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Project No. 101045956
Biomarker and AI-supported FX06 therapy to prevent progression from mild and moderate to severe stages of COVID-19

Deliverable 1.6

Report on virtual meeting with the other successful projects working on COVID-19 therapeutics funded under the Horizon Europe call "HORIZONHLTH-2021-CORONA-01"

WP1 – Project management and collaboration with other initiatives

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Revision history

Date	Authors	Revision
08/06/2022	Andreia Cruz (accelCH)	Draft version
10/06/2022	Benjamin Ginski (GUF)	Revision
15/06/2022	Andreia Cruz (accelCH)	Final version

Contents

Partner short names

GUF	Johann Wolfgang Goethe Universität Frankfurt am Main
accelCH	accelopment Schweiz AG

Abbreviations

COVID-19	Coronavirus disease
CTEG	Clinical Trials Expert Group
CTFG	Clinical Trials Facilitation and Coordination Group
D	Deliverable
DG RTD	Directorate-General for Research and Innovation
DG SANTE	Directorate-General for Health and Food Safety
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
ECRAID	European Clinical Research Alliance for Infectious Diseases
EMA	European Medicines Agency
EU	European Union
GCP IWG	Good Clinical Practice Inspectors Working Group
HaDEA	European Health and Digital Executive Agency
HERA	Health Emergency preparedness and Response Authority
HEU	Horizon Europe
HMA	Heads of Medicines Agency
ICU	Intensive Care Unit
JAAM	Joint Access Advisory Mechanism
M	Month
MS	Milestone
TCB	Trial Coordination Board

Executive Summary

The Report on virtual meeting with the other successful projects working on COVID-19 therapeutics funded under the Horizon Europe Health Emergency preparedness and Response Authority (HERA) incubator call "HORIZON-HLTH-2021-CORONA-01" summarises the main presentations and outcomes of the meeting held online on the 6th of April. The virtual meeting was set up by the Directorate-General for Research and Innovation (DG RTD) in coordination with the European Health and Digital Executive Agency (HaDEA). This meeting gave the opportunity for adaptive platform trials and other projects introduce to each other and to identify areas for potential collaboration.

1 Introduction

To support the efficient clinical assessment of COVID-19 therapeutics, the Commission supported the establishment of the European network for COVID-19 therapeutic trials, which is currently based on three large-scale, multi-centre adaptive platform trials. Combined, these encompass more than 300 trial sites in 20 European countries. In addition to this COVID-19 trial network, the recently founded European Clinical Research Alliance on Infectious Diseases is establishing a long-term, sustained clinical research network in Europe capable of initiating and completing high-quality clinical studies. Despite the COVID-19 deaths are declining, the COVID-19 pandemic is not over yet and the recurrent emergence of variants of concern warns us to be prepared. Under the Horizon Europe HERA Incubator call, new research projects received funding for the early clinical development of different types of therapeutics against SARS-CoV-2 and its variants of concern. In a still fragmented trial landscape, it is of utmost importance to increase the efficiency of conducting clinical trials as much as possible in order to reach robust results in a more timely manner and, ultimately, to better support the clinical management of COVID-19 patients. Initiatives such as the European network for COVID-19 trials provide valuable opportunities for a more harmonised and coordinated approach for COVID-19 therapeutic trials in Europe.

1.1 Purpose and scope of the deliverable

A virtual meeting was set up by DG RTD in coordination with HaDEA between the projects working on COVID-19 therapeutics funded under the Horizon Europe call "HORIZON-HLTH-2021-CORONA-01". The main purpose of this meeting was to introduce each project to each other and to identify areas for potential collaboration. Deliverable 1.6 summarises the general topics of discussion and the main takeaways of the meeting.

