



Innovative Therapeutics:

Challenges and Opportunities in Developing Drug Combinations

Webinar - October 15th, 2024

Agenda

Challenges and Opportunities in Developing Drug Combinations

In today's webinar, our panel will address the following questions:



01

How do we identify and validate the synergistic mechanisms of action between drug combinations?



02

What strategies can be used to predict and manage potential drug-drug interactions in combination therapies?



03

How do we balance efficacy and safety in combination therapies to minimize adverse effects?



04

What are the costs and benefits of developing drug combinations?



Today's panelists

Innovative Therapeutics: Challenges and Opportunities in Developing Drug Combinations

Host:



Michael Ward

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Guest panelists:



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Drug combination challenges

1.

Understanding mechanism of action of individual drugs does not practically lead to understanding which drug combinations would be synergistic

2.

1000s of compounds at varied dose creates unlimited screening space

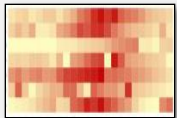
10 drugs ➤ 50 drug pairs 100 drugs ➤ 5,000 drug pairs

3.

Impracticality of screening makes use of network-based predictions critical

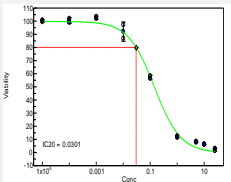
4.

Objective: leverage drugs / indications / OMICS data to build models that predict efficacious drug combinations



OMICS data

Gene expression, SNPs, Copy number



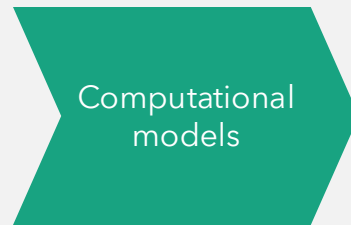
Drug information

Chemical properties
Titration curves
Toxicity information



Interactions

Drug-target
Target-indication
Biological pathways



Ranks for potential drug pairs

Team	Rank
Teaminf	1
Team#520	2
Team#352	3
Team#382	4
Team#383	5
Team#421	6
Team#354	7
Team#384	8
Team#571	9
Team#480	10
Team#173	11
Team#558	12
Team#556	13
Team#377	14
Team#405	15
Team#572	16
Team#456	17
Team#350	18
Team#435	19



Drug combination in the market

Regulatory Frameworks for Combination Therapies

Varying health policies, approval processes, and market access strategies across regions lead to distinct regulatory frameworks.



United States of America (FDA)

Approval Process: The FDA evaluates combination therapies through the New Drug Application (NDA) or Biologics License Application (BLA). Each component of the therapy must be individually approved, but the combination can be submitted together.

The FDA has specific guidance documents for combination products, which outline considerations for clinical trials, manufacturing, and labeling. Emphasis on the need for robust clinical data demonstrating the safety and efficacy of the combination, including interaction studies.



European Union (EMA)

Centralized Approval Process: The European Medicines Agency (EMA) allows for a centralized procedure for combination therapies, which can streamline the approval process across member states.

The EMA has specific regulations for combination products, which include drugs and medical devices, and it emphasizes the need for thorough clinical data supporting safety and efficacy.



China (NMPA)

Evolving Regulations: The National Medical Products Administration (NMPA) is rapidly evolving, with recent reforms aimed at accelerating the approval process for combination therapies. The NMPA has guidelines that may require separate clinical trial data for each component and their interactions.



Japan (PDMA)

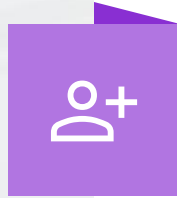
Regulatory Pathways: The Pharmaceuticals and Medical Devices Agency (PMDA) has its own guidelines, which require additional data for combination therapies, particularly if they involve different therapeutic areas.

Guidelines on the approval process for combination therapies, highlighting the need for comprehensive data on each component.

Japan often emphasizes innovative therapies and offers expedited pathways for promising combination therapies.

Overall, while there are common threads in regulatory approaches, the specifics can vary greatly, necessitating tailored strategies for each region when developing and marketing combination therapies.

Evolution of Guidelines



Increased Focus on Personalized Medicine: As precision medicine advances, regulations may evolve to reflect the need for tailored combination therapies.



Adaptive Trial Designs: Regulatory bodies may increasingly accept adaptive designs that allow for modifications based on interim results, particularly in combination therapy studies.



Streamlined Approvals: There may be a trend toward more streamlined approval processes for combinations that demonstrate clear synergistic benefits.



Post-Market Surveillance: Enhanced focus on post-market surveillance and real-world evidence to monitor the effectiveness and safety of combination therapies.

