The Oncology Combination Therapy Dilemma: Can Today's HTA Systems Support Tomorrow's Innovation? Lessons from Europe and the Future of Access in Asia-Pacific

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Introduction & Objectives

Branded-branded, free-dose oncology combinations are increasingly central to cancer care and are **projected to account for one in five developments of oncology medicine globally** over the next five years; up from one in ten in the prior five.[1]

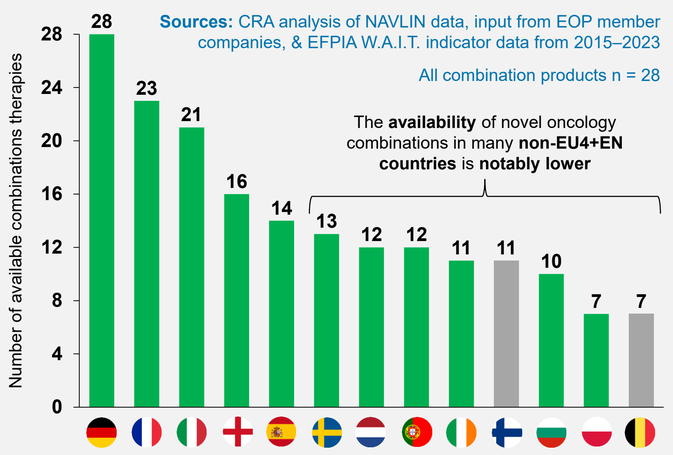
Despite many of these regimens delivering meaningful added clinical value to patients, they often **struggle to clear conventional HTA and pricing frameworks**. Current evidence demonstrates this problem in Europe most clearly. It is particularly challenging for **multi-sponsor combination regimens**, where value is evaluated at the regimen level (add-on + backbone), yet **prices are awarded and negotiated separately for individual constituents**, making it difficult to fairly attribute and reward the value created jointly.

The consequence for patient access is alarming; Europe shows that **only 54% of branded-branded combinations received a positive reimbursement recommendation**[2], taking an **average 193 days longer to reach patients**[3] than oncology medicines overall. As we explore in this poster, early evidence suggests APAC may be heading in the same direction.

Objective 1: Assess emerging access risks for branded-branded oncology combinations in Australia, Korea, Taiwan and Brazil.

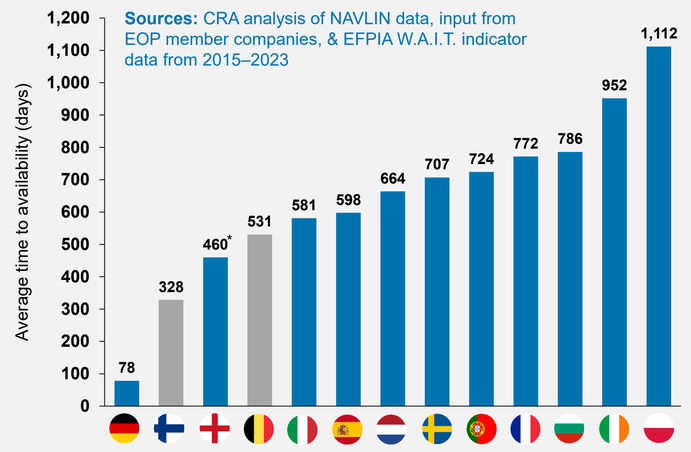
Objective 2: Identify lessons from European HTA experience to inform value framework adaptation and avoid access barriers.

Availability of Novel Oncology Combinations approved by EMA between 2015–2021 in selected European countries



In Europe, the **proportional availability of novel oncology combination therapies was 17% lower** than that of all oncology products across countries.[3]

Average time to availability, from EMA approval date, for novel oncology combinations approved between 2015–2021



Across all countries, novel oncology combination therapies took on average **193 days longer to become available** versus all oncology products.[3]

Methodology

Targeted literature review: Conducted web-based review of publicly available sources on oncology combination reimbursement barriers and enablers.

Database: Google Scholar and Google

Search terms: “oncology combinations”, “free dose combinations”, “HTA”, “pricing”, and “reimbursement”

Market scope selection: Markets across the Asia-Pacific and Latin America regions were selected to ensure the diverse approaches to oncology combination value assessment, including **cost-effectiveness and budget impact archetypical HTA processes**, are reflected in the analysis.

- **Australia:** Established cost-effectiveness-led HTA with explicit budget-impact assessment.
- **South Korea**: Pharmacoeconomic evaluation-led system, with exemptions for eligible high-need medicines.
- **Taiwan**: Globally budgeted NHI system with strong budget-impact and cost-effectiveness scrutiny.
- **Brazil**: Affordability- and budget-impact-sensitive public HTA, with formal cost-effectiveness assessment.

