HPR1

ComboConnect

Bridging Access Gaps in Combination Therapies: An Italian Project in Collaboration With ISPOR Italy-Rome Chapter

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INTRODUCTION AND OBJECTIVE

Over the past two decades, **combination therapies (CTs)** have addressed unmet needs in complex diseases, particularly in oncology. Despite their clinical relevance, access to CTs is hindered by disparate regulatory frameworks, a lack of clear value attribution for individual components, and misaligned reimbursement procedures.

The ***ComboConnect* project** aimed to analyze these challenges and provide actionable recommendations to support institutional decision-making.

METHODS

A mixed-methods approach was adopted. Quantitatively, EMA-approved CT indications evaluated in Italy from 2018 to 2024 were analyzed. A comprehensive database was built in MicrosoftExcel®, including CTs involving two or more APIs (at least one high-cost drug). Publicly available data from AIFA committees (UPC, CTS/CPR opinions, GU) were used to map P&R processes. CTs were grouped into four archetypes based on EMA label change and MAH ownership. Qualitative insights were gathered through expert meetings, involving national-level stakeholders.

RESULTS

A total of 41 CTs were analyzed (Figure 1). The average time-to-reimbursement was 467 days, significantly longer than the 327-day national average for single agents [1]. Timelines were particularly affected during the economic negotiation phase, except for CTs, including off-patent drugs (Figure 2). The archetype-based analysis revealed the longest delays in CTs involving different MAHs due to unaligned regulatory submissions. In cases where the backbone and the add-on followed separate negotiation pathways, procedural misalignment led to asynchronous timelines.

Figure 1. Flow-chart sample selection

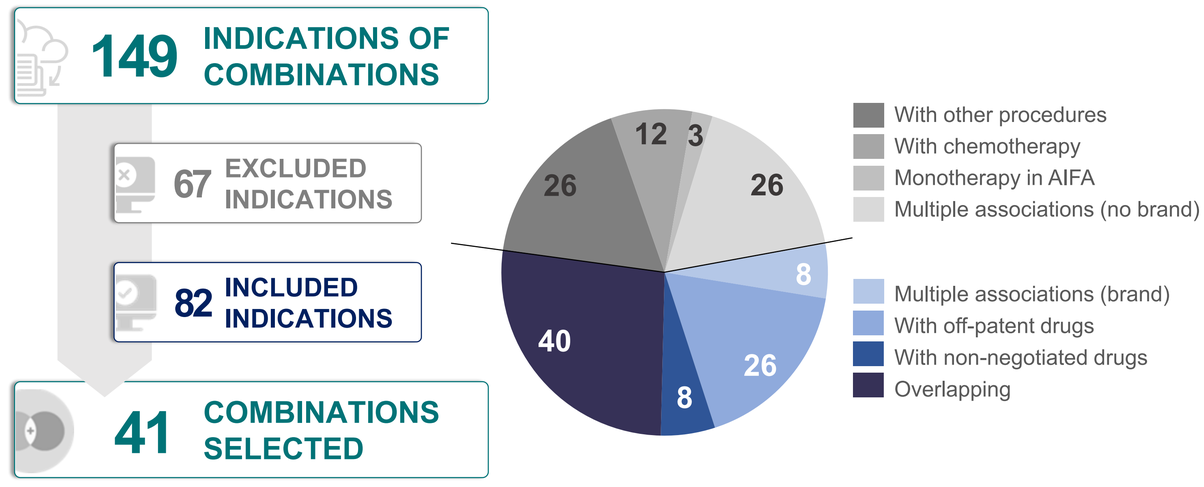
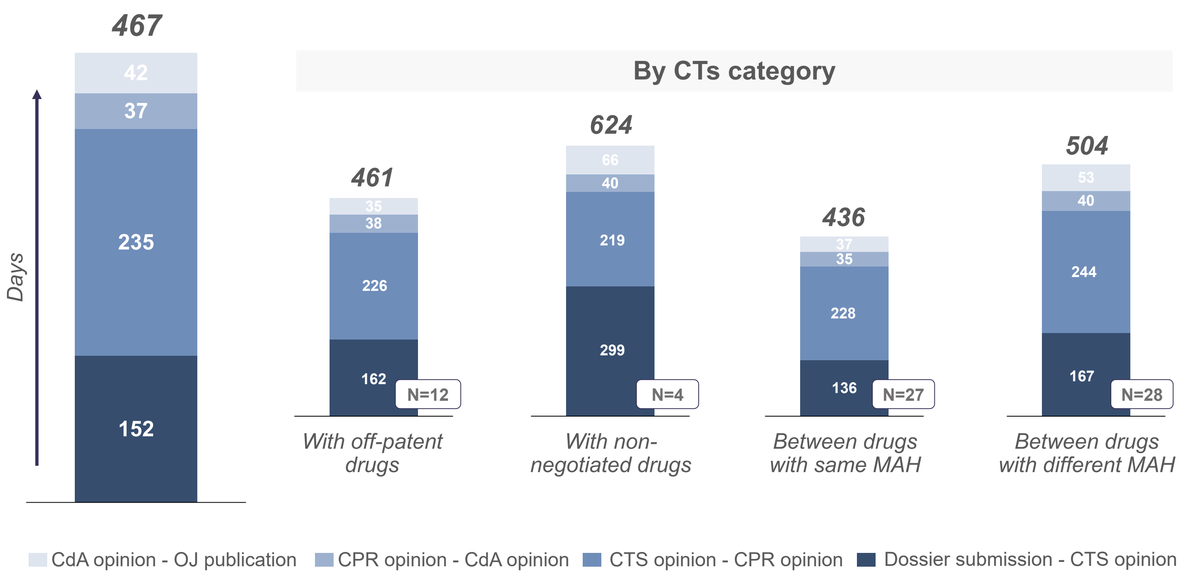


Figure 2. Average duration of assessment and negotiation pathway



CONCLUSIONS

Divergent timelines between backbone and add-on components lead to inefficient and prolonged evaluations, especially in cases with different MAHs. Additionally, delays may be due to the value uncertainty of each component, resulting in unfair prices that do not fully recognize CTs' actual value. The *ComboConnect* project highlights the urgent need for a methodological shift across regulatory, scientific, and economic domains, acknowledging the complexity of CTs through multi-stakeholder coordination, harmonized EMA/AIFA procedures, and flexible/ad hoc pricing models. Policy-specific actions are crucial for reducing procedural inefficiencies and ensuring timely access to CTs.

REFERENCES

[1] AIFA. Rapporto sulle Tempistiche delle Procedure di Prezzo e Rimborso dei Farmaci nel periodo gennaio 2018–2022. Aprile 2023.

ABBREVIATIONS

AIFA: Italian Medicines Agency; **API:** Active Pharmaceutical Ingredient; **CTs:** Combination Therapies; **CTS:** Technical Scientific Committee (Comissione Tecnico-Scientifica); **CPR:** Pricing and Reimbursement Committee (Comitato Prezzi e Rimborso); **EMA:** European Medicines Agency; **GU:** Official Journal (Gazzetta Ufficiale); **ISPOR:** International Society for Pharmacoeconomics and Outcomes Research; **MAH:** Marketing Authorization Holder; **P&R:** Pricing & Reimbursement; **UPC:** Centralized Procedures Office (Ufficio Procedure Centralizzate).

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