Strategies for Navigating Regulatory Challenges

Strategies to Overcome Challenges and Leverage Opportunities

01

Early and Ongoing Regulatory Engagement:

- Engage with regulatory agencies early in the development process to obtain guidance on the regulatory pathway, trial design, and data requirements.
- Use pre-submission meetings and consultations to clarify expectations and address potential issues early.

02

Comprehensive Clinical Trial Design:

- Design robust clinical trials that address both the individual and combined effects of the drugs. Consider adaptive trial designs to optimize dosing and efficacy.
- Ensure trials provide clear evidence of the combination's added value over existing therapies.
- Consider adaptive trial designs to allow for flexibility in response to emerging data.

03

Robust Data Management:

- Develop a detailed data management plan to integrate and present data from different sources in a cohesive manner.
- Collect extensive preclinical and clinical data on each component and their interactions.
- Ensure all data meets regulatory standards and addresses both the safety and efficacy of the combination.

04

Strategic Use of Regulatory Incentives:

- Explore opportunities for expedited review processes, orphan drug status, or other regulatory incentives that may be available for your combination product.
- Leverage regulatory support programs to assist in navigating the development and approval process.

05

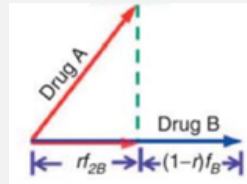
Collaborative Approaches:

- Consider partnerships with other companies, research institutions, or regulatory consultants to share expertise and resources.
- Collaborate with stakeholders to address complex challenges and enhance the development process.

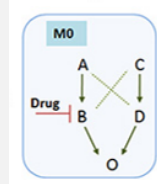


Drug combination prediction methods

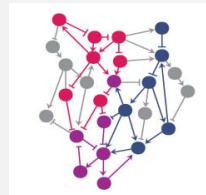
Mathematical methods



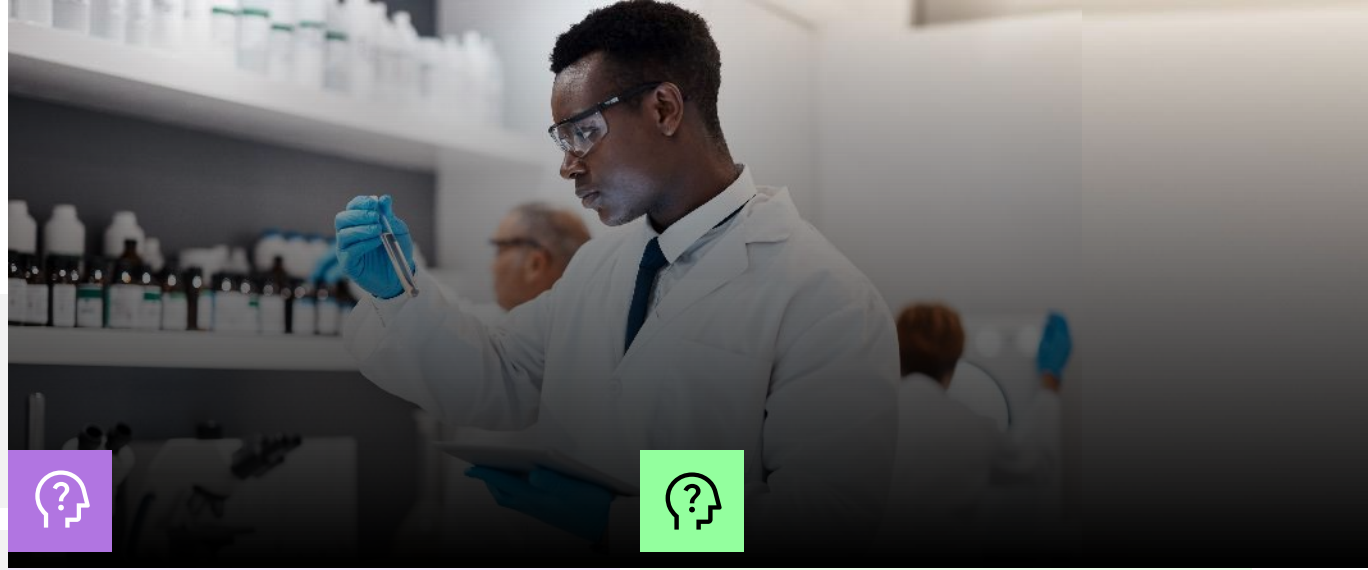
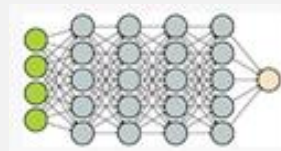
Kinetic Modeling



