



Informal consultation on the role of therapeutics in COVID-19 prophylaxis and post-exposure prophylaxis - **Post-exposure prophylaxis studies (PEP) subgroup**

Date, time and venue

Friday 10 April 2020 - 17:00 – 18:00 (CET) - Webex

Group Members

Group2: PEP Household / Contacts	
Ruanne Barnabas	University of Washington, USA
David R Boulware	University of Minnesota, USA
Jon Gilles	Columbia University, USA
Peter Dull	Bill & Melinda Gates Foundation, USA
Tom Fleming	University of Washington, USA
Frederick Hayden	University of Virginia
Phil Krause	Bill & Melinda Gates Foundation, USA
Hilary Marston	NIH, USA
Oriol Mitjà	Universitari Germans Trias I Pujol, Barcelona
Darrell Tan	University of Toronto, Canada

Unable to attend: Oriol Mitjà

WHO Secretariat: Ira Longini, Marie-Pierre Preziosi, Kolawole Salami and Siya Temu.

Agenda items

- Global clinical evaluation of chemotherapeutics for prophylaxis
 - Collective systematic assessment of the results of ongoing/soon-to-start PEP studies of households contacts / or of HCW
 - **Development of a global core protocol for the next studies/therapeutic agents**, building on the above
- Next steps



Overview of Deliberations

1. Collective systematic assessment of the progress of ongoing/ soon-to-start PEP studies

- WHO proposes a central DMC looking into safety and efficacy data of these trials. However, it is understood that some studies are already in advanced stages and may have their own DMCs. It was suggested for consideration that a central committee could include/liase with chairs of individual DMCs.
- The **University of Washington** study has just commenced with the recruitment of 43 subjects. The study has its own DSMB, chaired by David Griffin (statistician). Other members include Bob Cruz (Virologist) and Michael Boeckh (infectious diseases). The PI is pleased to liaise with DSMBs from other studies and that the study data is reviewed by a joint DSMB. The anticipated duration of the study is 6 to 8 weeks.
- The **Minnesota study** has recruited 50% of its sample size and had its first DSMB meeting on the 17th March. 25% individuals have completed 2 weeks of follow-up. The study involves just 5 days of dosing, with an anticipated duration of 2 weeks; although there is IRB permission to continue the study for up to 90 days if the need arises. The PI is pleased to pool data together.
- It was noted that although different studies use different dosing, safety assessment is a key element that DSMBs would look at. The different doses, however, provide a potential area of challenge for the joint DSMB. Primary outcome also differ from study to study (symptomatic disease, PCR+, with plans to do serologies).
- The **Toronto study** is yet to commence. A start of early next week is anticipated. 1200 individuals is the estimated sample size. The study is different as it would be evaluating the prophylactic efficacy of **lopinavir/ritonavir**. The study DSMB is yet to be assembled. The PI is pleased to share data and engage with other DSMBs. However, due to the difference in pharmacological agents, it might be challenging to pull together the data with data from other studies. The primary outcome is PCR+ on self-collected swab on day 14.



- The **Columbia study** has recently commenced with the enrolment of 10 subjects out of the planned 1600. Full enrolment should take ten weeks. The study is powered on an attack rate of approximately 11%, with a 30% reduction with treatment. The study already has a DSMB in place, but there are currently no plans for the interim analysis. The PI is pleased to share data. So, while a central DMC may help to resolve some unknowns (e.g., examine primary data from different studies to get a global answer), the absence of a plan for interim analysis makes it challenging.
- The importance of convening a unified DSMB was emphasized. This is especially so as these first-generation studies are impressive and share considerable commonalities. All are also united in their desire to have timely and reliable results. Therefore, having collective evidence would be key and a central DSMB helps to achieve this. The challenge of this group is to facilitate the emergence of this DSMB and shape the structure.
- All study PIs present at the meeting reiterated their commitments to the goal of having a unified DMC with the commitment to work towards actualizing this without interfering with studies that have already commenced.

2. Development of a global core protocol for the next studies/therapeutic agents

- Fully adaptive core protocols have been drafted for treatments and vaccines, and similarly such protocols would be developed for the next-generation PEP studies. This protocol would be developed to allow the evaluation of different agents. The core protocol will be premised on a universally agreed primary endpoint. In addition, sites are free to conduct add-on studies /collect additional data as they deemed fit.



Action points:

1. Participants to share research protocols with WHO to collate those
2. BMGF (Peter) to develop a summary table of salient differences between studies, together with WHO
3. WHO to propose a way forward (process, ToRs) for a central DMC
4. Ira/WHO to propose a first draft of the core protocol; suggestions for pertinent secondary endpoints should be forwarded to Ira.
5. Participants to go back to study teams and discuss issues raised

Next TC:

- Next Thursday, 16 April 2020, same time.