# Breakout Session #1
# Design of Master Protocols


EFPIA European Federation of Pharmaceutical Industries and Associations

PPD

Norwegian Medicines Agency

Day 1
5 October 2021

# Breakout session 1
# Design of Master Protocols

Multi-stakeholder workshop
5 - 6 October 2021

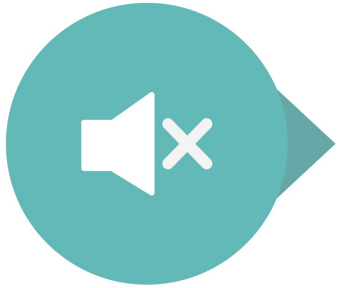
*Chairs:*

Christine Fletcher (GSK, EFPIA)
Lada Leyens (Roche, EFPIA)

Master protocols designs are supporting innovation strategies for evidence generation. This session will use 2 case studies, one in oncology and one in non-oncology, to illustrate some of the key challenges and sources of complexity when designing master protocols. The discussion will focus on key and critical points for different stakeholders. Their views will be shared and solutions proposed to enable recommendations and increased alignment across stakeholders regarding an optimal design of master protocols.

# House-keeping rules

## (For active participants in the Zoom call)



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# Agenda

- **Welcome (5 min)**
  - Aims and objectives
  - Stakeholders present today
  - Rules of engagement
- **Introduction to case studies (10 min)**
  - Morpheus
  - Piranga
- **Discussion (1h 40 min)**
  - Experience, robustness and stakeholder views
  - Key design challenges
  - New frontiers
  - Call for action: future for multi-sponsor master protocols
- **Wrap up discussion and key messages (5 mins)**

