Pooling of Endpoints WG

Liver Forum 15 Update
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on behalf of the pooling of endpoints WG

THE FORUM
For Collaborative Research℠

Berkeley Public Health

Working group progress:

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Co-chairs**: Jasmohan Bajaj** (VCU) and **Sharat Varma/Christina Klarskov Mogensen** (Novo Nordisk)

Meetings: Monthly, 3 meetings to date

- Cathy O'Hare
- Arie Regev
- David Shapiro
- Roberto Calle
- Ashish Dhawan
- Diogo Ferrinho
- Claudia Filozof
- Shirin Hemmat
- Massimo Siciliano
- Jörn Schattenberg
- Charmaine Stewart
- Vlad Ratziu
- Brenda Rodriguez
- Toru Matsubayashi
- Mazen Noureddin
- Jose Willemse
- Libette Luce
- Raj Vuppalanchi
- Margot Yann
- Juan Abraldes
- Jasmohan Bajaj
- Azza Karrar
- Sehyr Khan
- Madhuri Jerfy
- Veronica Miller
- Christina Mogenson
- Blue Neustifter
- Melissa Palmer
- Detlef Schuppan
- Radha Seetharam
- Amrik Shah
- Richard Torstenson
- Tram Tran
- Sharat Varma
- Julia Wattacheril
- Pam Young
- Michelle Long

Can we pool endpoints between F3 and F4 studies?

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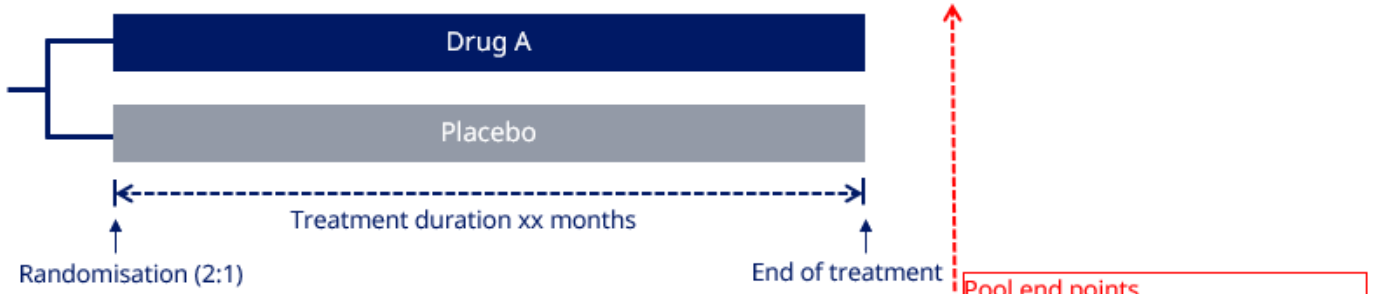
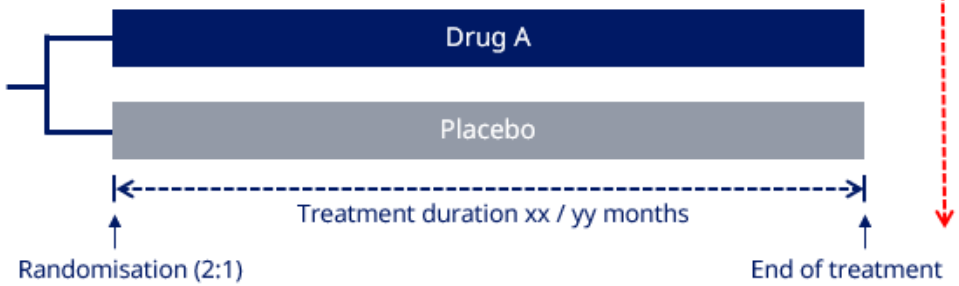
Trial 1
- Time driven by biopsy/histology
- NASH with **F3**



Trial 2
- Event driven
- NASH with **F4c**



Pool end points

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Challenge to pooling endpoints:

- **Pre-cirrhotic MASH**: aim to measure the clinical benefit of a therapeutic on the regression of disease (reduction in fibrosis or resolution of MASH).
  - Time-driven events
- **MASH with compensated cirrhosis**: aim to measure the halting of progression to decompensated cirrhosis.
  - Endpoint-driven events

3 Identified Workstreams

- 1: Pooling patient populations from *distinct trials in F3 and F4 patients* and ranking of endpoints to increase efficiency
  - Consider new, clinically relevant endpoints to add to a composite endpoint
- 2: Incorporate PROs in MASH clinical trials
  - For patients with F3 and F4c fibrosis, with and without signs or symptoms of portal hypertension
- 3: Potential for a *single trial* enrolling F3 and F4 patients
  - With considerations from expert statisticians

Focus: Workstream 1

- Aim: discuss and recommend a composite endpoint that would allow pooling endpoints in F3 and F4 patients
  - Addresses disease progression, disease stability (no progression, no regression) and disease regression
  - Relates to disease severity strata (F3, F4 with and without portal hypertension)
  - Consider phase 2 and phase 3 CT designs
  - Includes clinical, functional, histological, and non-invasive assessments
    - PROs to be added later (Workstream 1 discussion)
    - Innovative markers are important, but focus will be on considering **endpoints achievable in the near term**

Which measurements should be included in a composite endpoint with F3 and F4 patient populations in mind?

Next steps

- Mapping exercise of potential endpoints
  - Evidence base
  - Regulatory acceptance
  - Practicality
- **Please join us!**