EU HTA is like a box of chocolates, you never know what you are going to get – Necessity for EU PICO simulations

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OBJECTIVES

In the EU HTA process, manufacturers receive a list with the demanded evidence in form of PICOs (Population, Intervention, Comparator, Outcome) 100 days before the JCA dossier submission deadline, the so called "assessment scope". On the one hand, these PICOs define the (demanded) JCA dossier content. On the other hand, this evidence package is the basis for the national HTA ratings and price negotiations – and therefore a central component for the EU market access strategy. Manufacturers must not be surprised by the assessment scope, anticipation is highly relevant. HTA bodies offer an early consultation (JSC) to give a "fair" view on expected PICOs, however, it takes place years before the actual JCA. This analysis aims to understand the indication-specific dynamics within PICOs over time to educate on what and how to optimally anticipate the PICO scope for the future.

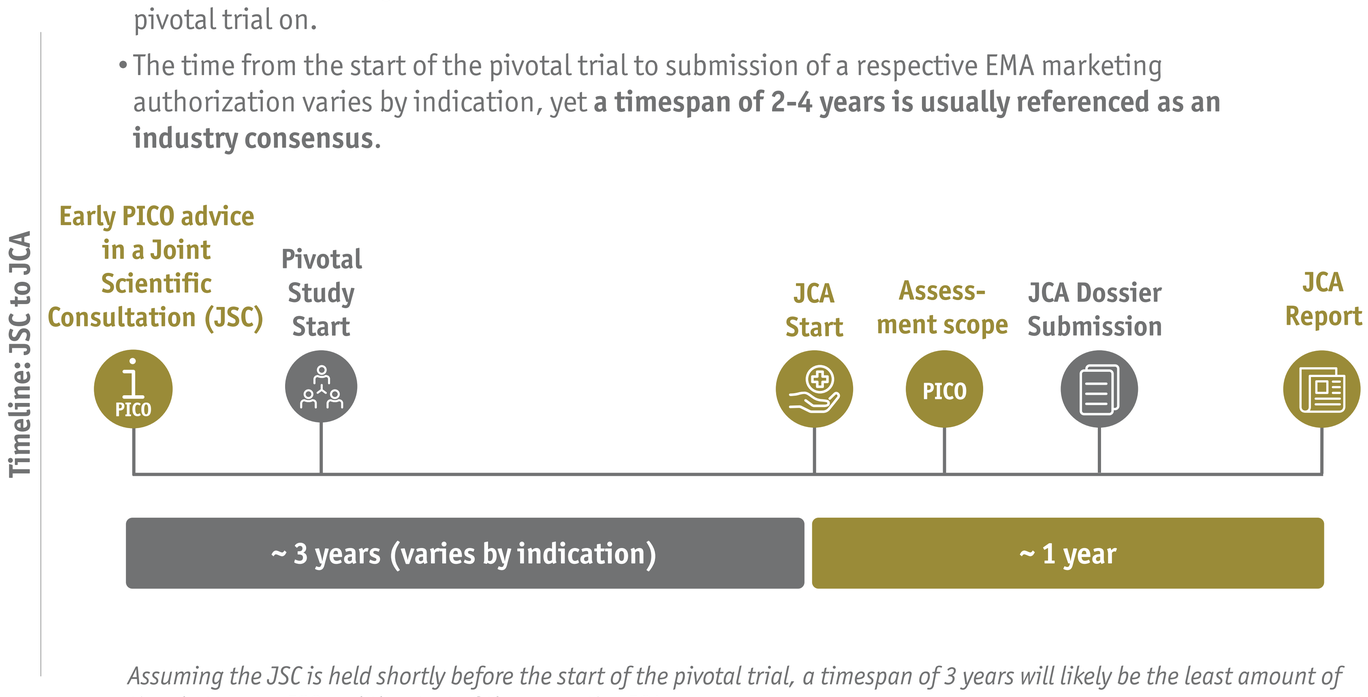
METHODS

1. Based on all German HTA procedures from 2011 to June 2024 (988), we analyzed average changes in the PICO scope to allow for extrapolation and categorization into less or more dynamic indications. Due to their imminent relevance in 2025 and overarching comparability, we focused on oncologic indications. In addition, a deep dive in plaque psoriasis was provided.
2. Indications were subdivided into reasonable and established categories, such as therapy lines, to account for both too small sample sizes and too broad areas of application. Both, assessments covering different therapeutic areas and potential reassessments were taken into consideration. A horizon scanning was performed to evaluate upcoming changes.

