refers to a set of one population, one comparator and all associated outcomes.

Results

PICOs from Published HTA Records

- Published HTA records yielded 24 PICOs for RCC and 9 PICOs for MCC pre-consolidation.
- Considerably more PICOs were identified for RCC than MCC, driven by the higher number of RCC comparators and subpopulations (**Figures 1** and **2**).
- Many single-state PICOs in RCC were observed; this was driven by the Portuguese appraisal, where 4 unique subpopulations contributed 8 additional PICOs.

PICOs from Guidelines

- Guidelines identified an additional 8 comparators and 1 subpopulation for RCC, and an additional 6 comparators for MCC, substantially increasing the total PICO number for both indications (**Figures 1** and **2**).
- Of PICOs identified in published HTA records, 68% (15/22) and 88% (7/8) were also found in guidelines for RCC and MCC, respectively.

Outcomes Included in Published HTA Records

- RCC and MCC records included 46 and 20 outcomes, respectively. The most frequent outcomes (in over half of appraisals) were common oncology endpoints:
  - **RCC:** Overall survival (OS), progression-free survival (PFS), number of adverse events (AEs).
  - **MCC:** OS, PFS, overall response rate, best objective response, duration of response, number of Grade ≥3 AEs.
- There was variation in the health-related qualify-of-life outcomes presented, with no single measure presented for over a third of member states in either indication.
- 50% (23/46) of RCC outcomes and 30% (6/20) of MCC outcomes were presented for one member state only.

FIGURE 1

Number of PICOs identified from published national HTA records and guidelines

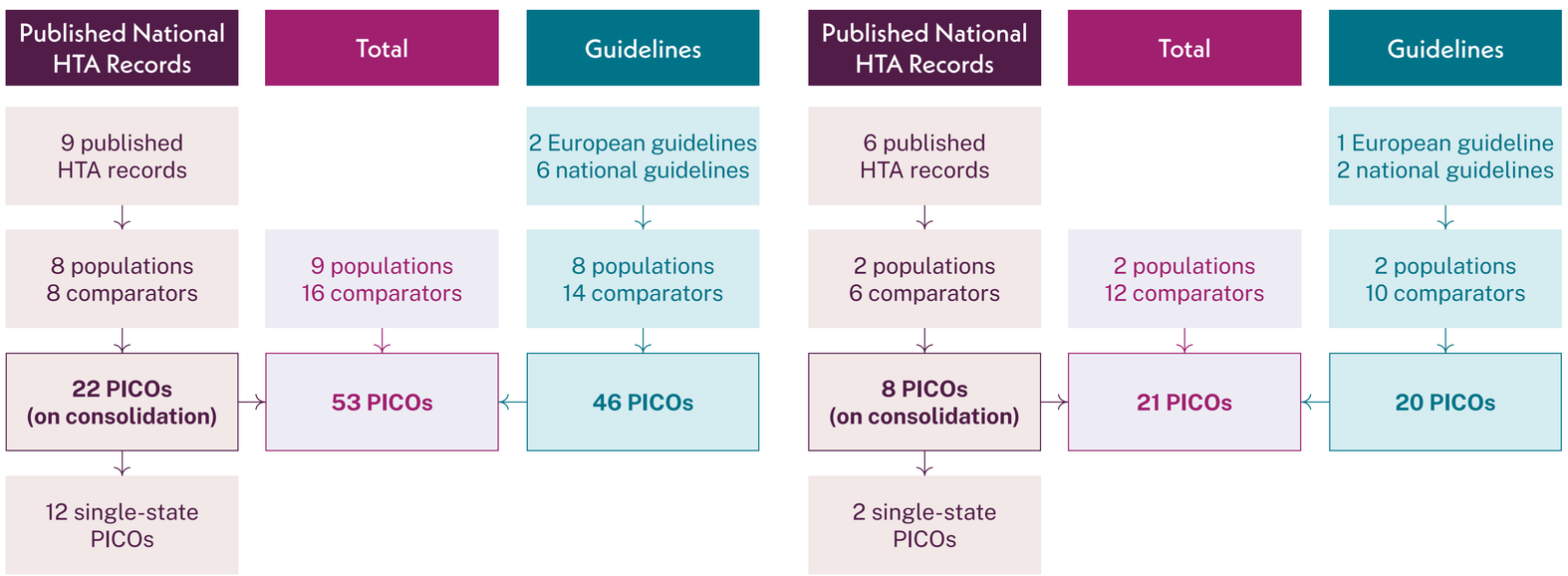
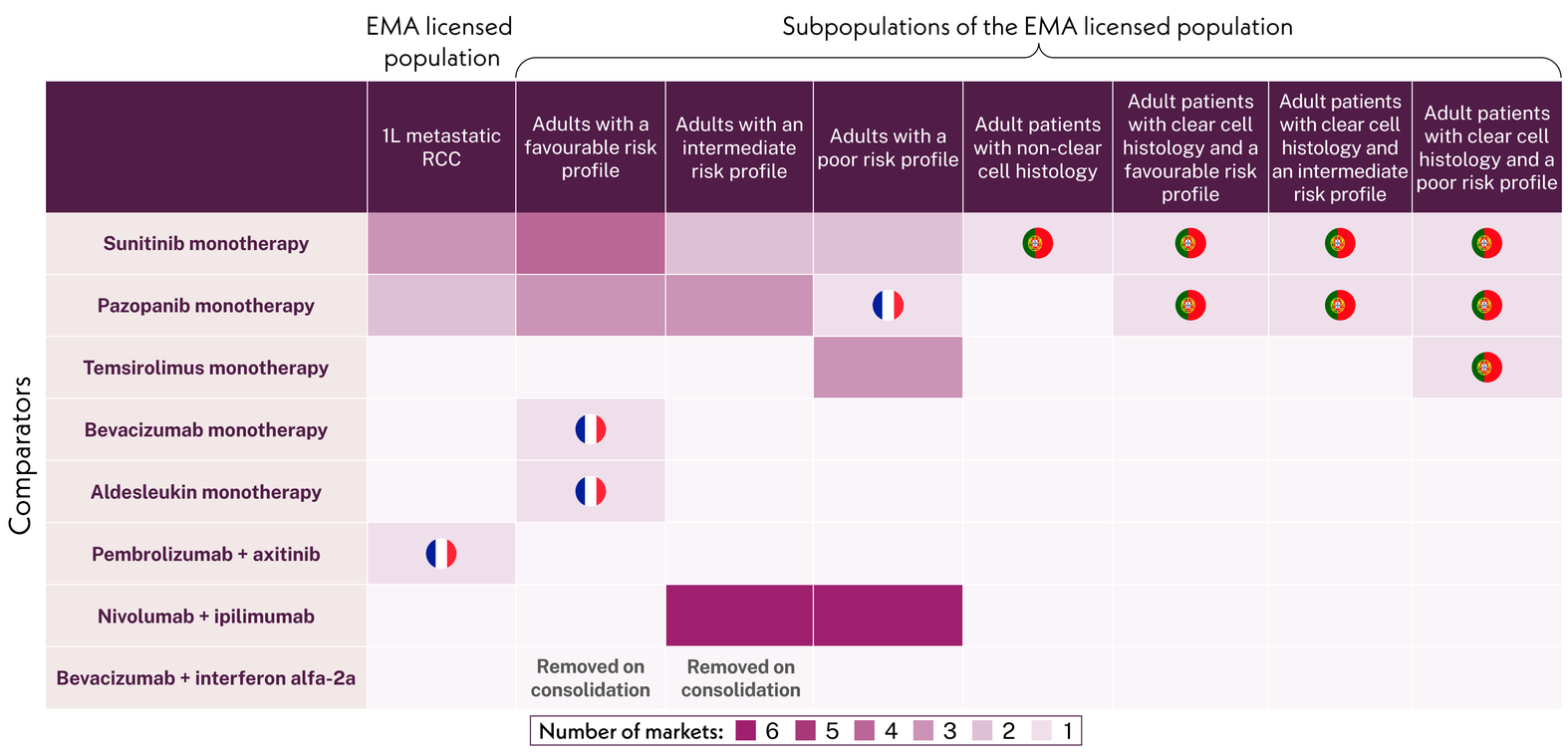


