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Value Attribution Frameworks for Combination Treatments: Are They a Viable Solution to Solving the Market Access Challenges?

Manufacturer perspective

ISPOR presentation

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Novel combinations help to address key unmet needs in oncology, and are increasingly becoming the standard of care

Combination treatments can help to **overcome tumor resistance** to therapies

Unmet needs in Oncology

- Despite huge progress in oncology, levels of unmet need among cancer patients remain high
- This is largely due to the ability of cancer cells to resist treatment
- Resistance mechanisms can vary between patients with the same cancer type, across tumors within a single patient or within the tissue of a single tumor

Benefits of combination therapies

- Combination treatments leverage distinct but complementary mechanisms of action to overcome treatment resistance in both solid tumors and hematological malignancies[1]
- Due to tumor resistance, targeted/precision agents may work better in combination with other anti-cancer drugs than in monotherapy
- There is a belief that most of oncology drugs will be combined with medicines from other manufacturers in the coming years[2]

References 1. **OECD**, 'Addressing Challenges in Access to Oncology Medicines, 2020; 2. **US National Cancer Institute**, 'Cancer Drug Resistance: Unraveling its complexity', 2020.

Despite clinical benefits, novel oncology combinations are currently facing price and access challenges

Combinations are valued as a single treatment, but often priced as individual components, creating inefficiencies and barriers to patient access

Key challenges

Launch planning

Reimbursement status

The backbone product may not be reimbursed in all markets, leading to greater reimbursement challenges in attempts to keep the combination cost-effective or affordable

Value assessment

Value attribution

There are no frameworks to attribute value between the components of a combination

Lack of WTP differentiation

Payers value incremental benefits equally across products, despite combos having potential to be unique therapeutic solution in more challenging indications

Pricing negotiation

Budget impact

Combination therapies are likely to be more expensive than monotherapies, payers have general budget concerns

Limited price headroom

Pricing combinations holistically often leave little willingness-to-pay 'headroom' for the add-on, which in some cases may not be cost-effective even at zero price

Competition laws

Manufacturers have to ensure they are adhering to all applicable competition laws in exploring pricing options together when they are willing to engage

Limited commercial incentives

Since in many countries a single price applies across all indications, this can lead to concerns about commercial viability

Challenges will affect combinations differently depending on their characteristics

Some aspects of combination development make them more vulnerable to PMA challenges			
Less vulnerable		**More vulnerable**	
Components owned by same manufacturer	**Component ownership**	Backbone and add-on owned by different manufacturers	Backbone MNFs have little willingness to negotiate on price, leaving the initiator of the combination to make all necessary price negotiations to secure access
Cheap generic backbone	**Backbone patent status**	Expensive branded backbone	Expensive backbones leave little willingness-to-pay 'headroom' for the add-on
Add-on already launched at established price*	**Launch status of add-on**	Add-on does not have established price	Existing prices can act as a high starting point for negotiations (although consider impact of price reductions on other existing indications)
Fixed dose combination	**Dosing**	Free dose combination	Fixed dose combinations are more amenable to HTA processes designed for monotherapies
Significant benefit over comparator	**Efficacy**	Minor benefit over comparator (especially if comparator is backbone alone)	Combinations with 1+1<2 clinical efficacy will struggle to get a 1+1=2 price

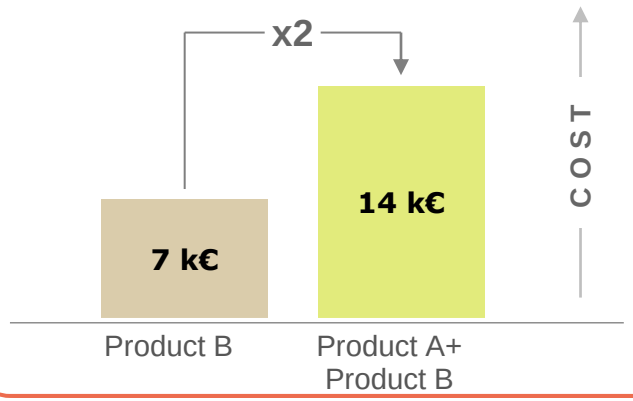
Note: From add-on product owner view point