Research framework: The research framework was applied during targeted literature review, assessing branded–branded oncology combinations across **three dimensions**: pricing and reimbursement, HTA and value assessment, and the broader system readiness and policy environment.

HTA & Value Assessment

Evaluate HTA assessment methodologies, evidence requirements, decision criteria and value attribution mechanisms for oncology combinations

Pricing & Reimbursement

Assess national price and reimbursement mechanisms and their application to oncology combinations

System Readiness & Policy Environment

Examine emerging policy discussions and initiatives and stakeholder perspectives on oncology combinations

Results

The research uncovers three cross-country access bottlenecks:

Assessment

There is **no suitable value framework to assess combinations in any market** – instead single-agent frameworks with rigid comparator rules & cost thresholds built for monotherapy, not multi-brand regimens

Affordability

Affordability rather than clinical benefit is the barrier when add-on prices stack against expensive backbone or an all-together novel regimen is stacked against a cheap mono comparator

Pricing

No way to split value across sponsors with **no value-attribution method**, limited scope for indication-based pricing, and competition law blocking coordination & collaboration

Australia

Combinations are assessed as regimens but reimbursed as separate PBS products, with confidential pricing offering some flexibility across a molecule's indications, though indication-specific pricing is possible but not routine.[4]

Country Policy Levers:

- **Confidential agreements:** Provide flexibility to improve cost-effectiveness without affecting list price, but do not provide a formal mechanism to split value between constituents.
- **Multi-indication reimbursement:** A weighted effective price can reflect value and volume across uses, including combinations, but does not isolate concessions to the combination indication.[4]

Case example: Olaparib + Bevacizumab – ovarian cancer
recommended only at the 3rd PBAC review after price cuts across three submission cycles, delaying access ~2 years longer than the oncology average.[5,6]

South Korea

Combinations are assessed and reimbursed at constituent level, requiring separate HTA, pricing and reimbursement decisions across manufacturers, which can delay access to the full regimen.[11,12]

Country Policy Levers:

- **ICER flexibility:** Considering greater flexibility in ICER thresholds for innovative combinations.[13,14]
- **Indication-based pricing:** Potentially allowing greater pricing flexibility across combination and monotherapy settings.[13,14]
- **Partial reimbursement:** Introduced in 2025 for selected branded-branded combinations, preserving reimbursement of the listed component while the partner remains patient-paid.[15]

Case example: Enfortumab vedotin + Pembrolizumab – urothelial carcinoma
reimbursed access delayed >2 years after MFDS approval as separate pricing negotiations with both manufacturers remained unresolved.[16]

Taiwan

Taiwan's NHI operates under a strict annual global budget cap, so combinations of premium-priced medicines can face particular affordability pressure. Combinations are assessed as regimens but priced separately, so the cost of each premium-priced constituent adds to the total.[7]

Country Policy Levers:

- **Drug-pairing agreements:** Can reduce total regimen cost through one sponsor’s concession, but do not establish a formal cross-sponsor value split.[8]
- **Cancer Drug Fund:** Provides temporary funding for eligible cancer medicines awaiting routine NHI coverage but does not resolve long-term regimen affordability.[9]

Case example:
TW has no publicly identified NHI-funded multi-MNF combination.
Lenvatinib + pembrolizumab – endometrial cancer
unfunded since its March 2022 approval, with further discounts required to make it cost-effective.[10]

Brazil

A rigid constituent-level price ceiling is set at market entry, so combinations are assessed as regimens but constrained by caps fixed before their combination value is reflected.[17]

Country Policy Levers:

- **Commercial discounts:** Constituent-level concessions can improve cost-effectiveness but cannot formally redistribute value across sponsors.
- **New negotiation committee:** Introduces confidential discounts and risk-sharing, but remains an emerging, non-combination-specific route.[18]

Case example:
Has no publicly identified SUS-funded multi-MNF combination.
Pembrolizumab + axitinib – renal cancer
rejected in August 2021 following unfavorable cost-effectiveness and budget-impact findings.[19]

Conclusions

The growing relevance of branded–branded, free-dose oncology combinations raises alarming concerns around patient access as existing HTA and pricing frameworks can create barriers and delays. This analysis draws lessons from Europe, where oncology combinations have faced lower availability and delays in patient access, and identifies key HTA, pricing and reimbursement gaps in APAC and Brazil. Multistakeholder collaboration and solutions that span across levers are urgently needed to deliver change in terms of current HTA processes and more importantly drive longer-term reform in value frameworks and expand funding.

Abbreviations: APAC = Asia-Pacific; EMA = European Medicines Agency; HTA = Health Technology Assessment; ICER = Incremental Cost-Effectiveness Ratio; NHI = National Health Insurance; PBS = Pharmaceutical Benefits Scheme; SUS = Sistema Único de Saúde.

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