Economic Evaluation of Advanced Therapy Medicinal Products (ATMPs) in France: Decision-Making Support or Methodological Challenge?

Justine Cortes, MSc[1], Sandrine Baffert, PhD[1], Anne-Line Couillerot, MSc[1]

1- CEMKA, Bourg-la-Reine, France,

Poster #HTA194

CONTEXT

In France, according to the revised 2022 eligibility criteria for health economic evaluation, Advanced Therapy Medicinal Products (ATMPs) are subject to health economic evaluation by the HAS (French Economic and Public Health Assessment Committee-CEESP) whenever an ASMR level I, II or III is claimed, regardless of the expected revenue level. As ATMPs are predominantly developed in rare diseases, their economic evaluation faces substantial methodological challenges.

OBJECTIVES

To characterize the economic evidence available for ATMPs in France and identify the methodological concerns and uncertainties limiting its use for decision-making.

METHODS

All CEESP economic opinions issued between 2020 and 2026 were reviewed. ASMR levels, incremental cost-effectiveness ratios (ICERs), their interpretability and reasons for invalidation (major methodological concerns or major overall uncertainty) were analyzed descriptively. ICERs per quality-adjusted life-year (QALY) and per life-year gained were examined separately, including alternative estimates where available.

CONCLUSION

ATMP economic evaluations can inform decision-making, but their contribution is frequently constrained by limitations in comparative evidence, long-term extrapolation and utility estimation. Better comparative and quality-of-life data, together with longer follow-up, would help reduce these uncertainties.

Nevertheless, an invalidated cost-utility analysis does not mean that the assessment provides no useful economic information. For EBVALLO and BREYANZI, the CEESP was still able to retain cost-per-life-year estimates, providing an economic result despite uncertainty about quality-of-life gains. This can also be anticipated when planning the economic evaluation, by considering alternative outcomes when robust utility data may be difficult to obtain.





COI: Cortes J, Baffet S and Couillerot A are employees at CEMKA, one of the first French consulting firms in the field of evaluation of products, programs and organizations in Health. The study was not sponsored.

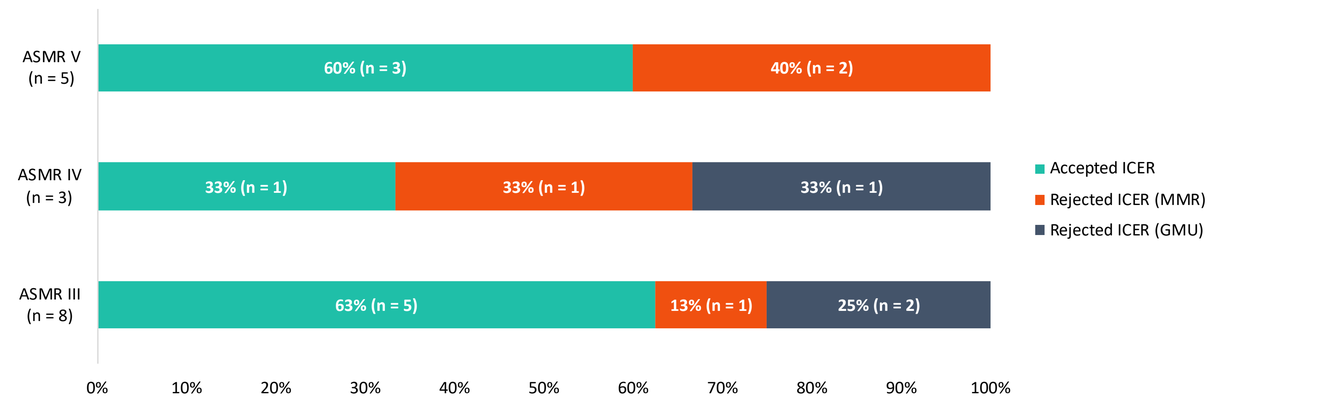
RESULTS

- **Between 2020 and 2026, the CEESP issued 122 economic opinions, including 16 for ATMPs:** 7 CAR-T cell therapies, 8 gene therapies, and 1 cell therapy.
- **All ATMPs targeted rare diseases**, compared with 39% of non-ATMP products, reflecting the challenges associated with limited evidence generation in small trial populations.

Interpretability of the economic reference result

The CEESP considered 7/16 ATMP economic evaluations non- interpretable (44%): **four due to major methodological reservations (MMR) and three due to global major uncertainty (GMU).** Three of eight evaluations coded ASMR III had non-interpretable reference results; clinical added value did not guarantee interpretable economic evidence.

FIGURE 1. CEESP reference-result status by recorded ASMR for ATMPs



Percentages are calculated within each ASMR category. EBVALLO (ASMR IV) and BREYANZI (ASMR III) received an MMR, which led to the unacceptability of the ICER per QALY. However, it was included in the "accepted ICER" section as the ICER per LY was validated.
ICER : Incremental cost-effectiveness ratio ; MMR : Major methodological reservation ; GMU : Global major uncertainty

The main methodologic barriers concerned **treatment effect estimation**, **quality-of-life estimation methods**, **small sample sizes, and insufficient statistical modelling.** Global uncertainty also reflected **long-term efficacy, limited comparative evidence and insufficiently robust quality-of-life data**. All three evaluations with major overall uncertainty relied on single-arm clinical evidence.

