Do we say “game over” when OS data is not mature at launch?

PT28

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A review of value drivers for oncology products in the absence of significant OS gains

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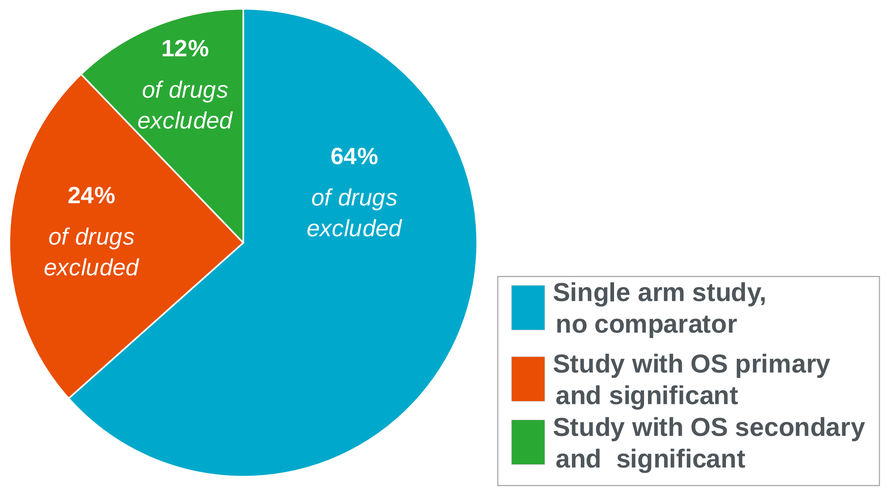
Background

- In the absence of mature data showing or statistically significant and clinically meaningful overall survival (OS) gains, novel oncology drugs face considerable challenges during health technology assessments (HTAs). This research investigated cases where therapies under such circumstances were reimbursed by HTA agencies by analyzing the key decision drivers and reimbursement restrictions underlying positive HTA outcomes.

Methods

- This study identified 59 novel oncology drugs through a comprehensive review of the European Medicines Agency (EMA) approvals from 2019 onwards, excluding generics, biosimilars and/or chemotherapy/radiotherapy. Of these 59 identified drugs, a total of 18 drugs were selected for further analysis. The selected drugs were those with clinical studies in which OS was a secondary endpoint and no statistically significant OS gains were shown (**Figure 1**).
- A thematic analysis of drivers of decision making and critiques of the 18 identified drugs was performed on HTA reports from four HTA agencies in Germany (G-BA), France (HAS), England (NICE), and Sweden (TLV).

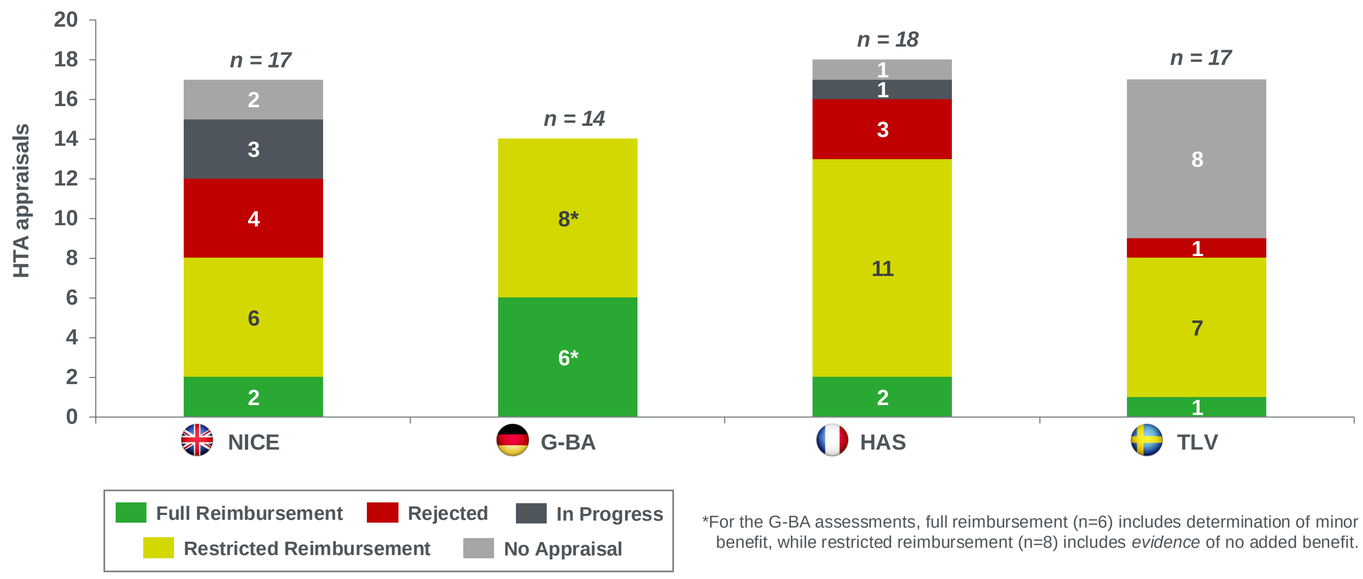
FIGURE 1: RATIONALE FOR EXCLUSION OF A DRUG



Results

- Among the 18 identified drugs, a total of 51 related HTA reports issued by G-BA, HAS, NICE, and TLV were reviewed. The outputs of these assessment reports were categorized into 5 distinct groups: full reimbursement, restricted reimbursement, rejected, in progress and no appraisal. Overall, 43 assessments resulted in a full or restricted reimbursement and 8 led to a rejection (**Figure 2**). The evaluation revealed that 74% of the appraisals were granted a **restricted reimbursement**, in contrast to 26% that received a **full reimbursement**.

