HTA302

A Retrospective Analysis of the Impact of Treatment Effect on HTA Outcomes for Oncology Treatments Assessed in France and Germany

Authors and affiliations

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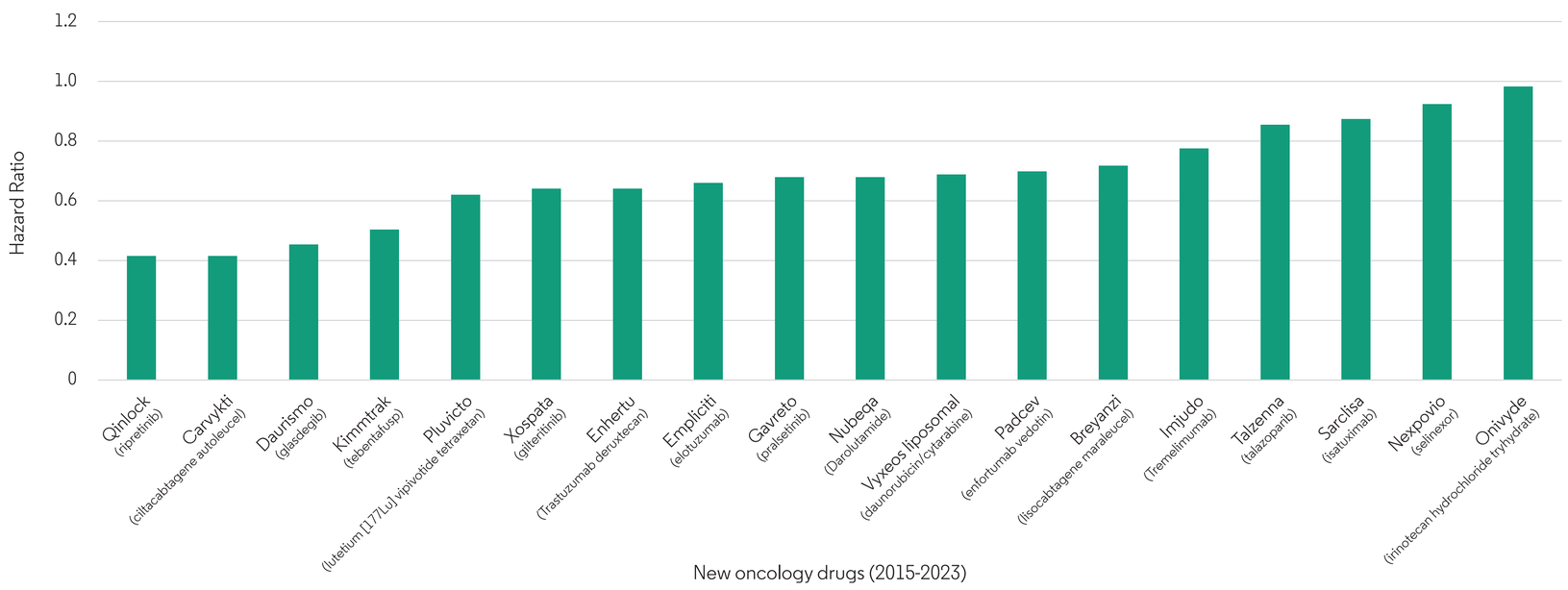
Introduction

- Clinical trials are essential in determining the safety and efficacy of new drugs and medical treatments. Hazard Ratios (HR), a statistical measure, have emerged as a pivotal tool in assessing and interpreting clinical trial data, particularly in the context of healthcare evaluation agencies across the globe.
- HRs provide a deeper understanding of the temporal aspects of treatment effects, offering a dynamic perspective beyond traditional summary statistics like odds ratios or relative risks. These ratios are particularly crucial in clinical trials where the time to an event, such as disease progression or death, is a vital outcome.
- HRs can quantify how the risk of an event changes over time in two groups, typically a treatment group and a control group. A hazard ratio less than 1 indicates a reduced risk in the treatment group, while a ratio greater than 1 suggests an increased risk. These ratios not only reveal the magnitude of a treatment's effect but also the direction and significance, making them valuable tools for healthcare decision-making.
- Healthcare evaluation agencies like the Haute Autorité de Santé (HAS) in France, and the Federal Joint Committee (G-BA) in Germany consider HRs to inform their decision-making processes regarding the adoption of new drugs and treatments. They consider various aspects when evaluating drugs, including clinical efficacy, cost-effectiveness, and safety HRs offer a nuanced view of treatment effects, contributing to these evaluations.
- HRs can allow agencies to assess the true impact of a drug on disease progression and patient survival over time. This nuanced perspective aids in determining the clinical effectiveness of the treatment, a critical factor in decision-making

