How impactful is time to next treatment on health technology assessment outcomes in indolent cancers?

Jonathan Hailwood
Avalere Health, London, United Kingdom

Avalere Health™
EVERY PATIENT POSSIBLE.

HTA179

Introduction

- In certain indolent cancers, patients may cycle through multiple lines of treatment. Therefore, there is value in a new product delaying the time until a subsequent treatment is required.
- Time to next treatment (TTNT) is a means of operationalizing this time as a clinical trial endpoint and is considered a clinically relevant outcome in a number of indolent conditions.[1,2] As a trial endpoint, TTNT can capture additional clinical benefits of a new treatment beyond delaying disease progression, including the length of active surveillance, as well as adherence and tolerance.
- Despite its clinical relevance, the extent to which TTNT data can impact health technology assessment (HTA) outcomes is unclear.
- Understanding the impact of TTNT as an outcome is particularly important in indolent cancers, as it is challenging to demonstrate a benefit for the "gold-standard" endpoint of overall survival owing to the relatively high long-term survival rates associated with these conditions.

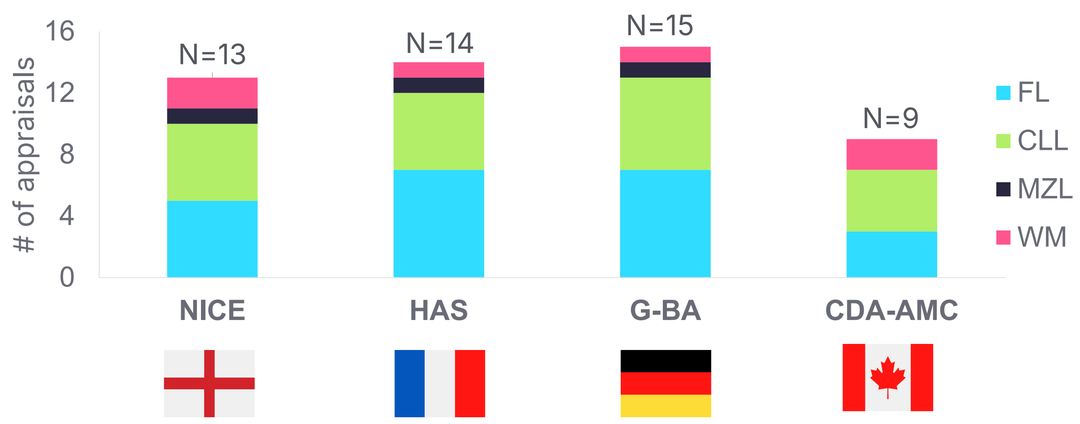
Objectives and Methods

- We conducted a targeted review of recent HTA reports of pharmaceutical products (March 2018-March 2025) from four influential HTA agencies: Canada (CDA-AMC), England (NICE), France (HAS), and Germany (G-BA).
- These agencies were chosen to include perspectives from both "cost-effectiveness" and "clinical-effectiveness" payer archetypes.
- Four indolent hemato-oncology conditions were included: chronic lymphocytic leukemia (CLL), follicular lymphoma (FL), marginal zone lymphoma (MZL), and Waldenström's macroglobulinemia (WM).
- HTA reports were manually screened for information relating to TTNT, including whether any data were submitted and whether any committees provided commentary on this outcome.

Results

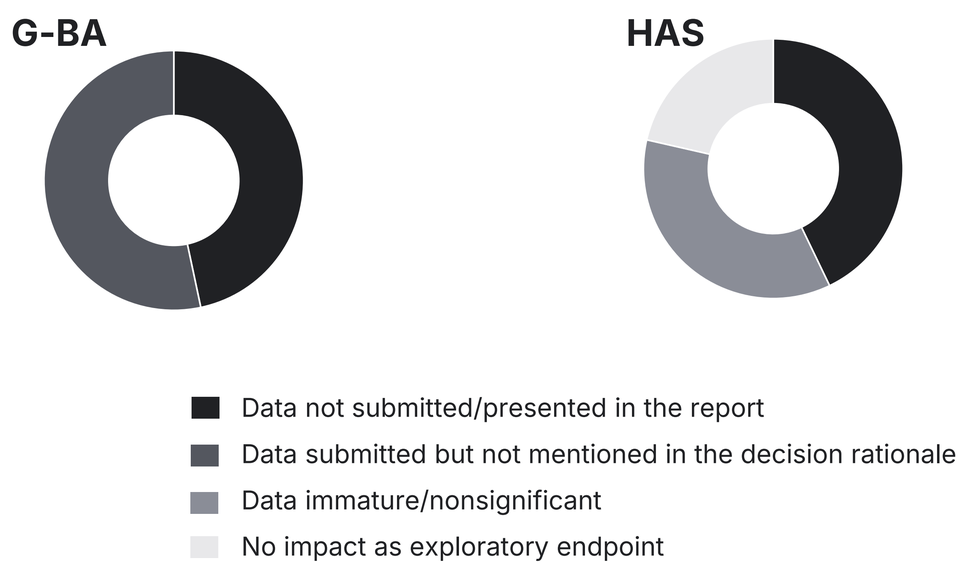
- Fifty-one HTA reports within scope were identified and reviewed (Figure 1).

