Oncology-Branded Multi-Company Combinations: Assessment of the Availability in France, Germany, Italy, Spain, England, Scotland, Canada, and Australia

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Introduction/Objectives

Introduction

- The therapeutic approach in oncology is increasingly based on the combination of different innovative medicines.[1] Making those regimens widely accessible to patients in the different healthcare systems has been challenging.[2] As clinical research continues to evaluate the potential of combination therapies to improve patient outcomes, it is essential to implement sustainable solutions to ensure patient access to these medical advances[3]
- It is expected that around 45% of the combination therapies launched in Europe between 2024 and 2027 will involve assets owned by different companies, referred here as Multi-Company Combinations or MCCs.[2] Competition law limits cross-company collaboration which could impact patient access to the combinations. Hence, it is important to understand how those combination therapies have been assessed by the healthcare systems

Objectives

- To assess the availability rate (AR) and the time to availability (TA) of oncology-branded MCCs in France, Germany, Italy, Spain, England, Scotland, Canada, and Australia, and to provide a descriptive comparison with AR and TA metrics for monotherapies

Methods

- Firstly, oncology-branded MCCs with a marketing authorization (MA) granted from 1 January 2020 to 31 December 2023, in 1 of the following countries – France, Germany, Italy, Spain, England, Scotland, Canada, and Australia – were identified through the IQVIA Health Technology Assessment (HTA) Accelerator. Secondly, oncology-branded monotherapies were identified. Only indication extensions were selected as all components of each MCC had at least 1 prior MA. The MA cut-off date was aligned with that of MCCs for each regulator
- The AR was calculated as the number of oncology-branded MCCs or monotherapies that were available to patients in a given country divided by the total number of oncology-branded MCCs or monotherapies with a MA in the country. The TA was calculated as the difference between the MA date and the availability date (AD) defined as per **Table 1**. Benefit ratings in France, Germany, and Italy were reported. The involvement of 1 or several companies in the regulatory and HTA processes for the MCCs was also described. All variables were captured as of 10 April 2024

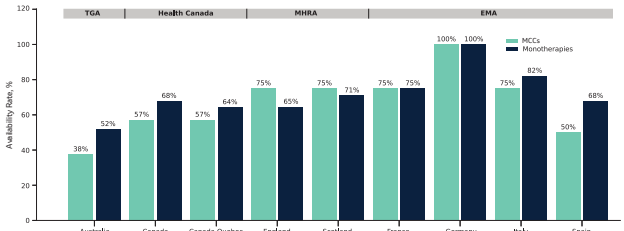
Table 1. Definition of availability and time to availability by country

General	The TA was the difference between the MA date and the AD. For MCCs, when the 2 components had a MA date, the most recent date was used. When only 1 component had a MA for a given indication, the AD of the combination was equal to the AD of this component. When a reimbursement decision was expected for each component, the combination was considered available if both decisions were published and the AD of the MCC was equal to the most recent AD of the 2 components.
Australia	A drug was considered available if its use was listed on Pharmaceutical Benefits Scheme (PBS) for a given indication, and the AD was the date of listing on PBS.
Canada	For all the provinces except Quebec, a drug was considered available if the negotiations with the pan-Canadian Pharmaceutical Alliance (pCPA) led to an agreement. The AD was the date of the agreement conclusion. In Quebec, a drug was considered available if it was included on the *Médicament d'exception* list, and the AD was the date of the inclusion in this list.
England	A drug was considered available if its use was recommended by National Institute for Health and Care Excellence (NICE) through baseline commissioning or within the Cancer Drugs Fund whichever occurred first. The AD was the publication date of the Final Draft Guidance.
France	A drug was considered available if it was listed on the public reimbursement list(s) for a given indication. In-patient drugs were considered available only if they were included on the *Liste en sus* for the given indication. The AD was the publication date of the listing on the appropriate list(s). If a drug was available through Early Access Program (EAP) publicly funded, it was considered available from the publication date of the positive EAP decision.
Germany	Given the scope of this research on indication expansions, a drug was considered available 1 day after the date of the MA.
Italy	A drug was considered available if it was listed on the public reimbursement list for a given indication. The AD was the publication date of the reimbursement decision in the *gazzetta ufficiale*.
Scotland	A drug was considered available if its use was accepted by Scottish Medicines Consortium (SMC) for a given indication. The AD was the publication date of the SMC advice.
Spain	The drug was considered available if it was listed on the nomenclator for a given indication. The AD was the date of the meeting of the *Comisión interministerial de precios de los medicamentos* (CIPM) that led to a positive recommendation.

