Assessment of Time to HTA Outcome for Novel Oncology Combinations and Decision Drivers Across UK and Europe

HTA195

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Background and Objectives

Advances in cancer biology have led to combination therapies becoming the cornerstone of treatment. Patient access to combinations remains challenging in the UK and EU, as supported by a 2022 analysis of time to decision for oncology combinations by Wilsdon et al.[1] versus the oncology EFPIA WAIT indicator.[1]

This research aims to evaluate the latest updates on time to HTA recommendation and the key drivers influencing decisions for novel oncology combination products.

Methodology

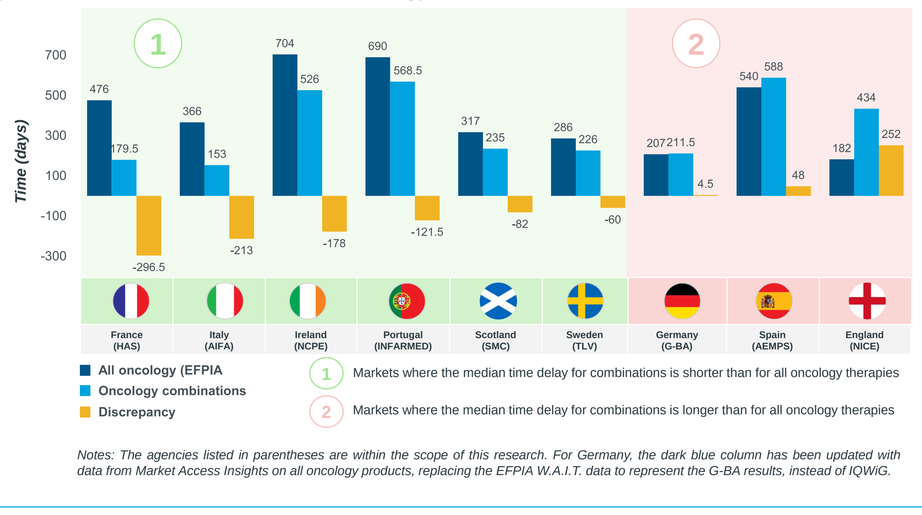
A review of 127 HTAs of oncology combinations was conducted. A search of an international HTA database (IQVIA's Market Access Insights) was conducted in October 2023, including HTAs with decision dates between July 2020 and September 2023. HTAs were restricted to double branded combinations for England, France, Germany, Ireland, Italy, Portugal, Scotland, Spain and Sweden. Data extractions included evidence under assessment, agency critique and recommendation. Time to decision was calculated as time between regulatory approval and date of positive HTA recommendation (with or without restrictions).

Results

The number of assessed combinations by HTA agency varied from 7 (Sweden) to 24 (France), with a mean of 10 across agencies. Most submissions leading to negative recommendations for oncology combinations came from Spain (N=6) and Ireland (N=5). Oncology combinations achieved faster positive decisions (median: 235 days, range: 153-588) compared to all oncology treatments (median: 366, range: 182-704), as shown in **Figure 1**. However, evidence indicated that time delays for combinations persist in Germany, Spain, and England.

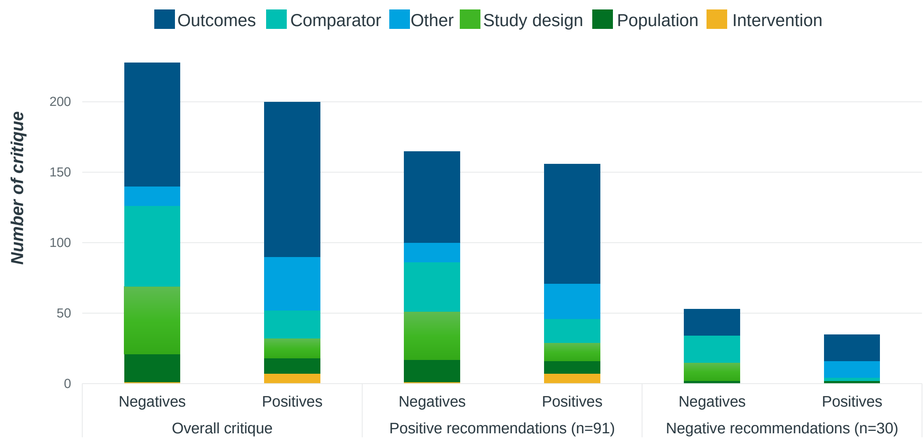
Compared to the 2022 analysis by Wilsdon et al.[2], the median time to positive decision for combinations improved in Italy, Portugal, Scotland, Spain and Ireland but increased in England, Germany, and Sweden. The greatest improvement in time to decision was noted in Italy, achieving quicker access by 348 days. Germany was found to have the largest increase in delays by 177 days; however, it is important to note that this analysis is only looking at G-BA decisions and excludes IQWiG.

