Beyond Overall Survival: The Value of Other Oncology-Related Endpoints in Supporting HTA Decision-Making

HTA88

Nishika Jain[1], Hannah Squires[1], Anna Alonso[1], Wenting Zhang[2], Ismail Ismailoglu[3]
[1]Trinity Life Sciences, London, UK; [2]Trinity Life Sciences, San Francisco, CA, USA; [3]Trinity Life Sciences, Minneapolis, MN, USA

Summary

- Oncology relevant endpoints beyond OS have the potential to bring additional value in the evaluation of novel oncology therapies, especially in early-stage cancers or indications with poor prognosis, where OS may not be the primary goal or may delay access to innovative medicines
- Payers across France, Italy, Spain and the UK find endpoints measuring delay to progression as the most impactful, whereas PROs measuring symptom and QoL improvement are most valuable in Germany
- RWE and HEOR studies evaluating the long-term clinical and economic impact of non-OS endpoints might be beneficial in increasing the value of these endpoints in the future

Introduction & Objectives

- Overall survival (OS) is regarded the "gold standard" endpoint in oncology trials due to its clinical robustness and direct relevance to patient outcomes
- However, OS has notable limitations as it fails to capture HRQoL, is more prone to confounding, and may lead to increased cost and delayed patient access to new therapies due to the long duration required to collect OS data
- Oncology-related endpoints beyond OS offer opportunities to address some of these limitations by accounting for patients' broader needs and QoL, while also enabling faster and more cost-effective access to innovative cancer therapies
- Therefore, this research aimed to understand payer perception and impact of oncology-related endpoints beyond OS in health technology assessment (HTA) submissions and payer decision-making

Methods

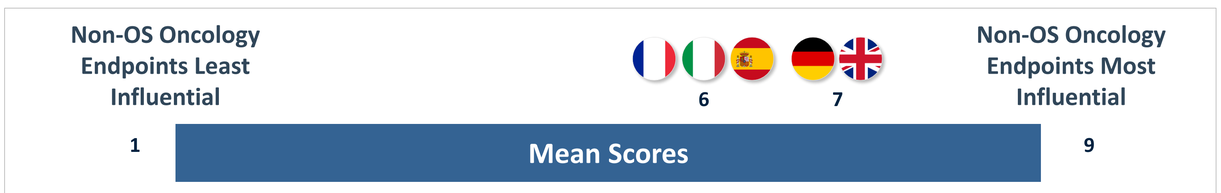
- A 15-minute online quantitative survey was completed by N=18 payers (N=4 DEU, FRA and ESP; N=3 ITA and GBR)
- Payer profiles included former G-BA advisors and members of the G-KV in Germany, former TC advisors in France, NHS representatives and former NICE advisors in the UK, and a mix of regional payers and former MoH members and AIFA advisors in Spain and Italy, respectively

Results

Acceptance of Oncology Endpoints Beyond OS in Drug Evaluations

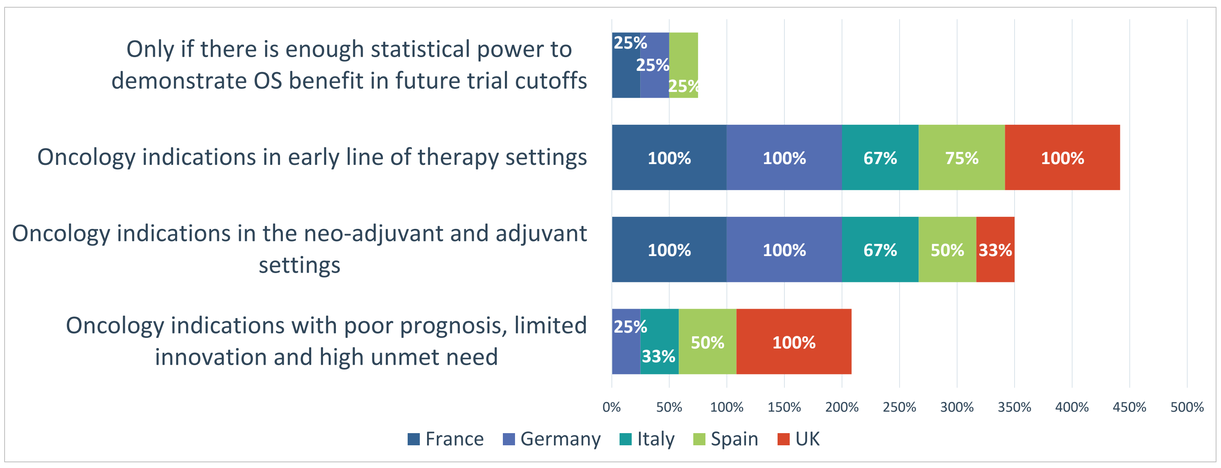
- The use of non-OS endpoints has a relatively moderate impact on HTA evaluations of oncology drugs, with varying payer acceptance of such endpoints (Figure 1)
- In Germany, while mortality (measured with hard endpoints like OS) is still the gold standard, non-OS endpoints can be influential in payer decision-making when they are symptomatically defined and therefore patient-relevant (and / or if the treatment is curative)