Combinations are often more expensive per month and used for longer than monotherapies, raising BI concerns

High budget impact of combination therapies

1 Increased cost[1] due to multiple products

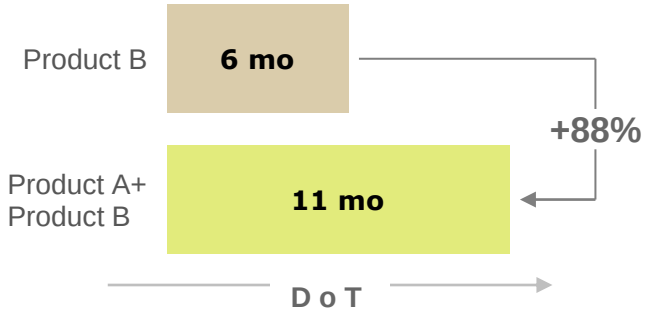
Monthly cost of treatment[2] of Product A + Product B vs. SoC (Product B) in Country X



2 Increased cost due to longer DoT

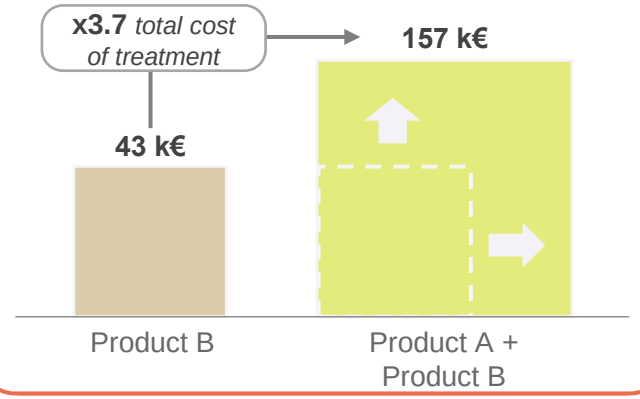
Exacerbated with increasing longer PFS/DoT

In its clinical study, Product A + Product B achieved 11.3 months of mPFS vs. 6.0 months for Product B in Melanoma



A double effect on total cost of therapy

Total cost of therapy in Country X for Product A + Product B



Affected markets

This challenge applies across **all markets** since all archetypes consider the overall treatment cost in pricing negotiations

Vulnerable products

Combinations with one or more **high cost components** or with **no fixed Tx duration**

Notes (1) Includes mandatory discounts (2) Cost of treatment per month (1 month = 4 weeks) is based on total cost of treatment divided by DoT. Indication: BRAF V600 mutation-positive patients with unresectable locally advanced or metastatic melanoma

There are no frameworks for attributing value between combinations

Value assessments consider combinations as a single therapy

Challenge overview

- At the clinical level, it is extremely **difficult to determine the relative contributions of the components to the clinical efficacy** of a combination, even in cases where monotherapy data is also available
- At the value assessment/payer level, there are **no specific frameworks in place** to manage this scientific challenge, and there is little interest from stakeholders to develop such a framework
- As a result, **combinations are assessed as a whole**, and no relative value is determined for the add-on vs the backbone when used in combination

Affected markets

- This challenge applies across **all markets** since it relates to difficulties interpreting the clinical dossier

Vulnerable products

- Combinations with a **backbone that has demonstrated substantial clinical efficacy as a monotherapy** are likely to face particular challenges

Notes (1) Includes mandatory discounts (2) Cost of treatment per month (1 month = 4 weeks) is based on total cost of treatment divided by DoT. Indication: BRAF V600 mutation-positive patients with unresectable locally advanced or metastatic melanoma
Source: GBA; Clinicaltrials.gov; Monitor Deloitte analysis
Figure originally in Sanofi Onco Combo Roadmap

How to support value recognition for combinations

Promote value-driven, fair, transparent, and efficient pricing and reimbursement frameworks

Value for combination therapies should be comprehensively defined by health authorities, encompassing clear and multidimensional criteria that reflects the full clinical, economic, and societal value of novel therapies

State-of-the-art HTA evaluation methodologies for novel combination therapies are instrumental to embracing the full value brought to patients

Country legal framework/competition laws should reflect the unique challenges of novel combination therapies

Thank you for listening!

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