Figure 1. Median Time for Positive Oncology Recommendations: Combinations vs. All Products



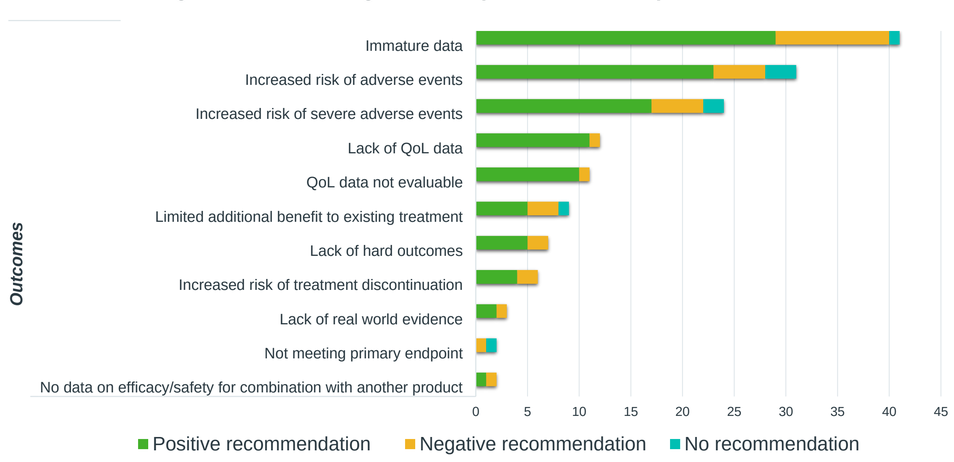
Notes: The agencies listed in parentheses are within the scope of this research. For Germany, the dark blue column has been updated with data from Market Access Insights on all oncology products, replacing the EFPIA W.A.I.T. data to represent the G-BA results, instead of IQWiG.

Figure 2. Clinical Negative vs. Positive Critique per HTA Recommendation



Notes: Positive recommendations include both recommendations with or without restrictions.
The number of the relevant HTA submissions is indicated by "n".

Figure 3. Clinical Negative Critique of Outcomes per HTA Recommendation



Note: Positive recommendations include both recommendations with or without restrictions.

Agency critique of combinations included sources of uncertainty commonly mentioned for monotherapies.[3] HTA agencies most often critiqued the choice of outcomes for the submitted clinical evidence, compared to other attributes of the evidence (**Figure 2**). ***Key insights from the negative recommendations indicate that the primary clinical factors that influence HTA bodies' decisions are outcomes*** (mainly due to data immaturity) ***and comparators*** (mainly due to poor quality of ITCs). Overall, regardless of recommendation, clinical negative critiques were most common for those submitting immature evidence and evidence for increased risk of (severe) adverse events (**Figure 3**).

Submissions lacking RWE (N=68) generally experienced longer decision times (median: 285 days; SD: 452.9); however, the decision times for submissions with RWE (N=51; median: 242.0 days) showed greater variability (SD: 508.1) (**Figure 4**).

For France, the majority of RWE comes from safety data and is the sole country utilising this type of data. Most common accepted RWE areas for England and Sweden were effectiveness/survival data followed by epidemiological evidence. Additional information on accepted RWE areas by country is shown in **Figure 5**.

Figure 4. Impact of RWE on Time to Decision

Figure 5. RWE Evidence Area by Country

Conclusions

- As is usually observed with the WAIT indicator, varied time to decision in accessing oncology combinations was observed across the UK and EU markets, despite similarities in agency critique to monotherapies,[3] indicating that other decision drivers influence combinations. This variation suggests that ***the challenges with access to combinations are being addressed differently across markets.***
- Notably, the ***time to decision has improved for most markets within the scope of this research, likely reflecting the implementation of processes that impact access to innovation***. The challenges with market access of innovative treatment like oncology combinations seem to be addressed on a policy level in some countries: France has introduced the Early Access Programme;[4] Ireland has implemented the Rapid Review[5] and Italy has adopted the Innovativeness Appraisal.[6] ***In England, access to oncology combinations remains problematic, as recent progress, including a new government level policy making it easier for drug firms to work together to ensure market access,[7] has not translated into quicker access.***
- Agency critiques of the evidence submitted for HTA of combination therapies frequently reflected the uncertainties observed with monotherapies, which were most commonly in reference to critiques of immature data submitted for clinical outcomes. This underscores the essential need for robust and mature clinical data to secure positive decisions for combination therapies, similar to monotherapies.[3] RWE remains an influential but less common source of evidence for HTA decision making, even for oncology combinations.

References
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Abbreviations
AEMPS, Agencia Española de Medicamentos y Productos Sanitarios (Spanish Agency of Medicines and Medical Devices); **EFPIA**, European Federation of Pharmaceutical Industries and Associations; **EU**, European Union; **G-BA**, Gemeinsamer Bundesausschuss (Federal Joint Committee in Germany); **HAS**, Haute Autorité de Santé (French National Authority for Health); **HTA**, Health Technology Assessment; **INFARMED**, Autoridade Nacional do Medicamento e Produtos de Saúde (National Authority of Medicines and Health Products, Portugal); **IQWIG**, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care, Germany); **ITC**, Indirect treatment comparison; **NCPE**, National Centre for Pharmacoeconomics (Ireland); **NICE**, National Institute for Health and Care Excellence (UK); **QoL**, Quality of Life; **RWE**, Real-World Evidence; **SMC**, Scottish Medicines Consortium; **TLV**, Tandvårds- och läkemedelsförmånsverket (Dental and Pharmaceutical Benefits Agency, Sweden); **UK**, United Kingdom; **WAIT**, Waiting Time for Access to Innovative Therapies.