Results

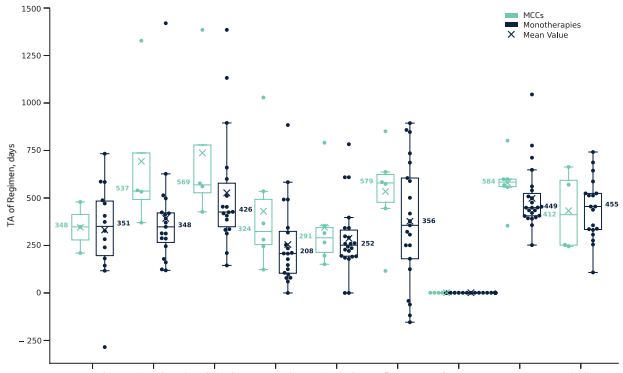
- The AR for MCCs varied from 38% in Australia to 100% in Germany for MCCs, and from 52% in Australia to 100% in Germany for monotherapies (**Figure 1**). In most countries, the AR of MCCs was lower than or equal to that of monotherapies except in England and Scotland. The largest differences were observed in Spain (-18 points) and in Australia (-14 points). The average of the mean AR across all countries was 67% for MCCs, compared with 72% for monotherapies
- The median and mean TAs for MCCs respectively fluctuated from 1 day in Germany to 584 days in Italy, and from 1 day in Germany to 738 days in Quebec (**Figure 2**). The median and mean TAs for monotherapies respectively went from 1 day in Germany to 455 days in Spain, and from 1 day in Germany to 527 days in Quebec. The median and mean TAs were longer for MCCs than for monotherapies in most countries except in Spain. The average of the mean TA across all countries for MCCs was 456 days, compared with 347 days for monotherapies
- In France, evidence of submission was not found for 2 of the 28 monotherapies with MA. 39% of the SMR issued for MCCs were found to be insufficient, while 21% were for monotherapies. None of the MCCs received an insufficient SMR for the entire indication, whereas 3 monotherapies did (**Figure 3**). An ASMR III was issued in 23% of the assessments for MCCs compared with 17% for monotherapies. An ASMR IV was issued in 23% of the cases for MCCs, compared with 45% for monotherapies
- In Germany, 14 benefit ratings were issued for MCCs. For monotherapies, evidence of submission was not found for 1 of them and 41 benefit ratings were determined. 86% of the benefit ratings issued for MCCs were no added benefit compared with 51% for monotherapies. While the proportion of considerable added benefit appeared similar between MCCs and monotherapies, minor and non-quantifiable added benefits were granted only for monotherapies in 15% and 19% of the cases
- In Italy, 4 and 20 reports related to the innovation status were respectively found for MCCs and monotherapies. None of the 4 MCCs had a full innovation status, while 8 monotherapies out of 20 (40%) received this recognition. For 3 out of the 4 MCCs (75%), an absence of therapeutic innovation was reported, compared with 8 monotherapies out of 20 (40%). 1 MCC (25%) and 4 monotherapies (20%) got a conditional innovation status
- For each country, when each component of the MCC was assessed by the HTA body, the benefit ratings issued were identical

Figure 1. Availability rates of regulatory approved oncology MCCs and monotherapies by country[a]



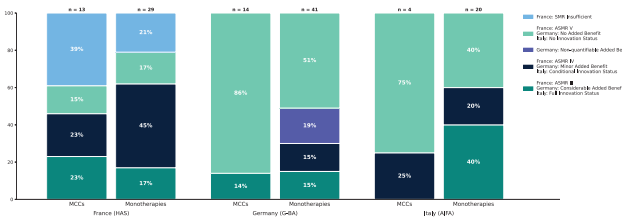
[a]Number of MAs: 8 MCCs and 27 monotherapies in Australia, 7 MCCs and 28 monotherapies in Canada, 8 MCCs and 31 monotherapies in England and Scotland, and 8 MCCs and 28 monotherapies in France, Germany, Italy, and Spain.
TGA, Therapeutic Goods Administration; MHRA, Medicines and Healthcare products Regulatory Agency; EMA, European Medicines Agency.