Figure 1 | Influence of Non-OS Oncology-Related Endpoints in Payer Decision-Making



- The value of oncology-related endpoints beyond OS may also differ depending on the tumor type and indication, disease stage or treatment setting (Figure 2)
- Across EU, non-OS endpoints are considered most appropriate in earlier lines of therapy; endpoints such as progression-free survival (PFS) are less likely to be confounded than OS as they are typically measured up to a disease-related event within one line of therapy, reducing the impact of subsequent treatments on outcomes of interest
- Similarly, most payers find non-OS endpoints more acceptable in the neo-adjuvant and adjuvant settings, where life expectancy of patients is often longer, and an analysis of OS may be less practical
- In countries like the UK, Italy or Spain, non-OS endpoints are also seen as particularly valuable in indications with poor prognosis, limited innovation and high unmet need

Figure 2 | Settings Where Non-OS Oncology-Related Endpoints are Most Relevant



Type of Non-OS Endpoints Driving Most Value in Oncology Drug Evaluations

- Most payers across EU consider delay to progression as the most impactful type of endpoint, whereas in some countries (e.g., France, Germany, UK), better tumor response is seen as the least valuable likely due to the lack of direct impact on patient benefit as these endpoints do not necessarily correlate with meaningful improvement in patient survival or QoL (Figure 3)
- In Germany, however, PROs measuring both symptom improvement and impact on QoL are considered most relevant as they can directly capture symptom improvement and QoL which are accepted as patient-relevant by the G-BA

Figure 3 | Most Important Value Drivers in Oncology Drug Evaluations (Beyond Survival)

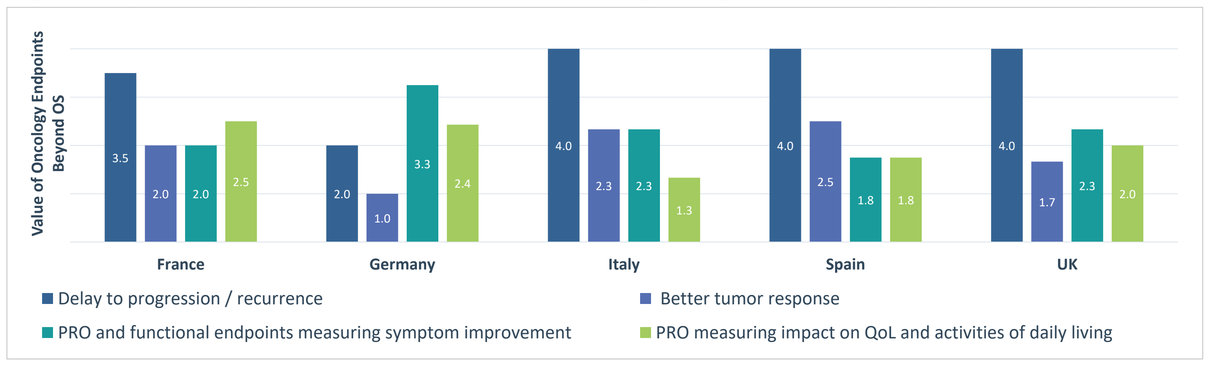
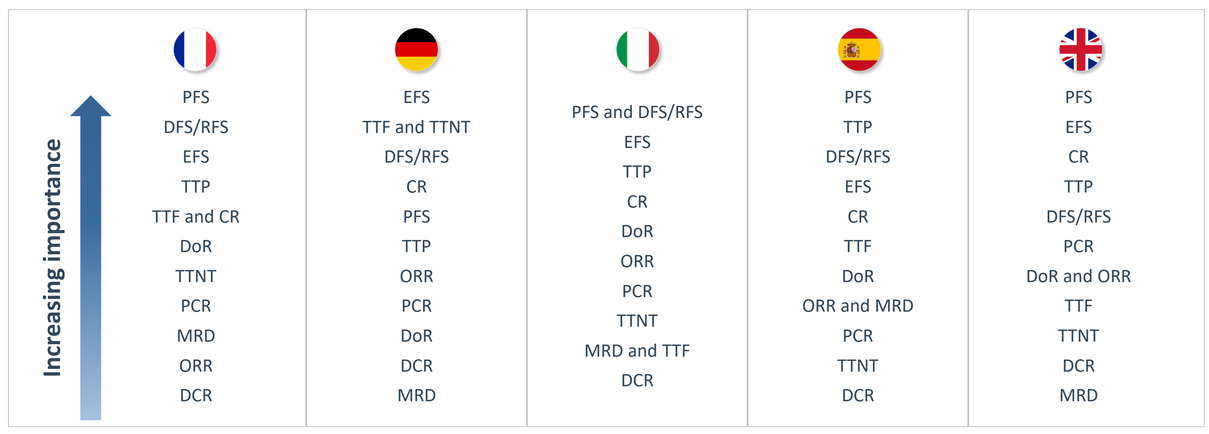
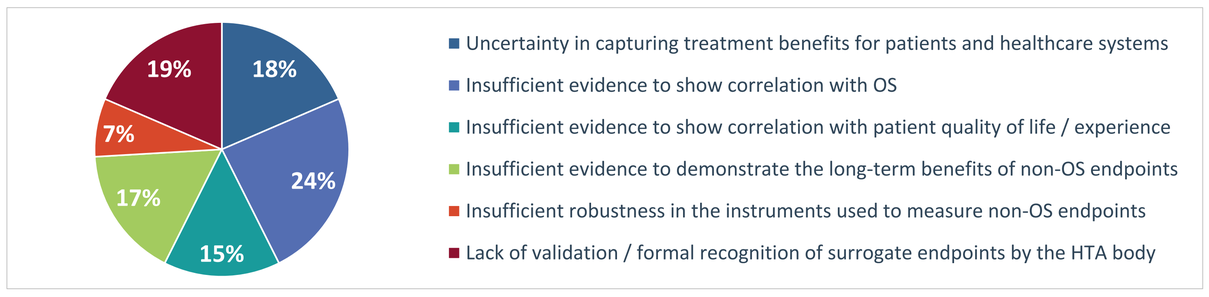


