

Addressing Public Health Emergencies

WHO R&D Working Group

- 2014-2016: Ebola Outbreak in Liberia, Guinea, & Sierra Leone
 - ✓ Need for randomized trials in public health emergencies...NAM & WHO
 - ✓ PREVAIL II RCT: ZMapp vs oSOC...71 of targeted 200 patients...
- 2016-2018: WHO R&D Working Group
 - ✓ Establishing principles/infrastructure in advance of public health emergencies
Ebola, ZIKA, Lassa, Chikungunya
- 2018-2019: Ebola Outbreak in DRC
 - Nipah, SARS & MERS CoV*
 - ✓ WHO Monitored Emergency Use of Unregistered & Investigational Interventions (MEURI)
 - ✓ PALM RCT: mAb114; REGN-EB3; Remdesivir; ZMapp
 - ✓ WHO MEURI & PALM RCT engaged 1/2 of 3000 patients in DRC outbreak
 - ✓ *“These efforts have created a paradigm to develop infrastructure to deliver compassionate care while efficiently and effectively attaining evidence needed to reliably assess benefits and risks of interventions to treat and prevent diseases in public health emergencies”* WHO MEURI DMC, 8/16/2019
 - NEJM 4/2/2020: *“Creating a Framework for Conducting Randomized Clinical Trials during Disease Outbreaks”* **The CORE Protocol**
- 2020-on: SARS-CoV-2 & COVID-19 Pandemic

Addressing the COVID-19 Pandemic

- 2020-onward: SARS-CoV-2 & COVID-19 Pandemic

- ✓ Developing **WHO CORE Protocol** for collaborative evaluation of Vaccines
(including efforts by Yunda Huang, Holly Janes, Peter Gilbert, Betz Halloran, T Fleming)

Endpt: Virologically confirmed COVID-19 disease...Severe disease? H_0 for VE? What about disinhibition?

- ✓ Developing **WHO “Solidarity” CORE Protocol** for Therapeutics

(including efforts by Ira Longini, Betz Halloran, T Fleming)

Endpt: Mortality

- In hospitalized patients: Lowering the risk of mortality
(Remdesivir, Lopinavir/ritonavir, Chloroquine)

**Adaptively adding & deleting
candidate regimens?**

- ✓ Developing Protocols for Therapeutics in PrEP, PEP, Early Dx & Adv Disease

- In PrEP, such as in Healthcare Workers (Chloroquine)

Endpt: infection vs sev dis, death?

- In PEP, such as in Household Contacts

Supply \Rightarrow Lowest effective dose?

(including efforts by Elizabeth Brown, UW/Gates Foundation)

(Hydroxychloroquine, Chloroquine, Lopinavir/ritonavir)

- In early diagnosis (including efforts by UW/Gates Foundation)

Endpt: hospitalization vs sev disease

- In Hospitalized Patients, preventing ventilator use and death

**How to efficiently proceed from
Phase 2 to Phase 3?**

(IL-6 inhibitors: Tocilizumab, Kevzara)

(using immuno-suppressive agents)

- Biostat 524: Design of Medical Studies M/W 8:30a- 9:50a