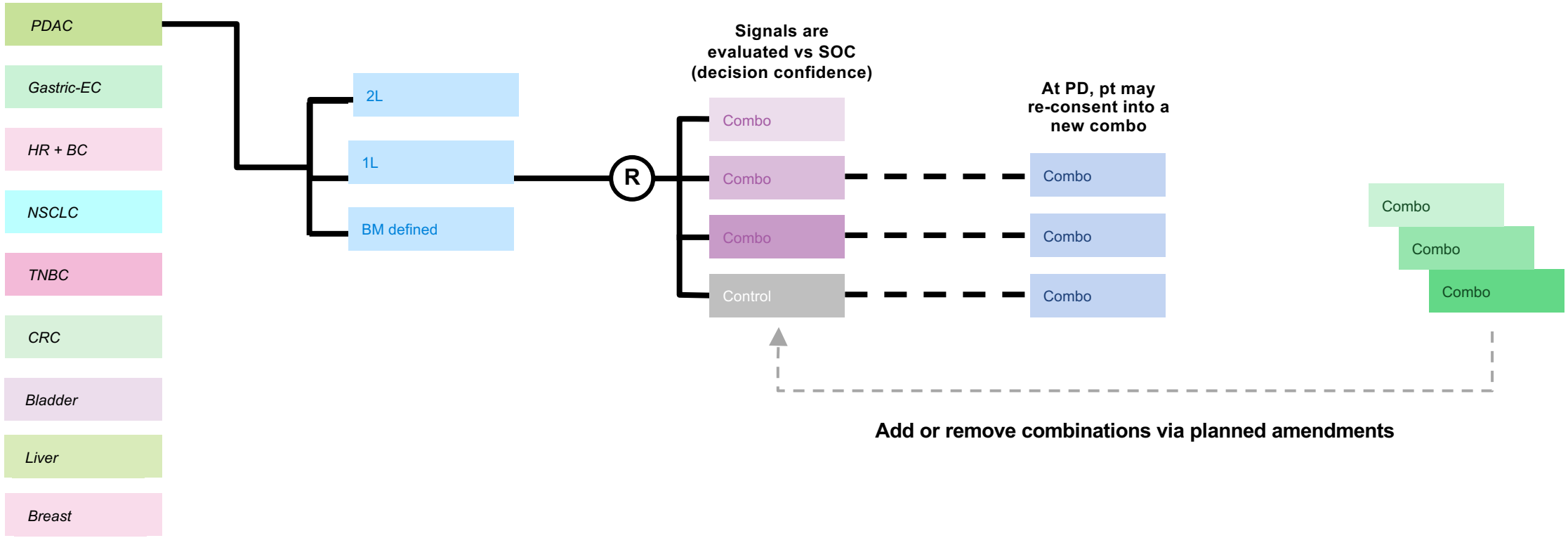
# Introduction to Case Studies

# **Drug combination development to treat tumours: Morpheus combinations platform** (Ruchi Upmanyu, Roche)

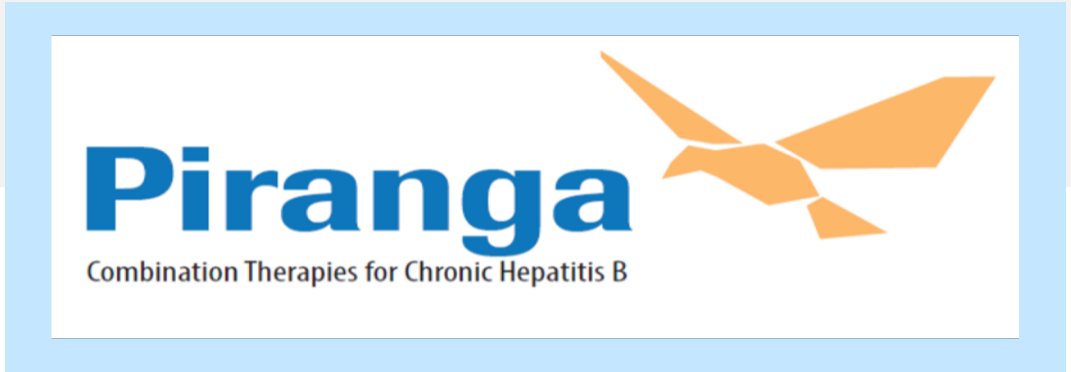
# MORPHEUS is...

**A suite of Phase Ib studies designed to generate signal-seeking data across a wide scope of combination treatments, to support cross-indication learnings and identify combinations with transformational potential**

| Multi-tumour type | Multi-basket | Randomised | Longitudinal | Adaptable |
|---|---|---|---|---|



# Drug combination development to treat infectious diseases : Piranga platform trial case study (Hans Joachim Helms )



# Piranga Adaptive Platform Study Design

**Platform -** multiple combinations in a single study

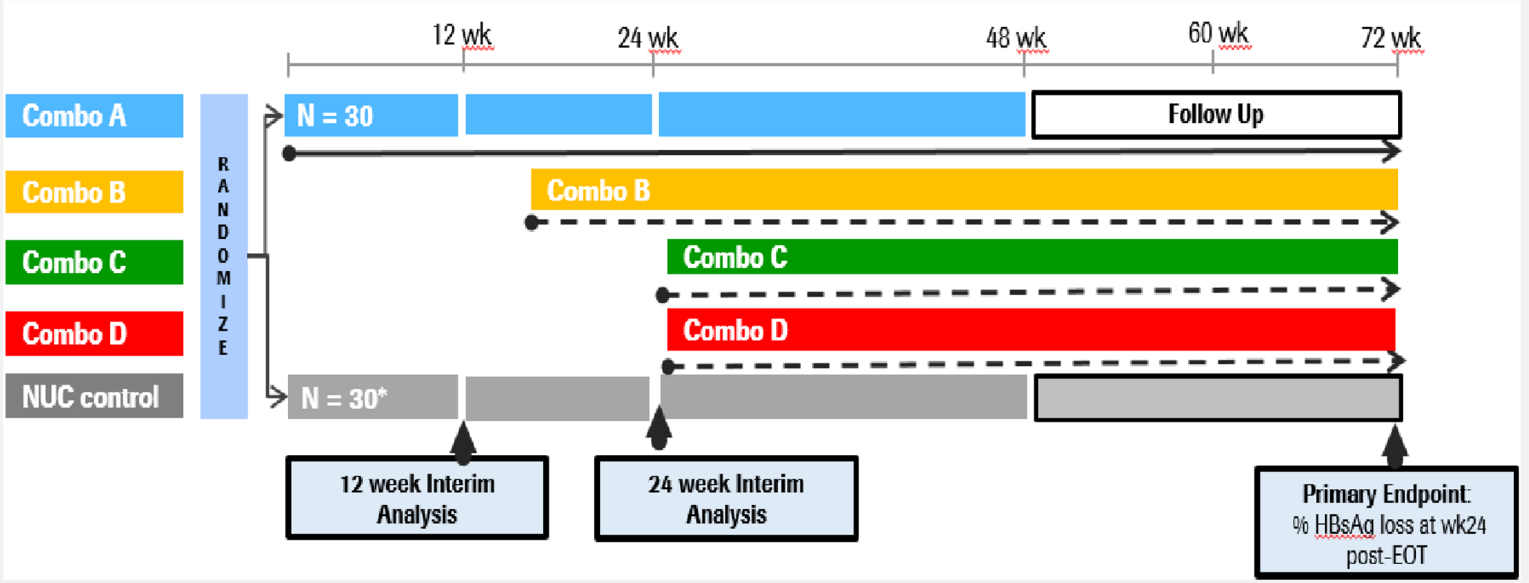
- answers multiple questions in one protocol allowing rapid advancement of scientific understanding e.g., on safety, MOAs individual drugs and MOA in combinations