RESULTS

1 JSCs take place years before the actual JCA process

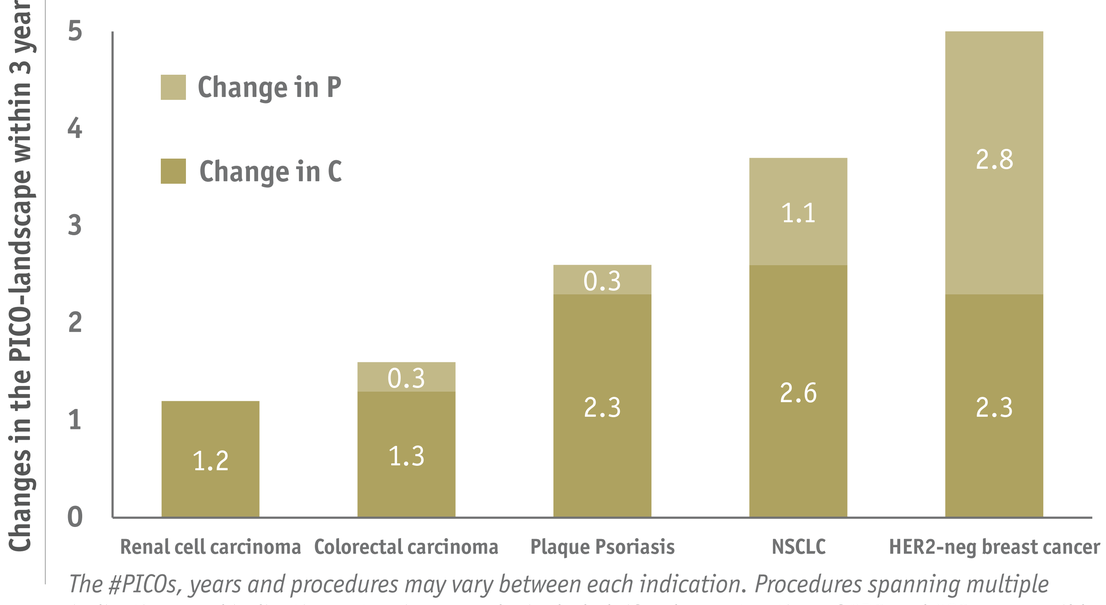
- JSCs shall provide a fair PICO recommendation but can only be done before the pivotal trials. According to the subgroup, the JSC will provide a basket of potential PICOs to build the pivotal trial on.
- The time from the start of the pivotal trial to submission of a respective EMA marketing authorization varies by indication, yet **a timespan of 2-4 years is usually referenced as an industry consensus**.



Assuming the JSC is held shortly before the start of the pivotal trial, a timespan of 3 years will likely be the least amount of time between a JSC and the start of the respective JCA.

