

Updates on design considerations for the SOLIDARITY PARTNERS core trial protocol

Professor Peter Horby

Dr Amanda Rojek

University of Oxford



R&D Blueprint

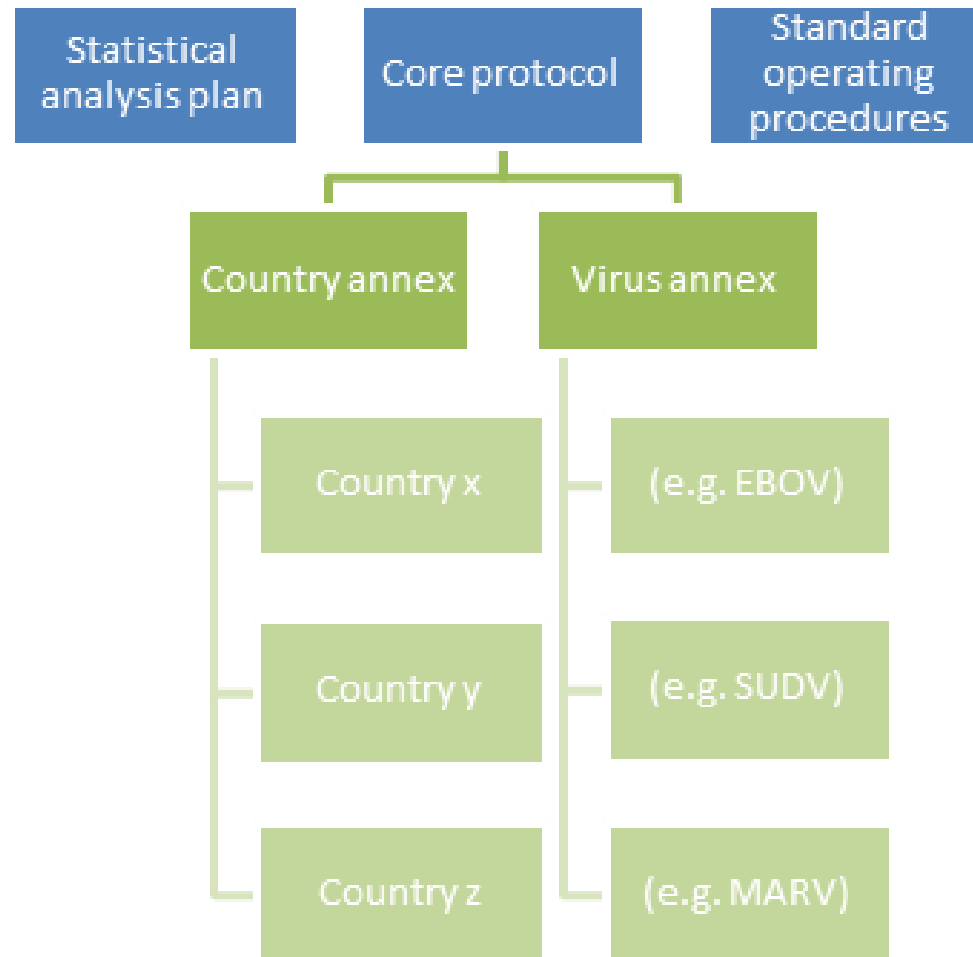
Powering research
to prevent epidemics

MARVAC meeting 4 April 2024

Key design features of proposed trial

1. **Pre-positioned:** to enable inclusion of early cases in an outbreak
2. **Streamlined core protocol**
 - a) **Conserved across outbreaks:** data from one outbreak contributes to findings in the next
 - b) **Conserved across viruses:** since certain interventions (e.g. broad spectrum antiviral and host-directed therapies) might be applicable to more than one virus subtype
3. **Adaptive platform design:** test multiple interventions simultaneously to identify the best treatment for a disease – focus on ‘disease’ not one particular drug
4. **Quality by design:** design optimised from the beginning to prevent mistakes and minimise waste

Design feature: Core protocol



Previous comparisons

Evaluation domain	MARV	SUDV	EBOV
Randomisation 1 Monoclonal	Monoclonal antibody vs no additional treatment (1:1)	Monoclonal antibody vs no additional treatment (1:1)	Receive approved Mab
Randomisation 2 Antiviral	Antiviral vs no additional treatment (1:1)		
Randomisation 3 Host directed treatment	Host directed therapy vs no additional treatment (1:1)		

Response to feedback from WHO R+D meeting in Kampala, February 2024

Inclusion of corticosteroids in the trial

Concerns raised about use of immune-modulating agent in the setting of viral kinetics of the disease (increasing viral load until death)

Design adaptation: initially restrict corticosteroids comparison to patients with Zaire (who will receive a licensed monoclonal antibody as standard of care)

Planned comparisons

Evaluation domain	MARV	SUDV	EBOV
Randomisation 1 Monoclonal	Monoclonal antibody vs no additional treatment (1:1)	Monoclonal antibody vs no additional treatment (1:1)	Receive approved Mab
Randomisation 2 Antiviral	Antiviral vs no additional treatment (1:1)		
Randomisation 3 Host directed treatment	<i>Inactive initially</i>	<i>Inactive initially</i>	Host directed therapy vs no additional treatment (1:1)

Duration of follow up

Request to extend follow up (initially 28 days) given risk of viral sequestration and recrudescence

Design adaptation: :

1. Increased all routine follow up to 60 days (pregnant women continue to post-birth)
2. Strengthened language around linkage to existing survivor follow up programs

Extending sampling duration

Request to extend duration of monitoring of viral kinetics and organ dysfunction.

Design adaptation:

1. We now take these measurements at day 0,3,5,7,10,13,16 (unless discharged)
2. We record data collected for routine purposes on any other day during admission (e.g. viral clearance prior to discharge)

Semen sampling

Request to include semen sampling in the core protocol

Design adaptation:

1. Strengthened language to be clear that sub-studies are supported and recommended, and this would be a priority
2. Decision not to include in the core protocol because this means we could not run the study in any site that could not support this extended sampling

Inclusion of pregnant women and children

Discussions regarding the benefits and harms of including vulnerable patients in clinical trials.

Design adaptation:

Improved clarity of language in the protocol to communicate

1. Pregnant women and children are eligible
2. There is due process that occurs (e.g. written advice from expert teratology service) before any specific drug is included to ensure there are no specific contraindications or concerns.

Interim analysis

Request to strengthen language around timing of pre-specified interim analysis in the protocol

Design adaptation:

Finalizing with our statistical team.



R&D Blueprint

Powering research
to prevent epidemics

Thank you