IMMATURE OVERALL SURVIVAL DATA IN FRENCH HTA: WHAT DIFFERENTIATES ASMR III FROM ASMR IV RATINGS?

Le Mao J[1], Garibello Garcia D[1], Gaugy P[1]

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

Acceptance code: HTA335

1. BACKGROUND AND OBJECTIVES

Background

- Overall survival (OS) is a key endpoint in oncology HTA and is considered the gold standard by the Transparency Committee (TC) when assessing clinical added value (ASMR).
- However, OS data are often immature at the time of initial assessment, creating uncertainty about long-term clinical benefit.
- In France, ASMR III indicates moderate added clinical value, while ASMR IV indicates minor added clinical value.

Objective

To identify the clinical and methodological arguments associated with ASMR III versus ASMR IV ratings when OS evidence is considered immature by the TC.

2. METHODS

Data source

Public HAS TC opinions issued between 2018 and 2025.

Inclusion

- Oncology opinions explicitly mentioning immature OS data or data maturity in the ASMR rationale.
- Only ASMR III and IV ratings were included (ASMR V excluded).

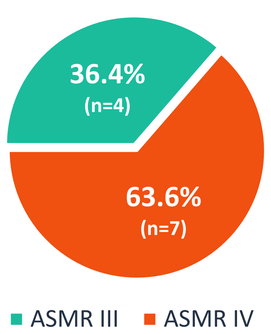
Data selection and analysis

- Retrospective benchmark analysis (targeted review).
- Identification of clinical and methodological arguments associated with ASMR III versus IV ratings (surrogate endpoints, treatment effect, unmet medical need, safety, QoL, positioning, etc.).
- Descriptive comparison over time.

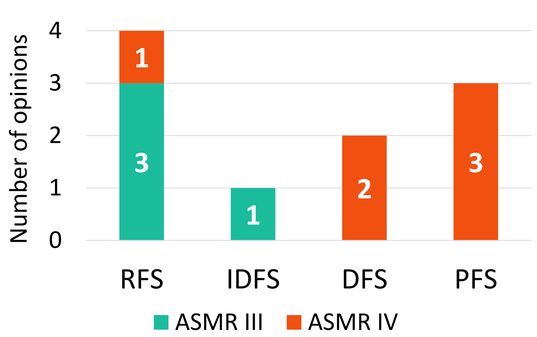
HAS TC opinions 2018-2025 ▶ **Oncology opinions with immature OS** ▶ **11 opinions (ASMR III or IV)**

3. RESULTS OVERVIEW

Distribution of ASMR ratings (n=11)



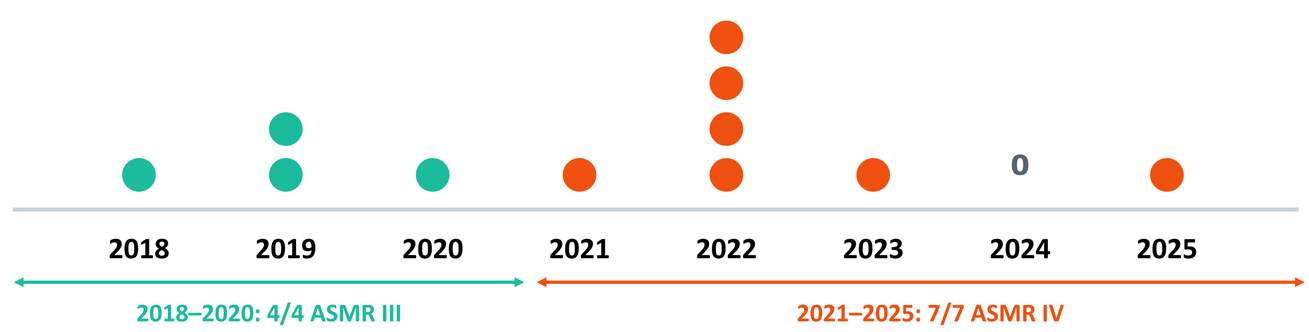
Primary endpoint by ASMR rating (n=11)



DFS, disease-free survival; EFS, event-free survival ; IDFS, invasive disease-free survival ; RFS, relapse-free survival

4. TEMPORAL PATTERNS

All four ASMR III opinions were issued between 2018 and 2020, whereas all seven ASMR IV opinions were issued between 2021 and 2025.
The highest number of ASMR IV ratings was observed in 2022 (4/7).



5. DIFFERENTIATING ARGUMENTS

Immature OS evidence was present across both ASMR groups.
The distinction between ASMR III and IV appeared to depend on the overall clinical evidence package, rather than OS maturity alone.

Assessment dimension	Factors supporting ASMR III (n = 4)	Factors limiting ASMR IV (n = 7)
Magnitude and relevance of benefit	• Substantial treatment effect on a clinically relevant surrogate endpoint (e.g., RFS, IDFS)	• Surrogate-endpoint benefit considered insufficient • Persistent uncertainty on long-term clinical benefit (no demonstrated OS gain)
Unmet medical need	• High unmet medical need and high risk of recurrence	• More favourable prognosis or existing therapeutic alternatives
Safety and QoL	• Acceptable safety profile (even with some uncertainties)	• Safety concerns (e.g., Grade ≥3 toxicities) • Non-conclusive QoL data
Comparators and positioning	• Relevant comparator (active or placebo) • Clinically meaningful effect in the disease setting.	• Uncertainties in therapeutic positioning • Indirect comparisons or heterogeneous populations

6. ILLUSTRATIVE CASES : SIMILAR BENEFITS, DIFFERENT ASMR OUTCOMES

A substantial surrogate-endpoint benefit does not guarantee ASMR III: clinical context, comparators and residual uncertainties also shape TC decisions.

KADCYLA (T-DM1) ASMR III (2020)	TAGRISSO (osimertinib) ASMR IV (2022)
HER2+ early breast cancer with residual disease after neoadjuvant treatment	EGFR-mutated NSCLC in the adjuvant setting
IDFS: HR 0.50 vs trastuzumab	DFS: HR 0.17–0.20 vs placebo
✓ Substantial benefit on a clinically relevant surrogate endpoint ✓ High-risk population and appropriate active comparator	✓ Substantial benefit on a surrogate endpoint ✓ Clinically relevant reduction in recurrence risk
• Immature OS • Increased toxicity and inconclusive QoL	• Immature OS, with no demonstrated survival benefit • Increased toxicity and non-demonstrative QoL

7. CONCLUSION AND KEY TAKEAWAYS

Immature OS evidence alone does not determine the ASMR rating. ASMR III decisions were supported by substantial benefits on clinically relevant surrogate endpoints, high unmet medical need and appropriate comparators.
Conversely, ASMR IV ratings were associated with greater residual uncertainty regarding long-term benefit, safety, QoL and/or therapeutic positioning.
Recent opinions predominantly received ASMR IV, although the small and heterogeneous sample limits conclusions regarding changes in TC assessment practices over time.

1. Immature OS does not preclude ASMR III.
2. Strong surrogate benefits may support ASMR III but do not guarantee it.
3. Safety, QoL and positioning influence ASMR ratings.
4. Recent ASMR IV predominance requires caution given the small sample.

ISPOR Europe 2026
8-11 November 2026 | Vienna | Austria

ASMR, clinical added value ; HR, hazard ratio; HTA, health technology assessment ; NSCLC, non-small-cell lung cancer; OS, overall survival; pCR, pathological complete response; PFS, progression-free survival; QoL, quality of life; RFS, relapse-free survival; TC, Transparency Committee.

COI: Le Mao J, Garibello Garcia D and Gaugy P 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.