Methodology

- All approved oncology products during 2015 to June 2023 that were evaluated by the G-BA and/or HAS between were included in this study
- Products included in this study were selected if they were: Oncology, approved by EMA 2015 or later, had no prior indication on label
- Products were excluded if they were: Chemotherapy combinations, Brand-brand combinations
- Sources included G-BA Assessment and HAS CT Opinion. Only the initial benefit assessment rating were captured unless a product was re-assessed based on additional clinical evidence. If a product was re-assessed because they were now in combination or if they had their orphan status lifted, this was not captured
- EMA EPARs were used for assessing the clinical evidence package with product that had submitted additional evidence towards their HTA assessment, the initial evidence package was used from EPAR
- For the incremental efficacy calculations, this is a combination of EPAR and new clinical evidence available or only EPAR data if no additional data was submitted at time of HTA assessment
- For pricing data annual cost, if a treatment had no stopping rule, the cost was calculated for 12 months. Where specified (i.e. a therapy could only be used for 5 treatment course), the cost was based on what was the recommended duration of therapy. With accommodation for dosing schedules made depending on the EMA label

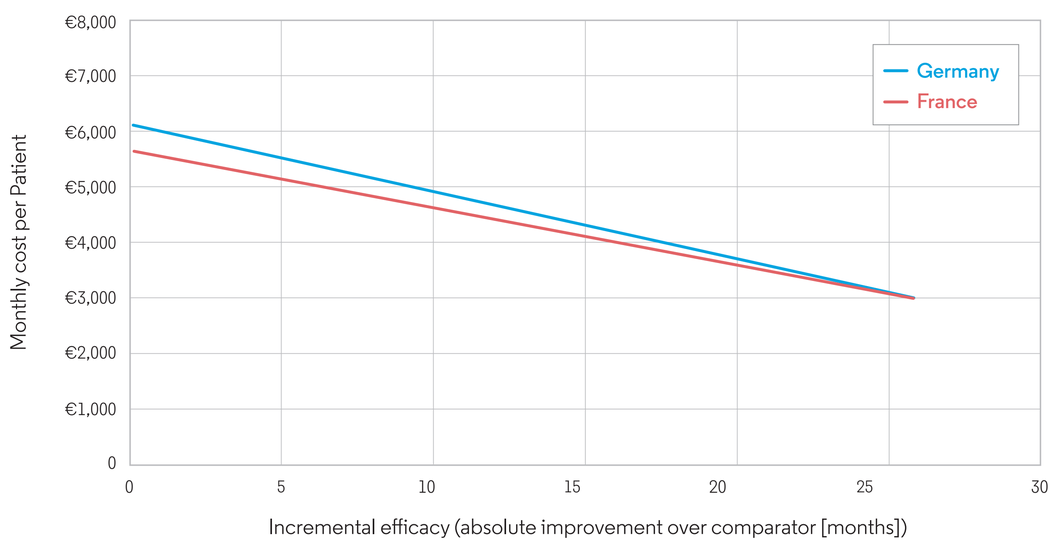
Figure 1. Hazard Ratio of new oncology molecules (2015 - 2023)



