Limited duration vs. treat-to-progression approaches for new therapies in hemato-oncology: impact at health technology assessment

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Introduction

Many therapies have been recently launched for late-line hemato-oncology indications. Barring one-off CAR-T therapies, most are used in a "treat-to-progression" manner; however, some have posology stipulating a maximum cycle number.

Decisions on posology consider the trade-off between maximizing therapeutic efficacy against toxicity and the practicalities of treatment.

- Hematological malignancies vary in whether long-term remission is plausible after cessation of treatment; this also depends on the drug's mechanism of action.
- However, there are examples of different posologies of therapies with the same indication and mechanism of action.

This research sought to understand the impact of these differences on HTA, as informative for future decisions on the posology of similar therapies.

Methods

HTA decisions were reviewed for three key hemato-oncology indications (DLBCL, FL, and MM) since 2022. Two examples were identified with a posology of maximum cycle number, both bispecific antibody therapies, plus for comparison examples in the same indications and/or drug class of "treat-to-progression" therapies (Table 1).

Published HTA documents from key agencies in Europe and Canada (as available as of May 2025) were reviewed to identify critiques relevant to the treatment approach.

The analysis of the impact on the cost of therapy used data based on list prices as available in TLV assessments.

Table 1: **Recently launched therapies in hemato-oncology with limited treatment duration/treat-to-progression therapies for comparison**

Drug	*Class*	*Indication*	*Licensed posology*	*Median duration of treatment (weeks)**
Glofitamab	Bispecific	DLBCL 3L+	Up to 12 cycles (36 weeks)	15
Epcoritamab	Bispecific	DLBCL 3L+	Treat-to-progression	18
Loncastuximab tesirine	ADC	DLBCL and HGBL, 3L+	Treat-to-progression	9
Mosunetuzumab	Bispecific	FL 3L+	8 cycles if CR (24 weeks), or up to 17 cycles (51 weeks) if PR or SD	24
Elranatamab	Bispecific	MM 4L+	Treat-to-progression	24
Teclistamab	Bispecific	MM 4L+	Treat-to-progression	37
Talquetamab	Bispecific	MM 4L+	Treat-to-progression	Not reached

*As reported in EPAR, or trial publication where not reported, calculated from the median number of cycles received.

Results

Impact by market

The impact of therapy approach on the assessment was clear in countries where cost-effectiveness was included as part of the published assessment (Canada, Sweden, and the UK), and also identified in Spain; no reference was made in the French or German assessments.

Impact on benefit for patients

The concept of patient benefit associated with a fixed duration was suggested in the UK and Spanish assessments.

- Patient comfort and safety are improved by limiting the number of treatment cycles.
- Treatment of finite duration, with duration adapted to response, avoids over-treatment and possible associated adverse effects.

Abbreviations: ADC, antibody-drug conjugate; CAR-T, chimeric antigen receptor T-cell; CR, complete response; DLBCL, diffuse large B-cell lymphoma; EPAR, European public assessment report; FL, follicular lymphoma; HGBL, high-grade B-cell lymphoma; MM, multiple myeloma; PR, partial response; PFS, progression-free survival; SD, stable disease; TLV, Dental and Pharmaceutical Benefits Agency; TTD, time-to-discontinuation.

Impact on cost of therapy

Median duration of treatment did not notably differ among indications (Table 1), likely reflecting low response rates/rapid discontinuation by patients owing to disease progression.

