HTA229

PICO criteria applied in Joint Action 3 differ from national HTA requirements: A review of oncology drug assessments in Denmark, France, Germany, and Sweden

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Background

- From 2016 through 2021, the European Network for Health Technology Assessment (EUnetHTA) collaboration, incl. 81 organizations from 29 countries, produced joint health technology assessments (HTAs) under the Joint Action (JA3).
- With the implementation of the European Union HTA regulation (EU HTAR), Joint Clinical Assessments (JCAs) will be introduced on an EU level and become mandatory for oncology drugs in 2025, building on previous joint work from EUnetHTA.

Objective

- To compare the PICO (population, intervention, comparison, outcomes) criteria applied in JA3 assessment reports and respective national HTAs for oncology drugs and to explore potential implications for the JCA.

Methods

- JA3 reports of oncology drugs published between 2019 and 2021 were compared to the national HTA reports in Denmark, France, Germany, and Sweden.
- In addition to the PICO criteria, the study types considered, the results, and the conclusion of the reports were compared.

Results

- Between 2019 and 2021, three oncology drugs, venetoclax, glasdegib, and polatuzumab, were assessed in the JA3 framework (**Figure 1**).[1-3]
- National HTA bodies in Denmark, France, and Sweden assessed venetoclax and polatuzumab, while all three drugs were assessed in Germany (**Table 1**).[4-12]
- JA3 and national reports aligned particularly well regarding the populations and interventions, although Germany requested a subpopulation analysis for venetoclax (**Table 1**).
- While the JA3 reports covered national requirements in terms of comparators and outcomes overall, there were differences seen between the four national assessments for venetoclax and polatuzumab (**Table 1**).
  - Overall, Germany was less restrictive than other countries for the comparator in the case of orphan drugs (glasdegib, polatuzumab), but more restrictive regarding (patient-relevant) outcomes and study types considered.
  - Denmark and France included data from studies other than randomized controlled trials (observational data, data from an indirect comparison, and compassionate use data) for polatuzumab, and Sweden recognized supportive phase 1b study data for venetoclax.
- Despite slight differences in PICOs, overall conclusions on the additional benefit of the drugs vs comparators were similar between countries (**Table 1**).
- Only in one instance was the JA3 report utilized in a national assessment: The Swedish Dental and Pharmaceutical Benefits Agency (Tandvårds-och läkemedelsförmånsverket, TLV) based part of their national assessment on the JA3 report of polatuzumab.

Results (cont.)

- The other countries did not utilize the JA3 reports, even if they were involved in the joint assessments, but in two cases (glasdegib and polatuzumab) the French National Authority for Health (Haute Autorité de santé [HAS]) mentioned the JA3 reports but did not draw conclusions from it.
- This could partially be due to overlapping timelines of the assessment processes (see **Figure 1**).
  - The national assessment in France and Germany of venetoclax was facilitated in parallel to the JA3 report development. However, for glasdegib and polatuzumab, there seems to be no overlap in timelines, and the JA3 report was not utilized regardless.