2 In a few years, the PICO landscape can drastically change

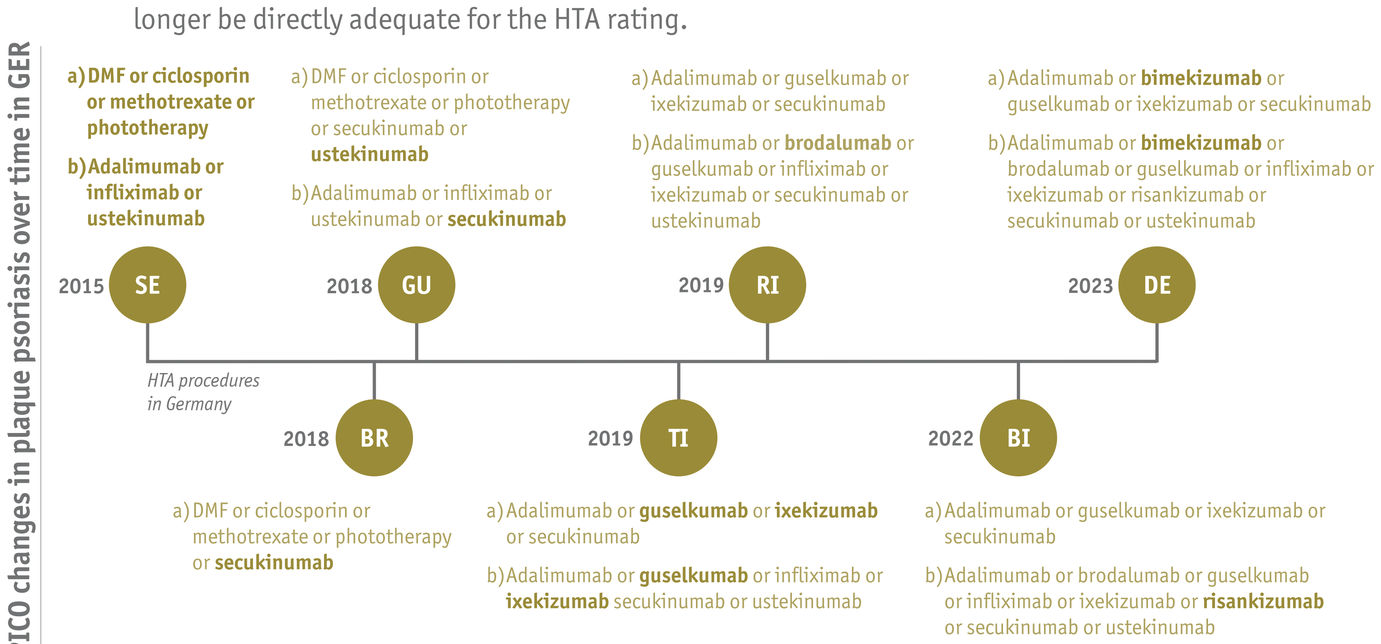
- We analyzed all German HTA procedures in view of changed populations ("P") and comparators ("C") within one indication.
- The median number of PICO changes during a 3-year timeframe was ~2.6 with a maximum of 5.1 changes of either a "P" or a "C" within one indication.



The #PICOs, years and procedures may vary between each indication. Procedures spanning multiple indications and indication extensions may be included, if a clear extraction of "P" and "C" was possible.