Figure 1: **HTA reports identified within scope**



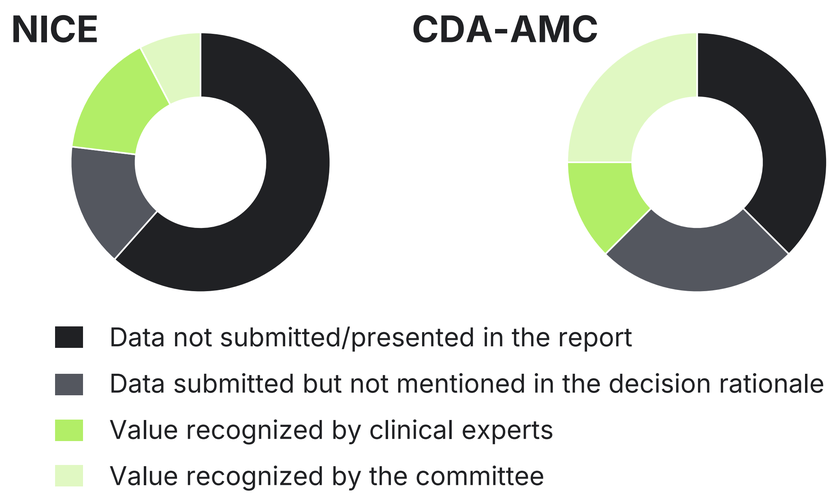
- For the clinical-effectiveness payer archetypes, methodological considerations meant that TTNT did not positively influence any decisions (Figure 2).

Figure 2: **TTNT in clinical-effectiveness HTA appraisals**



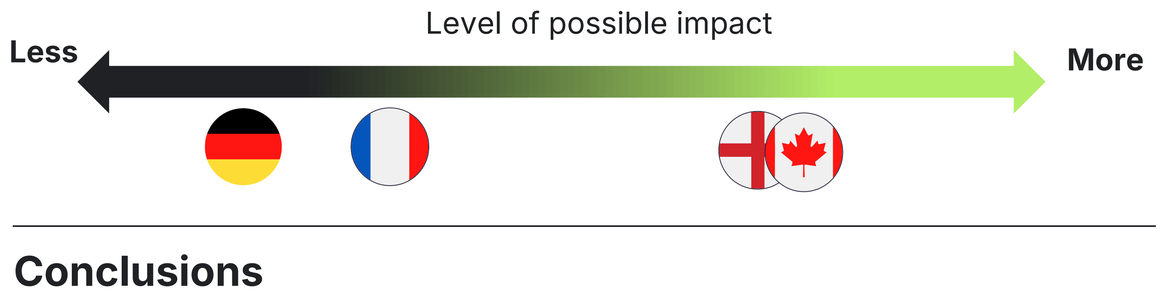
- In Germany, despite TTNT data being submitted in 7/15 assessments, it was not considered a patient-relevant measure of mortality, morbidity, or quality of life (QoL).[3] Consequently, TTNT was not mentioned in any decision rationale and did not influence any HTA outcome in Germany (Figure 2).
- In France, TTNT data were presented in the majority of assessments identified (8/14). In three assessments, the TTNT data were either immature or did not reach statistical significance. In the remaining five assessments, the committee could not consider TTNT data as the outcome was included as an exploratory endpoint (Figure 2)

Figure 3: **TTNT in cost-effectiveness HTA appraisals**



- A NICE committee noted that TTNT may be a more meaningful outcome than progression-free survival (PFS), which is the typical primary endpoint for indolent lymphomas. In such conditions, a disease can progress with minimal impact on symptoms or QoL. Therefore, the agency acknowledged that patients would more likely be concerned about the need to initiate a new treatment (Figure 3).
- However, the impact of TTNT on HTA outcomes in Canada was limited owing to difficulty in interpretation of TTNT when based on single-arm trial data, and separately, a lack of predefined clinically meaningful thresholds for TTNT also limits the interpretability of any results (Figure 3).
- From a cost-effectiveness perspective, TTNT can also inform cost-effectiveness estimates, as not all patients would receive subsequent therapy immediately post-progression. In several submissions to NICE and CDA-AMC, manufacturers used TTNT as a method of informing patient movement between health states.
- Commentary on the inclusion of TTNT in economic models was limited. In one NICE appraisal, the committee claimed that TTNT could have been implemented; however, it accepted that PFS was a suitable outcome for informing the model.
- Across markets, there was also no indication that TTNT had a greater impact on assessments of specific diseases.

Figure 4: **Potential impact of TTNT on HTA outcomes**



Conclusions

TTNT has the potential to be a trial outcome that can impact HTAs of indolent disease, particularly among agencies where methodologies allow consideration of its clinical value (Figure 4).

Despite this, challenges remain in delivering sufficiently robust data packages that allow agencies to recognize the benefits of new treatments based on TTNT.

Given the recognition of the clinical and patient relevance of TTNT by some influential agencies, manufacturers may wish to consider the benefits of including TTNT as a secondary endpoint in clinical trials and working to develop an understanding of clinically meaningful thresholds for TTNT in specific diseases.

References

1. Campbell B A, et al. ***Cancers.*** 2020;12:2311.
2. Jacobs R, et al. ***Future Oncology.*** 2024;20:39-53.
3. IQWiG. General Methods. Version 7.0. 2023.

Poster presented at ISPOR Europe, 09–12 November 2025, Glasgow, UK