Are Surrogate Endpoints a Way Forward in Non-Small Cell Lung Cancer? A Comparison of HTA Outcomes Across Germany, France, and the UK

Ergin Y, Malliou-Najjar K, Kassenaar S
Inbeeo, London

Introduction

In oncology, surrogate outcomes are increasingly being used to expedite the approval of new drugs.[1] Surrogate endpoints, including progression-free survival (PFS), disease-free survival (DFS), and response rate (RR), can be assessed earlier than clinically relevant outcomes such as overall survival (OS), which is considered the gold standard endpoint in oncology.[1,2]

Whilst filing with surrogate data may be sufficient to achieve early regulatory approval, this data may be challenged by health technology assessment (HTA) bodies due to an uncertain correlation with patient-relevant endpoints.

This research examines the relationship between surrogate endpoints and HTA outcomes in Non-Small Cell Lung Cancer (NSCLC) across Germany, France and the UK.

Materials & Methods

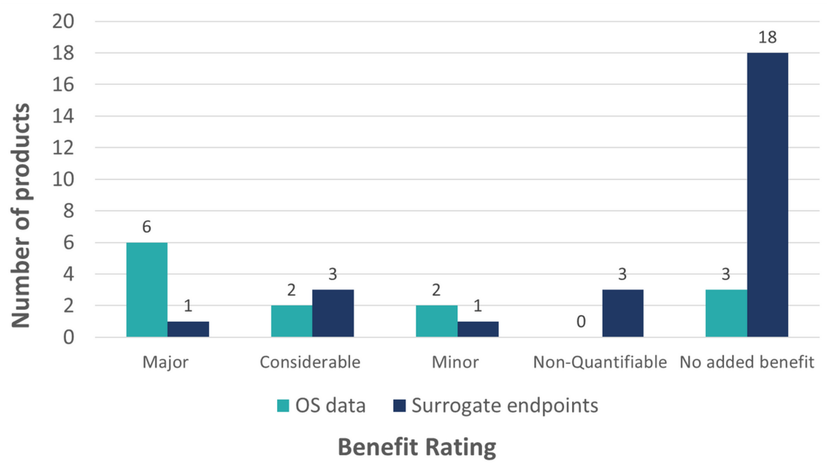
Products that received EMA marketing authorization for NSCLC between 2012-2022 were filtered to identify those with published appraisals from Germany's Federal Joint Committee (G-BA), France's National Authority for Health (HAS), and the UK's National Institute for Health and Care Excellence (NICE).[3-5]

Products were then categorized based on the endpoint for which they were granted regulatory approval: OS vs. PFS, DFS or RR.

HTA outcomes (benefit rating/ASMR/recommendation) of products with OS data vs. surrogate endpoints at first submission for the relevant indication were then compared in each country.

Results

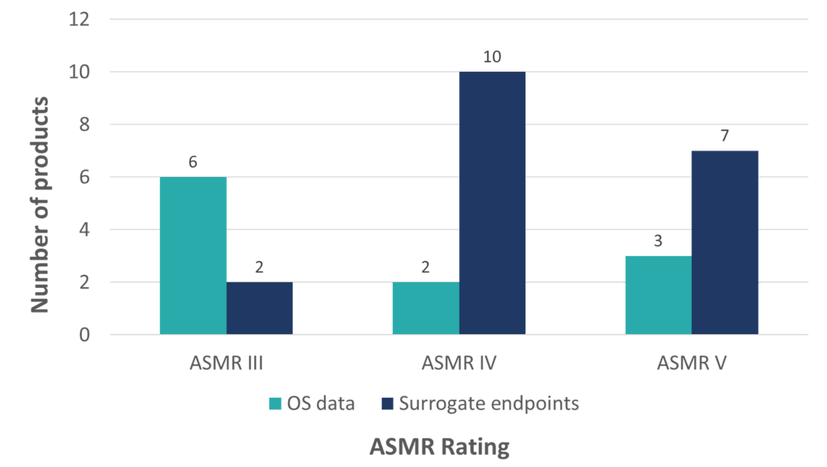
Figure 1: G-BA Benefit Ratings for EMA NSCLC Drug MAs from 2012-2022



Seventy-five percent of products with mature OS data received a positive added benefit rating (i.e. any rating above 'no added benefit') in at least one subgroup, compared to 27% of those with surrogate endpoints.