**Adaptive** – data driven flexible design, opportunity to seamlessly add and terminate different drug combinations,

- Pre-specified Interim Analyses inform incoming combos

Shared control arm

**Multi-stage –** combines phases (2a/2b)



# In Summary Adaptive data driven Platform Ph2 design: More nimble, de-risking & cost effective

| | Platform Design | Traditional – fixed duration, Ph2a shorter duration then Ph2b longer duration |
|---|---|---|
| **Pros** | • Adaptive, flexible add arms, stagger arms<br>• Potential to be more nimble Answer multiple questions in one protocol<br>• De-risks uncertainty & inform safety<br>• Less regulatory burden<br>  – One master protocol is designed to support different combinations.<br>• Shared control arm<br>• Potential to be more attractive to pts – increased chance for active Tx<br>  – Limited exposure to ineffective or unsafe therapies | • Starting with shorter Tx duration Ph2a study, with subsequent longer Ph2b study<br>• Simple to design and analyse.<br>• Clear answer from the single trial. |
| **Cons** | • More complex, need more internal experience<br>• Longer time planning are needed<br>• HA/EC acceptance is unknown to date in this disease area | • Not efficient – uses more patients.<br>• More patients on ineffective therapies<br>• Multiple protocols specific per molecule<br>• Difficult to compare combination arms due to site/country differences |

# Discussion

# Experience, robustness and stakeholder views

Question 1:  Has experience of master protocols confirmed the opportunities they bring to drug development e.g. increased efficiency?

Question 2:  What views do stakeholders have on the acceptability of evidence generated from master protocols?

# Key Design Challenges

Question 1: Are treatment effects of interest clear in master protocols and are multiplicity aspects being addressed sufficiently?

Question 2: What are key concerns relating to statistical methodology that need addressing?

# New frontiers

Question 1:  What have been experiences using flexibility of master protocols to add or remove arms in a confirmatory setting?

Question 2:  Are there opportunities to further innovate master protocol designs to include adaptive and/or seamless aspects, and/or use external control arms?

# Call for action

What is the future of multi-sponsor master protocols?

# Wrap-up & key messages

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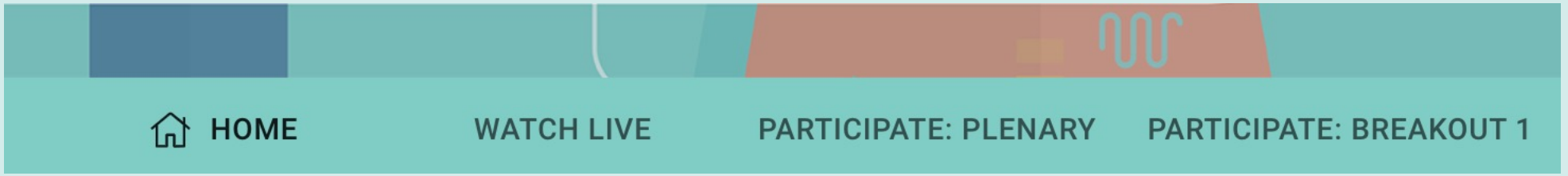


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