Results

- For Germany approximately 78% of products (35 out of 45) assessed in this analysis in Germany were reimbursed at <€8,500/month which would work out as approximately €100,000/year. None of the assessed products with an estimated prevalence >10 per 1000,000 achieved a price ≥€10,000/month. 13% (6 out of 45) of products achieved a reimbursed price >€15,000/month. Six products with an estimated prevalence <50 per 100,000 (orphan cutoff) and a >66% level of incremental efficacy achieved prices of >€10,000/month
- For France approximately 86% of products (24 out of 28) assessed in this analysis in France were reimbursed at <€8,500/month. None of the assessed products with an estimated prevalence >10 per 1000,000 achieved a price ≥€10,000/month. 11% (3 out of 28) of products achieved a price >€15,000/month
- For both France and Germany on average, a larger absolute PFS improvement in less aggressive tumor types did not correlate with a higher achievable price, suggesting they may not represent an urgent access issue. Overall, products that reported a greater than 10 months PFS improvement in areas of low unmet need (e.g. NSCLC, HR+ HER2- breast cancer) did not necessarily achieve a higher price
- Out of these, 18 of the 32 HRs published within the highest HR was for Onivyde pegylated liposomal (irinotecan hydrochloride tryhydrate) which was evaluated in 2022 for Epstein-Barr virus (EBV) with Post-transplant lymphoproliferative disease (PTLD). Despite a HR of 0.99, it was found to provide no additional benefit to the G-BA, however fared slightly better in France where HAS rated it ASMR IV
- The best HTA outcomes were for Nubeqa (Darolutamide) in Prostate Cancer with a seemingly modest HR of 0.68, HAS rated it ASMR III, and the G-BA found it has Significant Added Benefit, the second highest rating the agency could provide
- Most drugs evaluated fell into the range of a HR of 0.4-0.7, and had outcomes that fell between negative and mildly positive, with no clear association between HR and HTA outcome

Figure 2. Monthly cost in relation with incremental efficacy reported as absolute improvement in months for products reporting PFS



Conclusion

- Data maturity supersedes trial phase & line of treatment to achieve premium price. Comparator-controlled, Phase III programs were seen to be critical to achieve price points at or around €10,000 per patient per month. Overall Survival (OS) HR < 1, in a smaller patient population are ideal for premium pricing opportunity in Germany. In France increasing HR towards 1 didn't impact as significantly on monthly treatment cost. Line of treatment nor robustness of studies (Phases I/II vs. Phase III) have direct impact on monthly price per patient. As OS HR approaches 1 & beyond, monthly cost per patient tend to fall below €5,000, especially with increasing prevalence. OS HR < 1, in smaller patient population are ideal for premium pricing opportunity.
- In Germany, decreasing monthly price per patient was noticed as HR approached 1, irrespective of line of treatment & trial phases.
- The utilization of hazard ratios (HR) in the evaluation of clinical trials has become a cornerstone in the rigorous assessment of new drugs and medical treatments. These statistical measures offer a unique vantage point on the temporal aspects of treatment effects, particularly valuable when assessing critical clinical outcomes such as disease progression and survival.
- HRs enable a nuanced perspective that goes beyond traditional summary statistics, offering agencies the opportunity to evaluate clinical effectiveness, cost-effectiveness, and safety more precisely. As our study has revealed, the National Institute for Health and Care Excellence (NICE) in the UK, the Haute Autorité de Santé (HAS) in France, and the Federal Joint Committee (G-BA) in Germany, consider various factors when evaluating drugs, drawing upon as one element HRs to make informed decisions
- It is considered that HRs allow agencies to assess the efficacy of a drug in a dynamic manner, taking into account temporal aspects that might otherwise be overlooked
- Our analysis of HR utilization within the healthcare evaluation agencies of the France, and Germany revealed varying outcomes. In some instances, HRs seemingly had a significant impact on the pricing, while in others, they had no impact on benefit rating outcome. Specific cases, such as the assessment of Onivyde and Nubeqa, highlight the diverse parameters that are considered by these agencies beyond HR values for benefit assessment and pricing. In the case of Nubeqa, despite a seemingly modest HR, it garnered significant recognition from both HAS and G-BA, demonstrating the intricate nature of HR interpretation in healthcare evaluations
- It is evident from our study that HRs play a pivotal role in the assessment of new oncology drugs. However, the relationship between HR values and the benefit assessment i.e. HTA outcomes are not always straightforward. Multiple factors influence the final decision, including the overall clinical context, the specific patient population, and the ability to meet unmet medical needs
- In conclusion, HRs continue to be fundamental tools in the evaluation of clinical trials, enabling healthcare agencies to make well-informed decisions regarding the adoption of new drugs and treatments. While the HRs themselves are valuable, the interpretation and contextualization of these values within the broader clinical landscape are equally critical. Future research and collaboration between healthcare agencies can further refine the application of HRs, ultimately leading to more precise and evidence-based decisions in the field of healthcare evaluation and drug adoption

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References

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