1.2 Outcomes

With up to 80 participants, the meeting brought together the coordinators and members of the European network for COVID-19 therapeutic trials, the EU-funded COVID-19 clinical trial projects and the ECRAID foundation. From the European Commission, participants from several Directorates-General (DG RTD, DG SANTE) and the Executive Agency HaDEA were present, and included also participants from the European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA). After the presentations from the concerned COVID-19 clinical trial projects and initiatives, the discussion focused on possible opportunities for collaboration among the different projects and initiatives represented.

The meeting showed the potential for more efficient trial implementation when existing infrastructure and expertise are used, e.g., shorter delays to setting up new trial sites. Projects are strongly encouraged to further explore options for collaboration in this perspective. While there were several reminders of the commonly experienced hurdles for the implementation of multi-country trials in Europe, it was recognised that efforts are being made to overcome these, albeit in a complex environment. It is important for (academic) sponsors to be acquainted with the landscape of initiatives that exist to support addressing such barriers. The meeting provided the opportunity for the EU-funded clinical trial projects and other related initiatives to be introduced, and contact details were shared to allow individual follow-up.

2 Therapeutic clinical trials

Currently, three large-scale, multi-country adaptive platform trials are investigating treatment options in Europe for COVID-19 in hospitalized patients, including intensive care unit patients. A fourth adaptive platform trial looking for treatments in a primary care population is being set-up under the recently funded ECRAID-PRIME project. These four adaptive platform trials constitute the "European network for COVID-19 therapeutics" and effective coordination mechanisms between these trials are in place since autumn 2020 such as the trial coordination board (TCB) and the joint access advisory mechanism (JAAM). All these structures are described in more detail below.

2.1 Challenges

A pandemic is a global public health challenge that demands cooperation. While the greater good must take precedence, we know that problems can arise from likely competition. Nonetheless, some stakeholders are unaware of the existence of other players and initiatives, so in the end, the promotion of complementarity between trials, the optimisation of resources and the exchange of information are the main core tasks to avoid redundancies. Regulatory and ethics processes can lead to long review cycles, causing delays due to the assessment procedure, the completeness of the submission and to regulatory and Good Clinical Practice compliance that may be critical to the success of the clinical trials[1]. With the shared interest in making Europe more attractive for the conduct of clinical trials, in particular COVID-19 trials during the ongoing pandemic, the European Commission (EC), together with the European Medicines Agency (EMA), the Good Clinical Practice Inspectors Working Group (GCP IWG), the Clinical Trials Facilitation and Coordination Group (CTFG, a working group of the Heads of Medicines Agency (HMA) and the Clinical Trials Expert Group (CTEG), has published an EU-level harmonised guidance with necessary regulatory flexibilities and procedural simplifications for the rapid authorisation of COVID-19 trials.

2.2 European network for COVID-19 therapeutic trials

Early on in the pandemic, the Committee for Medicinal Products for Human Use at the European Medical Agency called for the pooling of EU research resources into large-scale, multi-centre, multi-arm clinical trials against COVID-19 with a view to delivering robust results as rapidly as possible. To support the efficient clinical assessment of COVID-19 therapeutics, the EC supported the establishment of the European network for COVID-19 therapeutic trials, which is currently based on three large-scale, multi-center adaptive platform trials.

[1] Accelerating clinical trial implementation in the context of the COVID-19 pandemic by Diallo et al, https://doi.org/10.1016/j.cmi.2021.12.027

2.2.1 REMAP-CAP

Community-acquired pneumonia (CAP) is a significant cause of hospitalisation and illness world-wide and it is severe enough to require admission to an Intensive Care Unit (ICU). Respiratory tract infections are the leading cause of deaths from infectious disease globally and are the leading cause of deaths in developing nations. REMAP-CAP is a global network of leading experts, institutions and research networks that uses a novel and innovative adaptive trial design to evaluate a number of treatment options. This study design is known as a REMAP, a Randomised, Embedded, Multifactorial, Adaptive Platform trial. The broad objective is, over time, to determine and continuously update the optimal set of treatments for community-acquired pneumonia. REMAP-CAP has implemented the Pandemic Appendix to the Core Protocol so that the platform can respond rapidly in the event of widespread disease resulting from the novel 2019 coronavirus. Any clinical site can participate by choosing the domain(s) and interventions (minimum of 2 per domain) - Figure 1. The University Medical Center Utrecht is the sponsor for the trial in Europe and some countries outside Europe.