Figure 2. Distribution of the time to availability for oncology MCCs and monotherapies available by country[a]



[a]The numbers reported next to each box corresponds to the median.

Figure 3. Benefit ratings determined by HAS, G-BA and AIFA for oncology MCCs and monotherapies[a]



[a]Benefit ratings from Haute Autorité de Santé (HAS) for France, Agenzia Italiana Del Farmaco (AIFA) for Italy and Gemeinsame Bundesausschuss (G-BA) for Germany were collected. The percentages of benefit ratings were based on the total number of subpopulations defined by the given HTA body for every indication. For the MCCs with an HTA report for each component, only one was considered when the benefit ratings were identical for all components. The cases where evidence of submission was not found were not included.

Table 2. Types of HTA submission for the MCCs in case of cross-labeling[a]

Single Submission	Dual Submission
Australia	**France**
• Cross-labeling in 50% (4/8) of cases – 3 single HTA submissions; no report found for 1	• Cross-labeling in 38% (3/8) of cases – Dual HTA submissions for the 3 MCCs
Canada	**Germany**
• Cross-labeling in 71% (5/7) of cases – For both HTA bodies,[b] single HTA submissions for 4 MCCs; no report found for 1	• Cross-labeling in 38% (3/8) of cases – Dual HTA submissions for the 3MCCs
Scotland	**Italy**
• Cross-labeling in 38% (3/8) of cases – Single HTA submissions for the 3 MCCs	• Cross-labeling in 38% (3/8) of cases – Dual HTA submissions for 1 MCC; no report found for 2
Mixed	
England	
• Cross-labeling in 38% (3/8) of cases – Dual HTA submissions for the first assessed and single HTA submissions for the next 2	

[a]This table captures results where each component of the MCC had a MA for the indication in combination refers as cross-labeling. The dual submission category corresponds to the situations where both companies owning 1 of the 2 components submitted a reimbursement dossier, whereas the single submission category represents the cases where only 1 of the 2 companies submitted a dossier. Those findings were derived either from the number of HTA reports found or by the name of the submitting company or companies. In Spain, the publicly available information does not allow for conclusions to be drawn about the number of submitters.

[b]Canada Drug's Agency (CDA) and Institut National d'Excellence en Santé et Services Sociaux (INESSS).

Discussion/Conclusions

- This research shows significant disparities of availability for oncology-branded MCCs across Germany, France, Italy, Spain, England, Scotland, Canada, and Australia. MCCs are less available than monotherapies in Spain, Australia, Canada, and Italy. On average, MCCs took 109 additional days than monotherapies to be made available to patients across all countries
- Certain countries have begun implementing new reimbursement approaches. For instance, in case of cross-labeling, ie, all MCC components have a MA for the combination indication, in the cost-effectiveness driven countries, only 1 company submits a dossier whereas in the clinical-effectiveness driven countries, the tendency is to maintain dual submissions (**Table 2**). In Europe, the newly released EU HTA regulation does not specify yet the process for MCCs. Additionally, in France new measures have been recently implemented for MCCs without cross-labeling, with the objectives of avoiding access inequalities to MCCs across hospitals[4]
- In conclusion, this research highlights the need to continue strengthening collaboration among all stakeholders such as companies, regulators, HTA bodies, payers and patients, to streamline pricing and reimbursement processes for multi-company combinations that address unmet medical needs, while acknowledging the inherent complexities
- **Limitations:** This research is based on a limited sample, particularly for MCCs. For most countries, the availability dates only capture the national reimbursement and pricing processes. The restriction of use such as duration of treatment, dosing or subpopulations is not reported

References

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