Table 1. Similarities and differences between JA3 and national assessments

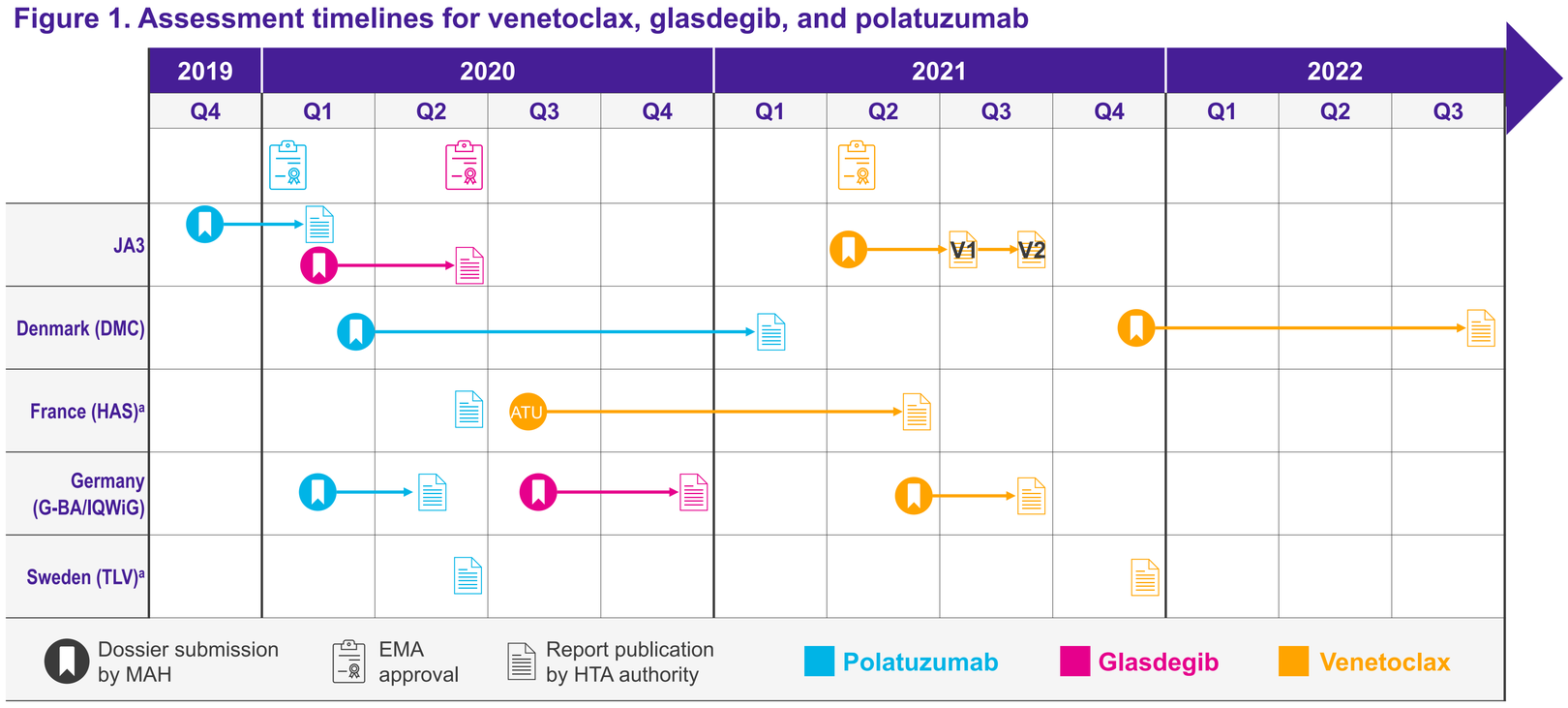
	Venetoclax				Glasdegib	Polatuzumab			
	DK	FR	DE	SE	DE	DK	FR	DE	SE
Population	✓	✓	✓ Subgroup analysis	✓	✓	✓	✓	✓	✓
Intervention	✓	✓	✓	✓	✓	✓	✓	✓	✓
Comparator(s)	✓	✓	✓	✓	X OD – no comparator predefined	✓ Considered additional comparators	✓	X OD – no comparator predefined	✓ Considered additional comparators
Outcome(s)	✓	✓	✓	✓	✓	✓	✓	✓	✓
Study types	✓	✓	✓	✓ Considered non-RCT data	✓	✓ Considered observational study data	✓ Considered IC and CU data	✓	✓
Conclusions on benefit[a]	✓	✓	✓	✓	NA	✓	✓	✓	✓

Key: DE – Germany; CU – compassionate use; DK – Denmark, FR – France; IC – indirect comparison; JA3 – Joint Action 3; NA – not applicable; OD – orphan drug; PICOS – population, intervention, comparison, outcomes, study types; RCT – randomized controlled trial; SE – Sweden.

Notes: ✓ National PICOS were in line with PICOS in the JA3 (ie, the nationally considered components were included in the JA3 report. This does not necessarily mean that for example all comparators, outcomes, or studies reported in JA3 have been considered in national assessments. ✓ National assessments were in line with JA3 reports but more restrictive compared to other countries. X PICOS included in JA3 were not considered.

[a] The conclusion on benefit was compared only for the individual countries since the JA3 reports do not include any judgments on the additional benefit of the drug. The comparison is made based on overall positive/negative conclusions from the assessments. Please note that assessment criteria differ between countries.

Figure 1. Assessment timelines for venetoclax, glasdegib, and polatuzumab



ATU – Authorization for Temporary Use; DMC – Danish Medicines Council; EMA – European Medicines Agency; G-BA – Gemeinsamer Bundesausschuss; HAS – Haute Autorité de santé; HTA – health technology assessment; IQWiG – Institute for Quality and Efficiency in Health Care; JA3 – Joint Action 3; MAH – Marketing Authorization Holder; TLV – Swedish Dental and Pharmaceutical Benefits Agency.

[a] The date of dossier submission is not known.

Conclusions

- Based on our findings, we conclude that national differences in European healthcare systems and treatment guidelines may lead to extensive PICO criteria in the JCA.
- To accelerate the overall HTA process in EU countries, it will be crucial that PICOs consolidated during the JCA scoping process are streamlined, while adequately addressing national requirements from all EU countries.
- From this analysis, additional data requirements from individual countries are to be expected, which could delay the entry of affected drugs in these countries.

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