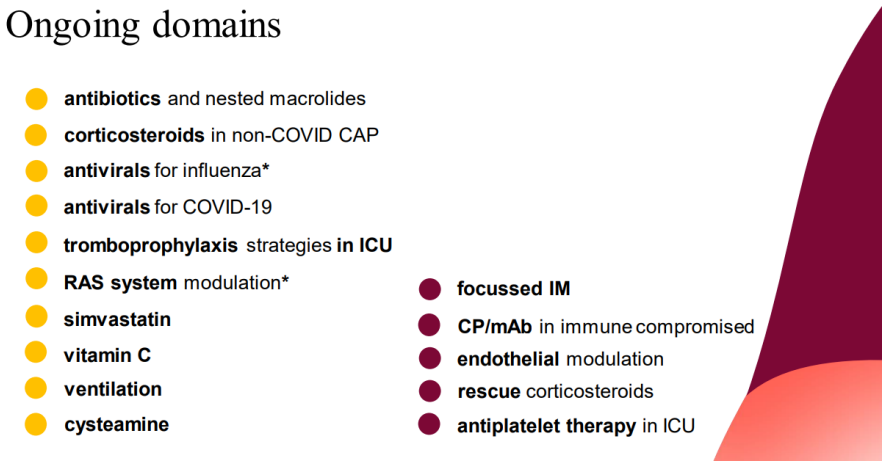

Figure 1 – REMAP-CAP randomizes multiple interventions simultaneously, nested within domains.

2.2.2 EU-RESPONSE

The EU-RESPONSE is a 5-year project aiming to build a multinational, adaptive European COVID-19 and emerging infectious diseases trial network, based on existing initiatives, experience and expertise, allowing European expansion of DisCoVeRy (WP1) and the establishment of a COVID-19 adaptive platform trial: EU-SolidAct (WP2).

EU RESPONSE

EUROPEAN RESEARCH AND PREPAREDNESS NETWORK FOR PANDEMICS AND EMERGING INFECTIOUS DISEASES

21 Partners | **16** Countries | **H2020 grant 15.7 M€** | **2020-2025**

WP	Title	Lead
1	Extending **Discovery** in Europe	**Inserm** Université Libre de Bruxelles Centro Hospitalar Sao Joao
2	**EU-SolidAct**	**Oslo University Hospital** Inserm Universita degli Studi di Verona
3	Coordination of the European COVID-19 Adaptive Platform trials	ECRIN Norwegian Institute of Public Health
4	Project management, coordination, communication and dissemination	Inserm Inserm Transfert

Figure 2 – EU-RESPONSE key facts.

2.2.2.1 DisCoVeRy

DISCOVERY

The DisCoVeRy study is a phase III, open-label, adaptive, randomized, controlled, multi-centre clinical trial designed to evaluate the safety and efficacy of medicinal products in hospitalized adult patients diagnosed with COVID-19. DisCoVeRy has implemented a new a new therapeutic arm to test a long-acting antibody (LAAB) combination developed by AstraZeneca. The initial design was composed of four different treatments evaluated in adults (≥ 18-year-old) hospitalized for COVID-19, added to standard cares (oxygen therapy, drugs in prevention of phlebitis and pulmonary embolism, and dexamethasone which reduces inflammation and lung damage) and compared to standard care alone. Their efficacy was evaluated 15 days after treatment initiation. This study is a multi-centre/country trial involving 10 European countries, led by the French national institute for Health and Medical Research (Inserm), and is conducted in partnership with the Solidarity trial, coordinated by the World Health Organisation (WHO).