3 Case example – the therapeutic progress and its impact in plaque psoriasis

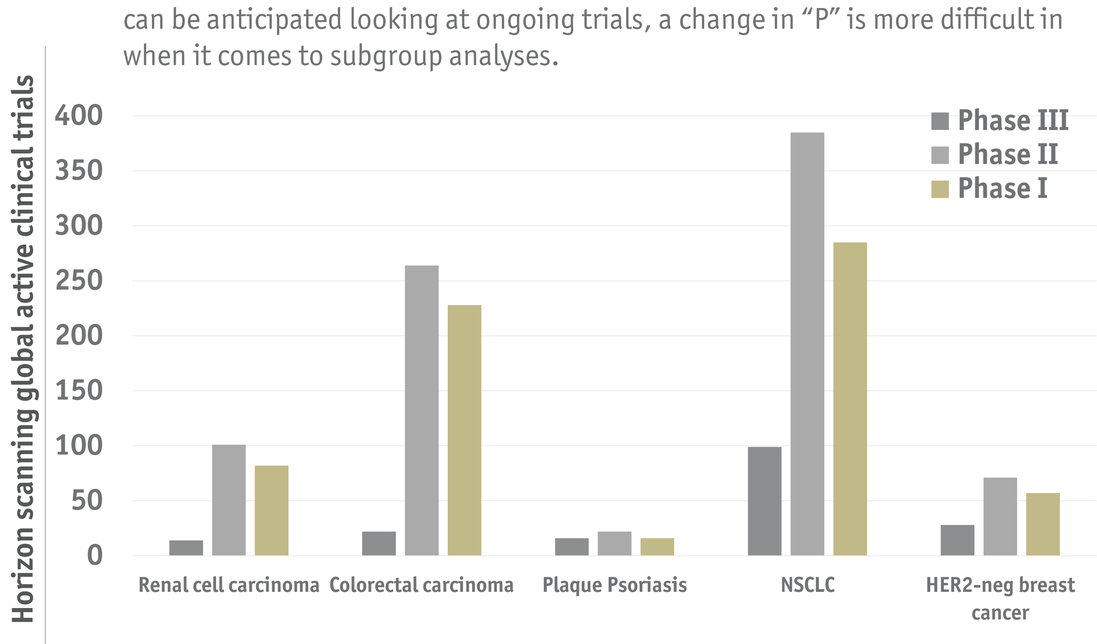
- Over the course of 9 years, the PICO landscape in plaque psoriasis successively changed.
- 5 out of 7 new entries became part of the comparator basket after their HTA process. Several 2015 comparators lost their relevance within 4 years, a respective controlled study would no longer be directly adequate for the HTA rating.



a) and b) describe the ACT for each requested PICO-population. The number of letters indicates the number of requested populations. If a same product was evaluated more than once, it is only shown once. Not all medicines that are approved for this therapeutic area are depicted.
Abbr.: BI: Bimekizumab; BR: Brodalumab; DE: Deucravacitinib; DMF: Dimethyl fumarate; GU: Guselkumab; PP: Plaque Psoriasis; RI: Risankizumab; SE: Secukinumab; TI: Tildrakizumab.

4 Ongoing clinical trials can be an indicator for indication dynamics

- Clinical development, especially in broader oncologic indications, shows no sign of slowing down in the next years.
- Horizon scanning should be part of a PICO simulation. Usually, a change in "C" can be anticipated looking at ongoing trials, a change in "P" is more difficult in when it comes to subgroup analyses.



All global clinical trials (as of Oct 2024) per indication are shown. If the same product is studied in different phases, all studies are shown.

CONCLUSION

- **PICOs change**: Considering the time from a JSC to actual submission of the JCA dossier, there is a **high likelihood of receiving different PICOs** in the assessment scope compared to the study planning phase.
- **Market dynamics need to be considered**: Especially in a **dynamic indication**, it can be expected that the **PICO landscape is affected by combinations of influencing factors** such as new entries as direct or indirect competitors, new distinct subgroups, derivations of the treatment cascade, complete paradigm shifts, e.g., with gene and cell therapies, and, for all of them, the evolving price spectrum.
- **Anticipation of PICOs is crucial:** The **PICOs fundamentally influence the chances of success or failure at the negotiation table**. And it is not only about the current situation, but also about anticipation of the situation when actually undergoing the EU HTA process. Manufacturers have to build **scenarios to foresee and evaluate all potential changes to their PICO scope**.
- **It can be done:** One could claim that nothing has changed - and it would be at least partially right. For an **optimal position at the negotiating table**, manufacturers must **anticipate the requirements and circumstances**, for example **regarding the SoC and the associated price level, as well as all relevant (future) influencing factors** along the way. Obviously, now the complexity and required efforts are higher, emphasizing the need for a more focused and tactical prioritization – yet **it can be done**!

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All analyses have been generated by data from SKC's proprietary MAIS (**Market Access Intelligence System** = MAIS) database. This database contains and links information on completed and ongoing benefit assessments according to §35a SGB V of the German Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA). The MAIS-database records and evaluates relevant information from the dossier, the benefit assessment by IQWiG or the G-BA, the G-BA resolution as well as the Lauer-Taxe. It also contains an up-to-date overview of all procedures and their status.

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