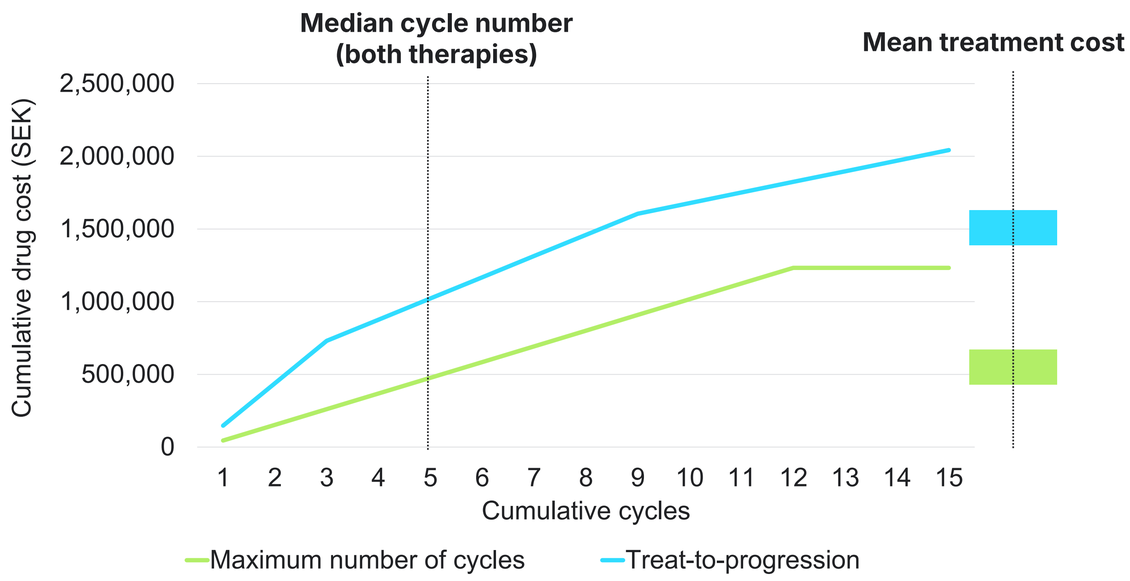
However, the mean therapy cost is relevant for economic analyses; hence, it was of interest whether a treat-to-progression approach leads to higher costs owing to the minority of patients receiving an extended duration of treatment.

Comparison of two therapies in DLBCL (Figure 1) using available data highlighted:

- the mean treatment cost of the "treat-to-progression" therapy was more than double,
- but owing to the higher upfront cost associated with higher dosing in initial cycles, rather than extended treatment duration.

Given that higher initial dosing/lower maintenance dosing is common in the examples identified, this suggests that the treatment approach has a limited impact on costs.

Figure 1: **Comparison of cumulative treatment costs**



Impact on cost-effectiveness analysis

No model included health states that differentiated time on- *vs.* off-treatment.

Submissions for "maximum cycle number" therapies used trial data for treatment continuation (hence therapy consumption) directly for costs.

In contrast, HTA agency critique on model inputs for therapy consumption was common for "treat-to-progression" therapies (Figure 2).

Figure 2: **HTA critique around model inputs for therapy consumption for treat-to-progression therapies**

Extrapolation of trial TTD data To estimate total therapy consumption	• Use of mean TTD *vs.* considering distribution of TTD • Selection of distribution for TTD extrapolation • Interpretation of difference between TTD and PFS curves
Stopping rules in model Proposed maximum duration for treat-to-progression therapies	• Plausibility that a patient in remission will stop therapy in clinical practice • Proposed timepoint for stopping • Whether the treatment benefit can be assumed as maintained after stopping therapy
Correspondence with cure assumptions	• Whether it is valid to consider a patient continuing therapy long-term, as in long-term remission/functional cure

Conclusions

- Treatment approach (posology) appears to have a limited impact on HTA assessments for these drugs.
  - This is caveated by the late-line nature of indications, as time to progression is regrettably short for many patients.
- Identified impacts might be more prominent if these therapies were used in earlier treatment lines.
  - If there is greater uncertainty in duration, the value of time off-treatment is more important, increasing the impact of the stopping rule on costs.
- Future work to explore these issues could look for examples of such therapies in earlier lines, as and when these launch.

Poster presented at ISPOR Europe 2025, 9–12 November, Glasgow, UK