FIGURE 2

Composition of PICOs identified from published national HTA records only, and number of markets requiring each PICO



Key Takeaways for Industry

- Manufacturers may face a potentially large number of PICOs, particularly in dense treatment landscapes but also in less crowded indications where there are many subgroups.
- As guidelines captured the majority of PICOs, prospectively examining guidelines could provide a reasonably comprehensive assessment of likely comparators; local clinician consultation could address any remaining gaps.
- Investigating pragmatic HTA decisions and discussing different member state requirements with affiliates could help to further consolidate and prioritise PICOs, reducing their overall number.
- The large number and heterogeneity of outcomes presented across HTA submissions amplify difficulties associated with addressing a broad range of PICOs.
- Overall, this simulation exercise further highlights the challenges facing manufacturers in meeting evidence requirements for all identified PICOs.

PICOs identified from guidelines are not presented in this figure

Abbreviations: AE: adverse event; **CAV:** cyclophosphamide, doxorubicin and vincristine; **EU:** European Union; **EMA:** European Medicines Agency; **HTA:** Health Technology Assessment; **JCA:** Joint Clinical Assessment; **MCC:** Merkel cell carcinoma; **OS:** overall survival; **PFS:** progression-free survival; **PICO:** Population, Intervention, Comparator, Outcome; **RCC:** renal cell carcinoma.

References: [1]Eur-Lex. Document 32024R1381: Commission Implementing Regulation (EU) 2024/1381. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202401381 [Last accessed 13 Sep 24]; [2]European Medicines Agency. Bavencio Product Information. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/bavencio. [Last accessed 13 Sep 24]; [3]EUnetHTA 21. D4.2 Scoping Process. Available at: https://www.eunethta.eu/d4-2/ [Last accessed 13 Sep 24]; **Acknowledgements:** The authors thank Courtney Gray, Costello Medical, for graphic design assistance. We also thank Catherine Bunting and Alex Porteous for their review and editorial assistance in the preparation of this poster.

Presented at ISPOR Europe 2024 | Barcelona, Spain | 17–20 November