2.2.2.2 EU-SolidAct

The EU-SolidAct trial is an Adaptive Platform Trial and the master protocol is developed for evaluating treatments in hospitalised patients with COVID-19. While the master protocol is currently designed to test medications in hospitalised patients in phase 3 clinical trials, it will be expanded to other interventions, trial phases and involve patients outside of the hospital, when necessary. The protocol is designed such that it functions as the basis of a joint European response to combat infectious agents both now and in the future. EU-SolidAct is adaptive and enables the inclusion of hospitals in Europe and beyond, regardless of the severity of epidemic waves or available resources. The protocol is divided into two main parts: part A is for patients with moderate disease, and part B is for patients with severe to critical disease (Figure 3). The trial is sponsored by Oslo University Hospital, Norway.

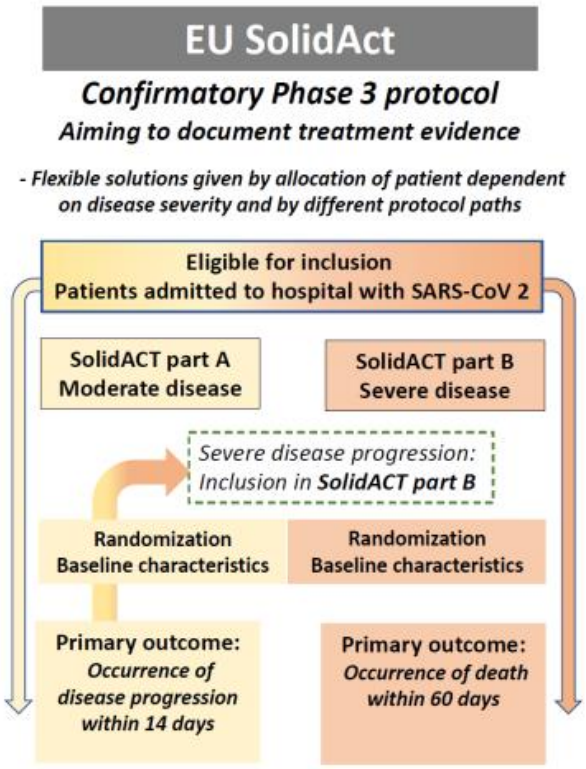

Figure 3 – Modular data capture in the EU-SolidAct.

The three large-scale, multi-center adaptive platform trials combined (REMAP-CAP, DisCoVeRy, EU-SolidAct) encompass more than 300 trial sites in 20 European countries.

2.2.3 ECRAID-PRIME

The European Clinical Research Alliance on Infectious Diseases is the primary care adaptive platform trial for pandemics and epidemics. The overall goal of ECRAID-Prime is to establish safety and efficacy, and thus suitability of COVID-19 treatments. This is a unique project that will assess COVID-19 treatments for non-hospitalized patients with the aim to speed up recovery and/or to prevent deterioration of illness and hospitalisation. By focusing on early phase clinical trials, the ECRAID-PRIME platform will be able to assess safety and efficacy of various treatments, helping to streamline them towards Phase III trials. ECRAID-PRIME will run the trials in a pan-European primary care Network.

2.2.4 Trial Coordination Board

The importance of cross-border cooperation and coordination in the fight against the global COVID-19 pandemic has been highlighted since it began. In particular, international clinical research efforts need to be connected and synchronized to ensure that results are obtained rapidly while remaining robust, reproducible and reliable. With this aim in mind, two ambitious projects financed by the EC, EU-RESPONSE (mentioned above) and RECOVER, established a joint coordination module between them. This module allows them to address the most pressing research questions through large adaptive platform trials (APT), while avoiding duplications and maximizing the use of resources.
The Trial Coordination Board (TCB) gathers the main actors, playing a role in the successful implementation and development of the European COVID-19 adaptive platform trials (APT). It aims to ensure collaboration and cooperation between the European COVID-19 APTs, and to create and maintain a constructive dialogue with regulatory bodies, policy makers and global COVID-19 trials.