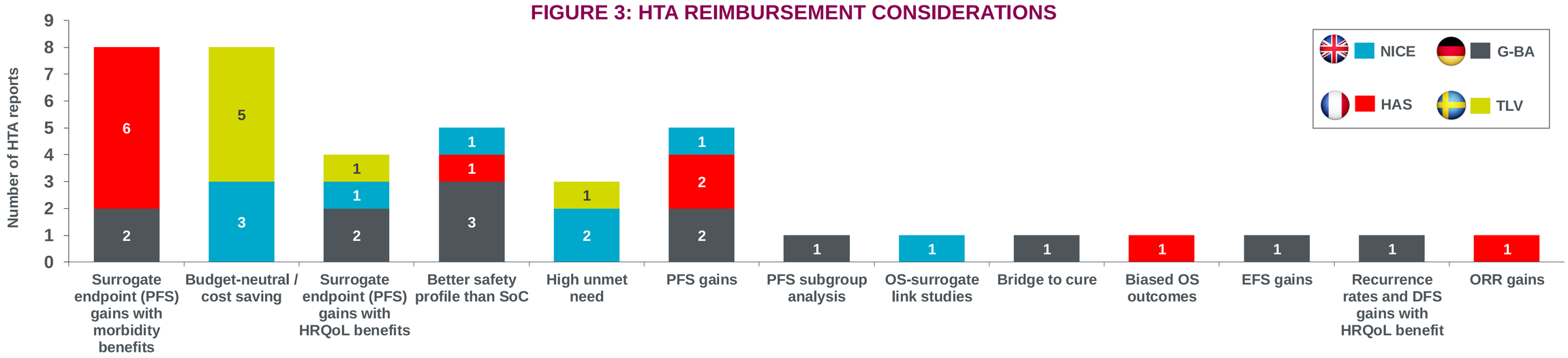
FIGURE 2: NUMBER AND STATUS OF HTA APPRAISALS (n = 18 drugs)



*For the G-BA assessments, full reimbursement (n=6) includes determination of minor benefit, while restricted reimbursement (n=8) includes *evidence* of no added benefit.

- The demonstration of concurrent benefits in the primary surrogate endpoint (e.g., PFS) and either morbidity or HRQoL was a key driver leading to reimbursement by HAS (n=6) and G-BA (n=4). In contrast, evidence around budget neutrality or cost-effectiveness were a common focal point for TLV (n=5) and NICE (n=3). In the remaining reimbursed cases, HTA bodies cited multiple factors contributing to their decisions (e.g., improved safety profile, high unmet need, benefits in specific subpopulations or cancer stages, and bridging to a potential cure) (**Figure 3**).

FIGURE 3: HTA REIMBURSEMENT CONSIDERATIONS



Conclusions

- This investigation revealed that HTA agencies evaluate novel oncology drugs with unproven OS gains on a case-by-case basis and may be willing to accept other value elements, besides OS, if sufficient justification and evidence can be provided. As anticipated, G-BA and HAS prioritized clinical-effectiveness outcomes, while NICE and TLV focused on economic arguments. In all cases, depending on the maturity of the data package, clients may need to balance the benefits of early time to market against the impact that this may have on reimbursement levels.
- In light of these findings, a modelling approach can enable manufacturers to proactively identify data gaps and optimize investment returns either in clinical or economic outcomes to strengthen the evidence package and mitigate reimbursement uncertainty, especially in anticipation of JCA implementation.

ABBREVIATIONS

DFS: Disease Free Survival; EFS: Event Free Survival; HAS: Haute Autorité de santé; HRQoL: Health-Related Quality of Life; G-BA: Gemeinsamer Bundesausschuss; HTA: Health Technology Assessment; JCA: Joint Clinical Assessment; NICE: National Institute for Health and Clinical Excellence; OS: Overall Survival; ORR: Overall Response Rate; PFS: Progression Free Survival; SoC: Standard of Care; TLV: Swedish Dental and Pharmaceutical Benefits Agency (Swedish: Tandvårds- och läkemedelsförmånsverket)

REFERENCES

[1] EMA website for oncology drugs from 2019 onwards. Accessed: 06th March 2024.

[2] NICE, G-BA, HAS and TLV website for the 18 oncology drugs identified: relugolix, elacestrant, acalabrutinib, alpelisib, lisocabtagene maraleucel, asciminib, ripretinib, selinexor, idecabtagene vicleucel, isatuximab, niraparib/abiraterone acetate, lorlatinib, polatuzumab vedotin, relatlimab / nivolumab, duvelisib, pertuzumab/trastuzumab, talazoparib, dacomitinib. Accessed: 30th May 2024.

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