Filovirus Research Consortium Summary

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Tedros in Tanzania, partners in country, cohesive response plan. Importance of global collaborative response and high level of participation in this call is very encouraging

Marburg research, with goal to generate reliable and relevant evidenceto support response that promotes equity and trust. This fits into WHO's viral/pathogen family approach, will be conducted with the Collaborative Open Research Consortium for filoviruses. This builds on previous MARVAC group work to develop strategies including core protocols for vaccines and therapeutics.

Original strategic roadmap gaps: MCM lack, poorly characterized viruses, mechanisms of viral persistence, virus ecology, integrated social science research. Anticipation, Reinforcement (including multivalent vaccines), Cure.

20 January 2025 Outbreak confirmed in northern Tanzania (index case 16 December, 1 confirmed case, 25 suspected cases). Mobile lab (RT-PCR), investigations, more information pending. Cluster of 8 deaths await confirmation. Original source unclear in Tanzania, under investigation

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Diagnostics and basic/translational research priorities

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Response based on Epidemiologic investigation, biological characterization, testing: biofire, QS7 systems, NGS using Illumina and Nanopore for metagenomics, probe capture sequencing, ELISA, multiplex serology by Luminex. Can be used for animal studies as well. DRC collaborating with Tanzania.

Research priorities: Expanding virus family. Vaccines research includes GP and vectored vaccines (replicating and non-replicating). Key issues: duration & breadth of protection. Treatments include antibodies, small molecules, mixed (need to be given early, usually within 5 days, a bit later with combination). Research publications: EBOV is 75%, Marburg 15%, other filo 10%. All viruses have similar life-cycle, which can promote antiviral via proviral and antiviral host factors. Differences in biology/virulence determinants can lead to different infection outcomes. Key is to expand understanding of less studied viruses by applying knowledge form the more thoroughly studied viruses.

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Ecology and available therapeutics and vaccines

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Ecology: Rousettus aegyptiacus cave dwelling fruit bats are reservoir for Marburg and Ravn. 80% of females are pregnant, two birthing seasons per year which correlates with outbreaks. EBOV usually goes through intermediate NHPs, while MARV is due to direct bat interactions. Human ERB interactions, mining, speed/ease of travel, climate change.

Several vaccines have NHP efficacy data. Licensed vaccines are vectored (VSV, Ad, MVA). Mappbio: recombinant IgG1 from survivor, protected NHPs, t1/2 21 days. EA: no SUSARs. Animal rule unless human data are available. Inquiries/requests MAPP & Barda. Gilead: Remdesivir & Obeldesivir prodrug. IV RDV is efficacious in NHP infected with MARV. ODV works as oral PEP post-exposure prophylaxis against NHP lethal challenge with reduced viral load. RDV made available under EA in Rwanda. PHV: VSV pseudotyped Angola vaccine 100% protective in GP, hamster, cyno NHPS. Dose escalation Ph I study complete. 1 dose immunogenic & durable. IAVI: VSV vectored: Ph 1 planned Q3 2025, DP may be available end Q1 2025. Sabin: cAd3-MARV: NHP studies 75 protection@ 1 yr. Ph 1 56 participants complete (no SAEs and immunogenic) Ph 2 underway (total ~2K, 1 MARV infection in Rwanda), planned animal rule pathway. Vaccine requests to Sabin/BARDA. Oxford/SII ChAdOx in Ph 1, thousands of doses available.

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Vaccines and therapeutics evaluation in the next outbreak

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Four vaccines have been evaluated by prioritization committee, all considered suitable for inclusion in trials. MAPPBio and Gilead (RDV) are recommended for clinical trial core protocol including combination therapy.

Vaccine core protocol is flexible, meets vaccines where they are, considers outbreak and interoutbreak phases. During outbreak is a ring vaccination trial of delayed vs immediate vaccination.

Therapeutics protocol has factorial design that can randomize separately to monoclonal, antiviral, host directed therapies. Primary outcome: all cause mortality @ 28 days. No host directed therapy component for MARV. Successfully implemented in Rwanda with strong support, some challenges e.g., supply chain/logistics, clinical load for physicians, transition from off-label/expanded access, use of verified lab methods for 2ndary outcomes

Performing research during outbreaks is an essential component of response. Each outbreak we aim to do even better in initiating clinical studies to collect key data. Steps: prioritizaiton, availability, clinical trials, agreements, funding, open mechanism

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Typical Outbreak Challenges/Considerations

Transmission and epidemiology
Animal model research
Evaluate and deploy state of the art rapid & sensitive diagnostics
Define optimized clinical standard of care
Promote development and evaluation of new therapeutics
Promote development and evaluation of vaccines
Follow defined regulatory pathways
Good participatory practices
Integrate research into outbreak response
Embrace collaboration and coordination

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