Figure 4 | Non-OS Endpoints Ranked by their Impact / Influence on Payer Decision-Making



- PFS emerged as the preferred non-OS endpoint by payers across EU, with the exception of Germany where several other endpoints were prioritized; namely event-free survival, time to treatment failure, time to next treatment, disease-free or relapse-free survival (Figure 4)
- On the contrary, disease control rate and measurable residual disease were consistently rated as the least influential in payer decision-making

Figure 5 | Main Barriers to Broader Adoption and Acceptance of Non-OS Endpoints



- The limited evidence showing a correlation between OS and non-OS endpoints, combined with the lack of formal recognition of surrogate endpoints by the HTA agency, remain as the most common hurdles to achieving broader acceptance of such endpoints (Figure 5)
- As such, most EU payers (N=9/20) cited RWE and HEOR studies that evaluate the long-term clinical and economic impact of non-OS endpoints as one of the most important actions to help increase the acceptance of such endpoints in the future
- Additionally, most EU payers also found standardized / methodological guidance from HTA bodies and/or relevant societies (e.g., ESMO) on the use of surrogate endpoints helpful to validate such endpoints in drug assessments

Conclusions

This research showed that while OS is still considered the gold-standard in HTA evaluations of oncology treatments, alternative non-OS endpoints can still measure patient-relevant outcomes and support the clinical efficacy value proposition to varying degrees.

Non-OS endpoints, particularly those measuring delay to recurrence, are likely to have the most impact in the UK, France, Italy or Spain, whereas PROs capturing QoL benefits are most likely to have a positive impact on payer evaluations in Germany. Payer perceptions of the level of influence and acceptance of such endpoints also varied depending on the indication, suggesting that goals of treatment might be changing in some oncology indications (e.g., early line of therapy or adjuvant indications) where improving QoL while surviving may be the first goal.

Uncertainty around the correlation of oncology-related endpoints beyond OS with OS remains a key barrier to their use in HTA / payer decision-making. However, there is opportunity for future evidence generation to demonstrate the long-term clinical and economic value of non-OS endpoints and potentially support HTA / payer methodological guidelines that validate the use of such endpoints in oncology drug evaluations.

Abbreviations

CR: Complete Response; **DCR:** Disease Control Rate; **DFS:** Disease-Free Survival; **DOR:** Duration of Response; **EFS:** Event-Free Survival; **ESMO:** European Society for Medical Oncology; **G-BA:** Gemeinsamer Bundesausschuss; **G-KV:** Gesetzliche Krankenversicherung; **HTA:** Health Technology Assessment; **HEOR:** Health Economics and Outcomes Research; **MRD:** Measurable Residual Disease; **NICE:** National Institute for Health and Care Excellence; **ORR:** Objective Response Rate; **PCR:** Pathological Complete Response; **PFS:** Progression Free Survival; **PRO:** Patient-Reported Outcome; **QoL:** Quality of Life; **RFS:** Relapse Free Survival; **RWE:** Real-World Evidence; **TC:** Transparency Committee; **TTF:** Time to Treatment Failure; **TTNT:** Time to Next Treatment; **TTP:** Time to Tumor Progression

Ask A Question: aalonso@trinitylifesciences.com

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