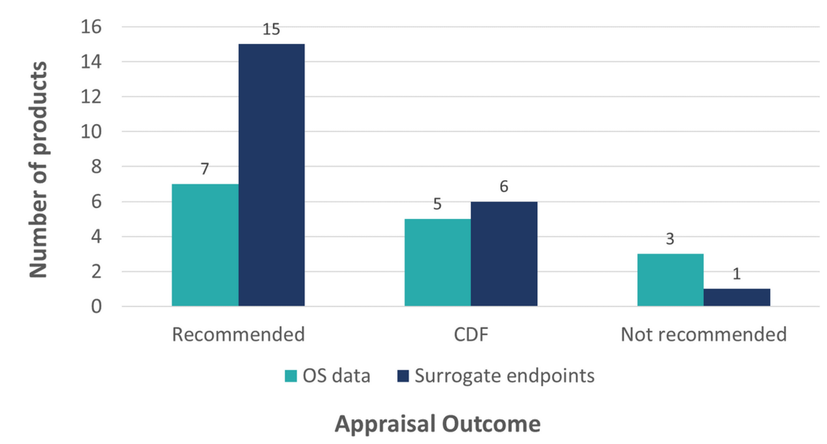
Thirty eight percent of drugs with mature OS data were awarded a 'major added benefit' rating vs four percent of those with surrogate endpoints.

Figure 2: HAS ASMR ratings for EMA NSCLC Drug MAs from 2012-2022



Fifty-five percent of products with OS data received an ASMR III compared to only 11% of products with surrogate endpoints.

Figure 3: NICE Guidance for EMA NSCLC Drug MAs from 2012-2022



Ninety-five percent of products with surrogate outcomes were recommended for routine use or for use within the Cancer Drugs Fund, compared to 80% of products with OS data.

Conclusion

In Germany and France, products submitting with mature OS data received more favourable HTA outcomes compared to products that filed with surrogate endpoints.

However, in the UK, products submitting with surrogate outcomes were more likely to receive a positive recommendation compared to those with mature OS. It is important to note that in addition to the Cancer Drugs Fund, which allows for temporary reimbursement of products with high clinical uncertainty, the modelling approach used by NICE allows surrogate endpoints to be factored into cost-effectiveness estimates.

Overall, manufacturers must consider that launching NSCLC products without mature OS data may have adverse consequences on HTA outcomes in Germany and France, which could impact pricing and access. The UK however may be more accepting of surrogate outcomes for NSCLC drugs.

Abbreviations

ASMR: Amélioration de Service Médical Rendu;
CDF: Cancer Drugs Fund
DFS: Disease-Free Survival;
EMA: European Medicines Agency;
G-BA: Federal Joint Committee;
HAS: Haute Autorité de Santé;
HTA: Health Technology Assessment;
MA: Marketing Authorization;
NICE: National Institute for Health and Care Excellence;
NSCLC: Non-Small Cell Lung Cancer;
OS: Overall Survival;
PFS: Progression-Free Survival;
RR: Response Rate;
UK: United Kingdom

References

1. Kemp, Robert, and Vinay Prasad. "Surrogate endpoints in oncology: when are they acceptable for regulatory and clinical decisions, and are they currently overused?." BMC Medicine. 15.1 (2017): 1-7.
2. Delgado, Amanda, and Achuta Kumar Guddati. "Clinical endpoints in oncology-a primer." American Journal of Cancer Research. 11.4 (2021): 1121.
3. Gemeinsamer Bundesausschuss. n.d. [online] Available at: <http://www.g-ba.de>
4. Haute Autorité de Santé. n.d. [online] Available at: <https://www.has-sante.fr/jcms/r_1455134/en/about-has>
5. NICE| The National Institute for Health and Care Excellence n.d. [online] Available at: <https://www.nice.org.uk/>