The PARTNERS trial protocol

Platform Adaptive Randomised Trial for NEw and Repurposed Filovirus treatmentS

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R&DBlueprint
Powering research to prevent epidemics

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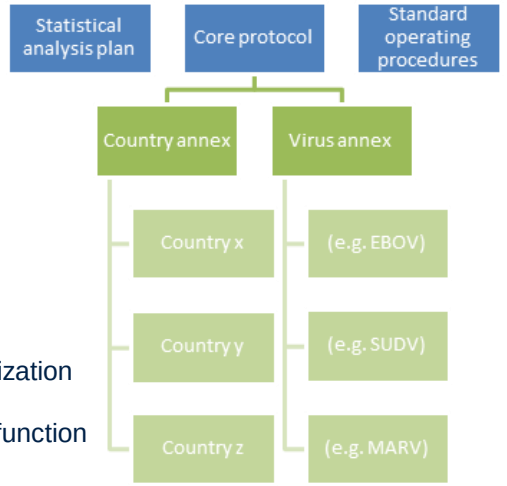
Key design features of PARTNERS

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. **Factorial design:** by therapeutic domain for efficient evaluation of >1 drug and to assess combination therapies

** N Engl J Med. 2020 Apr 2;382(14):1366-1369.*
Creating a Framework for Conducting Randomized Clinical Trials during Disease Outbreaks

Core protocol + annexes

- Open-label
- Randomised
- Controlled (WHO recommended standard of care)
- Adaptive platform trial
- For patients with lab-confirmed acute Filovirus disease
- Primary outcome: All-cause mortality 28 days after randomization
- Secondary outcomes: viral clearance, viral load, organ dysfunction
- Safety assessments



Three therapeutic "domains"

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)

Where licensed monoclonal antibody treatment exists, patients will receive these as standard of care

Marburg virus disease investigational products

MBP091

- Single IgG1 lambda mAb recovered from a MVD survivor. MBP091 binds to the MARV glycoprotein and neutralizes the virus by occupying the conserved receptor-binding site
- Efficacy in non-human primates (rhesus macaques) challenged with MARV/Angola
- Well-tolerated in phase I human studies

Remdesivir

- Small molecule antiviral
- Efficacy in non-human primates (cynomolgus) challenged with MARV/Angola
- Approved for SARS-CoV-2 infection

Factorial design

All patients receive optimised standard of care		**Antiviral randomisation**	
		Allocated to antiviral arm (50%)	Allocated to no additional treatment arm (50%)
Monoclonal randomisation	Allocated to monoclonal arm (50%)	Receives antiviral + monoclonal	Receives monoclonal alone
	Allocated to no additional treatment arm (50%)	Receives antiviral alone	Receives no additional treatment

Factorial design with SOC comparator throughout

1. Will generate most easily interpreted evidence
2. Efficient evaluation of multiple interventions
3. Evaluation of additive or synergistic effects
4. Reduces confounding that may be introduced by non-randomised treatments

MVD Rwanda October 2024

MON	TUE	WED	THU	FRI	SAT	SUN
				27 **Outbreak declared**	29	29
30	1 Approval: Rwandan RNEC	2	3 Research team assembled	4	5	6 Redzone access granted at site
7	8	9	10	11	12 Rwandan FDA approval	13
14 WHO ethics approval	15 **Trial open**	16	17	18	19	20
21	22	23	24	25	26	27

Operational lessons from Rwanda activation

Successes	Challenges
Coordinated approach to a single trial	Slow supply chain and logistics
Strong scientific support from Government	Simultaneous clinical load of trial physicians
Acceptance of randomization & SOC comparator	Transition from off-label and expanded access use
Use of a central referral hospital with high-quality care	Verified & calibrated laboratory methods and viral load assessment

Thank you