ACCEPTABILITY OF IMMATURE SURVIVAL DATA IN HEALTH TECHNOLOGY ASSESSMENT DECISION-MAKING IN FRANCE AND GERMANY

HTA29

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INTRODUCTION

- There is no formal definition for what constitutes 'immature' survival data, however, in general this term refers to datasets in which only a limited proportion of patients (≤20 – 50%) have experienced a defined event (e.g. death, when considering overall survival).[1,2]
- Health Technology Assessment (HTA) submissions for oncology medicines increasingly rely on early or interim clinical trial evidence to enable faster patient access, resulting in immature overall survival (OS) data at the time of assessment.[1]
- Consequently, statistical modelling is repeatedly relied upon to extrapolate survival beyond observed trial periods; however, variation in modelling approaches can substantially influence projected survival and ICER estimates.[3]
- This is compounded by inconsistencies across European HTA bodies in the acceptance of surrogate endpoints (e.g. DFS, EFS, PFS) when OS data are immature.[4,5]
- This raises questions about the impact of immature OS data on HTA decision-making and reimbursement outcomes.

Study objectives

The main objectives of this study were as follows:

- ✓ Assess the impact of OS maturity on HTA and reimbursement outcomes in France and Germany*
- ✓ Examine how uncertainty from immature OS data is handled in G-BA and HAS decision making

METHODS

- Oncology HTAs published by the Gemeinsamer Bundesausschuss German Federal Joint Committee (G-BA) in 2025 were identified from the G-BA website.[6]
- Corresponding French assessments were retrieved from the Haute Autorité de Santé (HAS) website.[7] HAS assessments without an exact indication match to identified G-BA assessments were not included in downstream analysis.
- Indication, comparator, endpoints, OS data maturity, and HTA outcomes were noted from each assessment, where available.

G-BA website searched for 2025 oncology assessments

HAS website searched for corresponding assessments with matching indications

Clinical benefit and reimbursement outcomes extracted from French (HAS) and German (G-BA) mature and immature OS datasets

RESULTS

- 41 G-BA oncology assessments were documented in 2025, 30 of which were submitted and assessed by HAS for the same indication.
- While OS data maturity was available for all 30 HAS assessments, this information was only obtainable for 21/41 (51%) assessments from G-BA. Only those with available OS maturity data were included in further analysis.

RESULTS

- Among G-BA oncology assessments, all submissions with mature OS data (n = 8) achieved a considerable (25%) or minor (75%) added benefit. Of those with immature OS data (n = 13), outcomes ranged from major (8%) to not proven/non-quantifiable (25%) (Figure 1A).
- For HAS, outcomes were similar regardless of OS maturity: 29–30% received ASMR III and 70–71% ASMR IV/V for mature (n = 9) and immature (n = 21) OS data (Figure 1B).
- 52% of G-BA assessments in 2025 received a not-proven rating, largely due to inappropriate comparator selection or reliance on single-arm studies.

Figure 1: Overall survival (OS) data maturity at HTA assessment, and outcomes among submissions with immature OS data in Germany (G-BA) and France (HAS)†

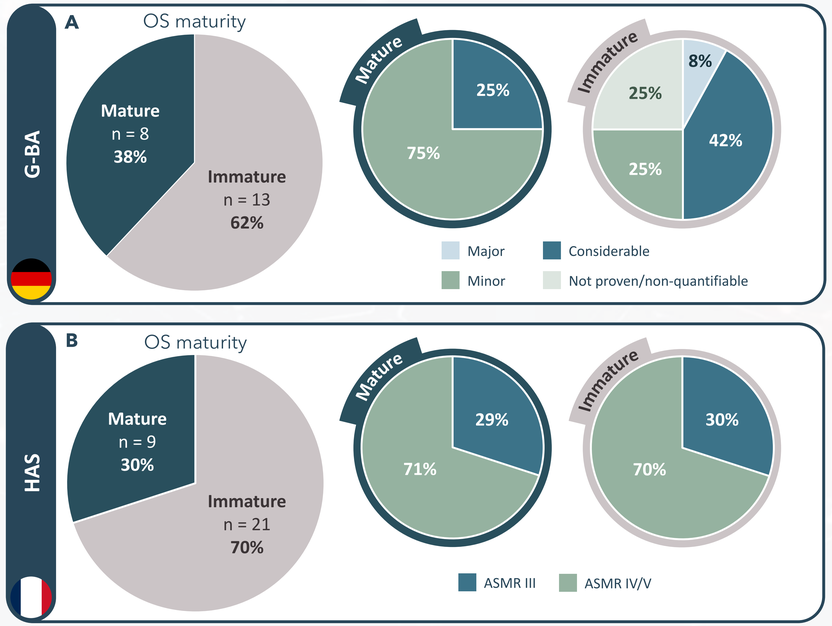
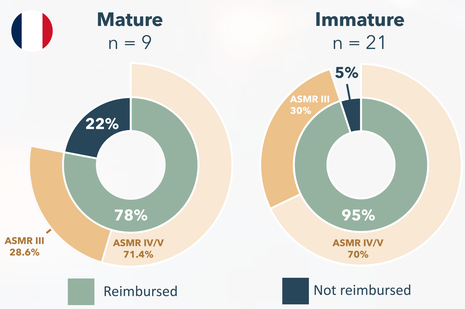