Systems Biology method



Machine Learning

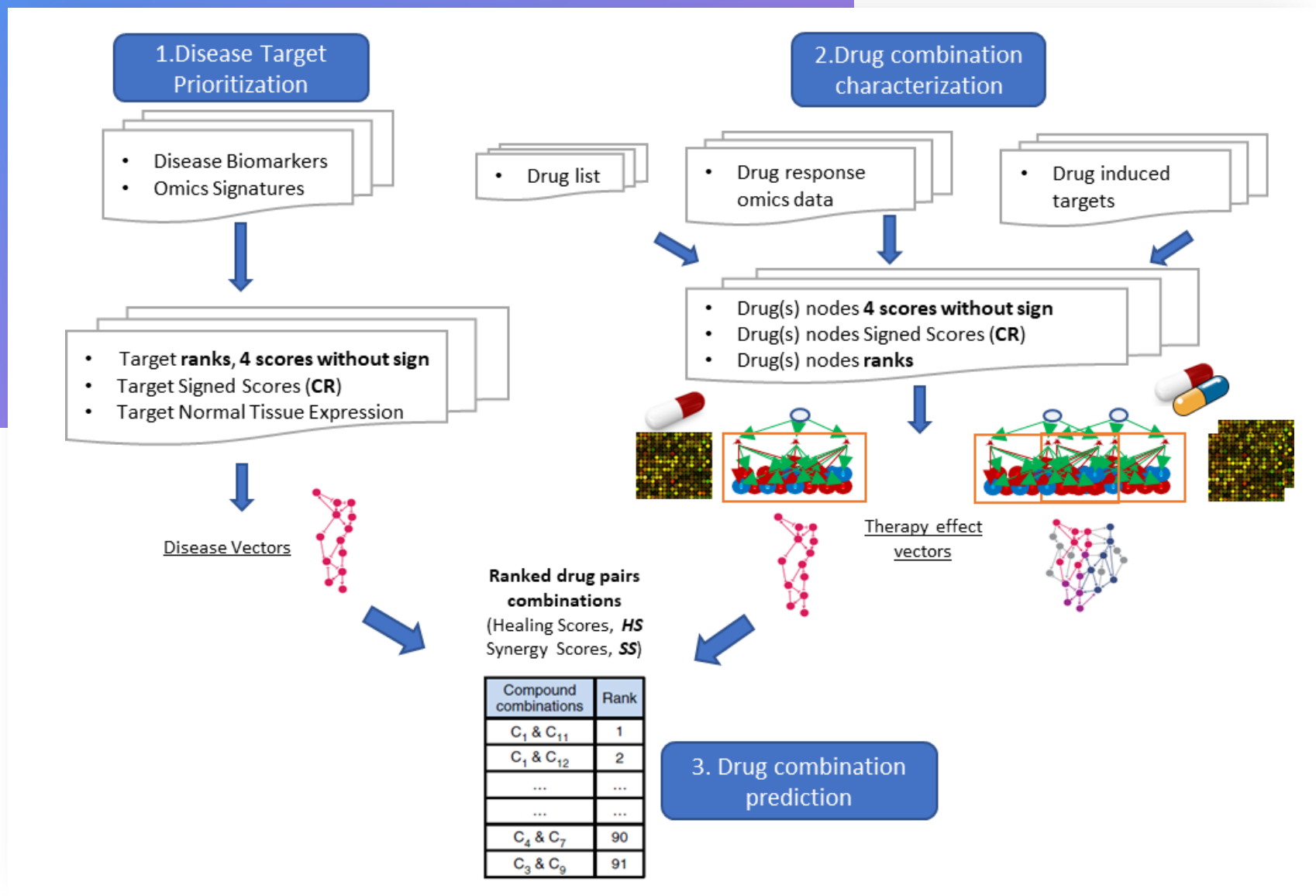


What type of methods are used to predict drug combinations?

What are the advantages and disadvantages of each of them?

Drug combination prediction in aging

Case study for the drug combination prediction service



Questions?



Use the chat feature

Q&A will take place
at the end of the
webinar

Thank you for joining us



How can Clarivate help?

Cortellis Drug Discovery Intelligence

Accelerate preclinical development and avoid late-stage failures with drug intelligence that integrates multi-source biological, chemical and pharmacological data into one platform.

Discovery and Translational Science Consulting Services

Helping you optimize each step of drug development, from discovery to clinical trials to bring treatments to market and patients faster.

OFF-X

A unique translational tool providing drug and class safety intelligence to anticipate risks and drive new competitive value.

Cortellis Regulatory Intelligence

Keep up to date with regulations, maintain regulatory compliance and make the right strategic decisions.



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