	Main driver	Evaluations concerned
MMR	Unreliability of efficacy sources ; lack of robustness of ITCs	**VYJUVEK; CARVYKTI (2022)**
MMR	Lack of robustness of utility sources and estimation methods	**BREYANZI; EBVALLO; CASGEVY (2024)**
MMR	Study objective and absence of efficiency frontier	**ROCTAVIAN**
GMU	Effect durability; prophylaxis costs; QALY overestimation	**HEMGENIX (2024)**
GMU	Non robust Indirect comparison; uncertain long-term disease progression and long-term benefits; limited quality of life data	**ZOLGENSMA (2023)**
GMU	Non robust indirect comparison; PFS estimation (ratio PFS/OS); extrapolation; utility transferability	**TECARTUS (2021)**

Economic information available

The five retained €/QALY estimates ranged from €41,545 to €379,317 with lower values for ASMR III and earlier lines of therapy, and a downward trend over successive assessments (Figure 2). **Other retained results were expressed per life-year gained** (Figure 3). These estimates concern different indications, comparators, populations and time horizons.

FIGURE 2. Retained reference estimates (€/QALY)

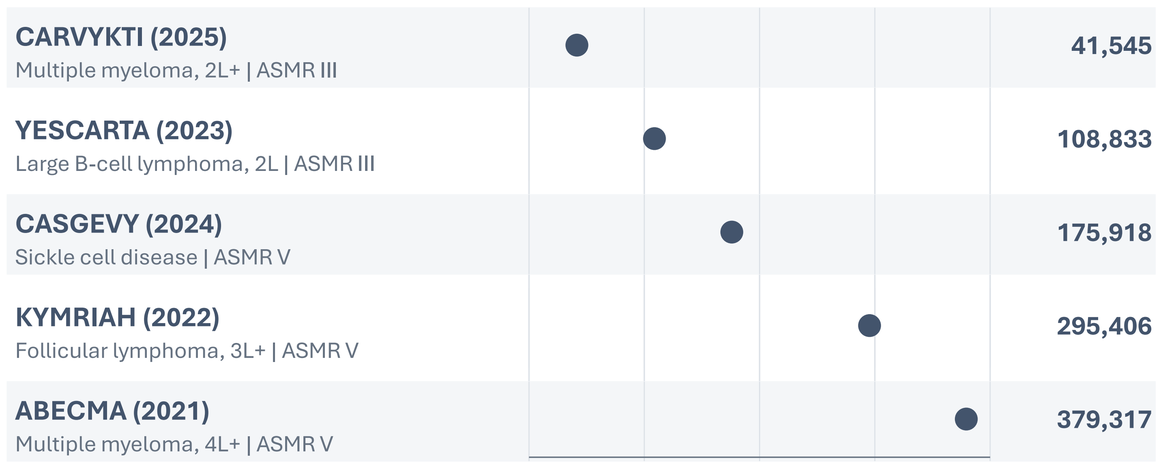
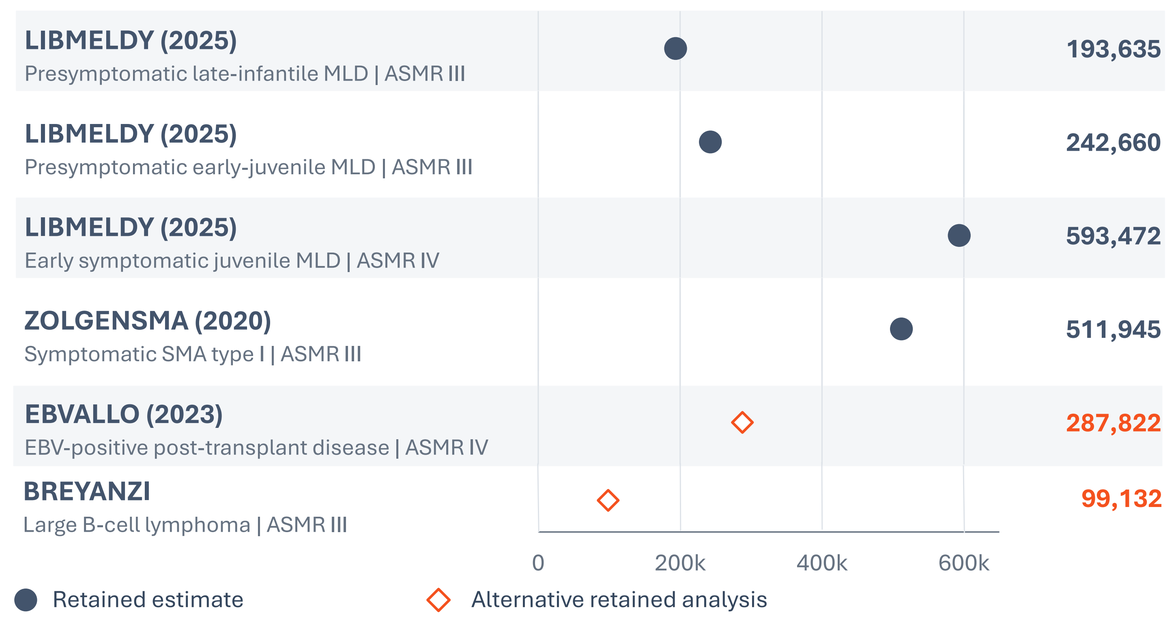


FIGURE 3. Selected retained estimates (€/life-year gained)



Importantly, **invalidation of a cost-utility analysis does not necessarily imply a lack of interpretable economic evidence**. For EBVALLO and BREYANZI, the CEESP retained estimates of €287,822 and €99,132 per life-year gained, respectively, despite invalidating their cost-utility analyses.