Figure 2: Reimbursement outcomes among 2025 HAS oncology submissions‡ (n = 30) by OS data maturity, with reimbursed ASMR ratings shown.



- Among HAS oncology assessments with mature OS data (n = 9), 7 (78%) were reimbursed and 2 (22%) were not (Figure 2).
- HAS assessments with immature OS data (n = 21) showed high reimbursement (95%; 20/21), with only 5% not reimbursed (Figure 2).
- Of reimbursements, ASMR ratings were similar between mature and immature data (ASMR III 28.6% and 30%; ASMR IV/V 71.4% and 70%, respectively) (Figure 2).

CONCLUSION

- Immature OS data accounted for over half of the oncology HTA assessments in both France and Germany in 2025, reflecting increasing reliance on early or interim clinical trial evidence to support earlier patient access to oncology therapies when mature data are not yet available.
- In France, OS data immaturity alone did not negatively impact reimbursement outcomes, with a high proportion of HAS submissions supported by immature OS data still achieving reimbursement‡, reflecting the broader and more holistic consideration of overall clinical benefit alongside recognised data uncertainty.
- OS data immaturity alone did not preclude positive HTA outcomes in either France or Germany, suggesting decision-makers consider OS alongside other factors such as study design, comparator relevance, and supporting clinical endpoints. This indicates that OS maturity functions as one component of a broader evidentiary package rather than a sole determinant of added benefit.
- G-BA typically do not recognise disease-free survival (DFS) or progression-free survival (PFS) as valid surrogate endpoints when OS data are immature, except in orphan indications, and accepted use requires formal surrogate validation by IQWiG.[4] As a result, submissions relying primarily on unvalidated surrogate endpoints face substantial challenges in demonstrating added benefit in the absence of mature OS evidence.
- Conversely, HAS typically does accept surrogate endpoints in the presence of immature OS data, including DFS, PFS, EFS, and overall response rate. At initial decision making, these endpoints are frequently accepted as interim measures of clinical benefit, with the expectation that mature OS data will be generated post-launch to support the confirmation of benefit.[5]
- Although HAS and G-BA differ in their treatment of surrogate endpoints, these methodological differences did not appear to influence added-benefit outcomes across 2025 oncology assessments with immature OS data.
- Findings from the total 51 analysed 2025 G-BA and HAS oncology assessments suggest that greater transparency around OS maturity definitions, alongside more consistent handling of uncertainty associated with immature OS data, could improve the predictability of HTA decision-making for oncology therapies across European markets.

Abbreviations: ASMR, Amélioration du Service Médical Rendu; DFS, disease free survival; EFS, event free survival; G-BA, Gemeinsamer Bundesausschuss (German Federal Joint Committee); HAS, Haute Autorité de Santé; HTA, Health Technology Assessment; ICER, incremental cost-effectiveness ratio; IQWiG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Independent Institute for Quality and Efficiency in Healthcare); OS, overall survival; PFS, progression free survival

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* Only France and Germany were included in the analysis as both make HTA/reimbursement decisions primarily on additional clinical benefit
† Inclusive only of HAS submissions with an exact indication match to corresponding G-BA oncology assessments (n = 30)
‡ Reimbursement outcomes based on SMR rating: 'insufficient' = not reimbursed; all others = reimbursed