2.2.5 Joint Access Advisory Mechanism

The EU-SolidAct, REMAP-CAP and ECRAID-Prime are part of the Joint Access Advisory Mechanism (JAAM), which provides a gateway to COVID-19 adaptive platform trials taking place in Europe. JAAM assesses requests from investigators and industry who are looking to test their compounds in one or more of these trials. Any independent investigator or private company can request access to the EU APTs via the JAAM, in order to assess their repurposed or investigational new drug.

2.3 HERA incubator call

Under the Horizon Europe HERA Incubator call, three new research projects (besides COVend) received funding for the early clinical development of different types of therapeutics against SARS-CoV-2 and its variants of concern.

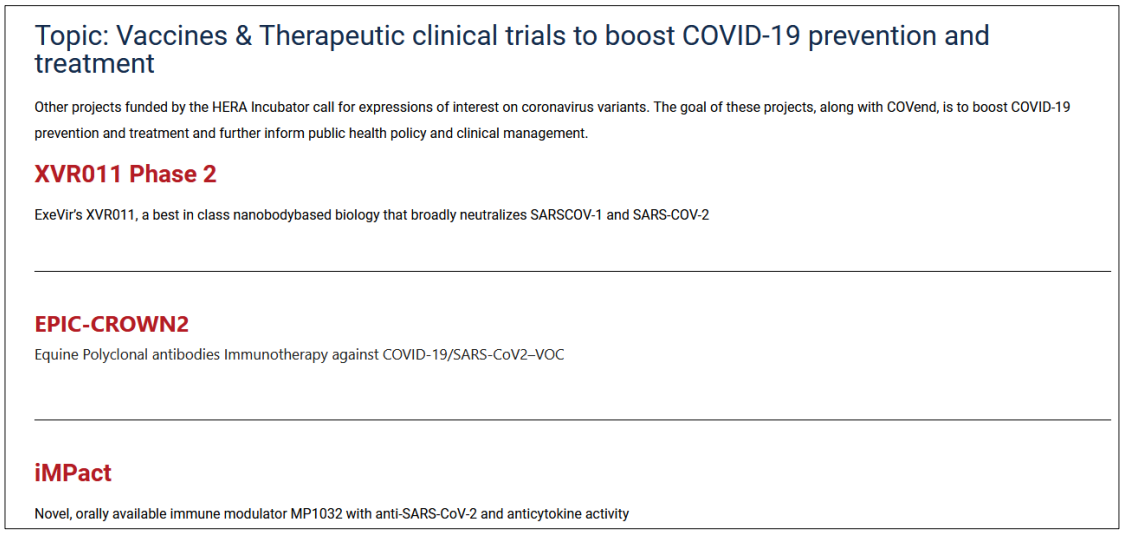

Figure 4 – New research projects featured on the COVend website.

The iMPact project aims to demonstrate that the asset MP1032 is a promising new candidate for the early intervention treatment of COVID-19 patients. MP1032 is a first-in-class drug candidate that reduces inflammatory markers such as TNF-alpha, IL-6, IL-12. These anti-inflammatory properties make it a highly promising compound for early intervention treatment of COVID-19.

EPIC-CROWN 2 seeks to rapidly clinically assess, in a phase 2 study, the safety and efficacy of FBR-002, a potent and broad neutralizing horse anti-SARS-CoV-2 polyclonal F(ab')2 antibodies in COVID-19 patients infected with either SARS-CoV-2 or its variants of concern.

The XVR011-Phase 2 led by ExeVir is an adaptive study, partially single blind, to evaluate efficacy and safety of XVR011 in immunosuppressed patients with a positive test for SARS CoV-2.

3 Main conclusions and next steps

The meeting showed the potential for more efficient trial implementation when existing infrastructure and expertise are used, e.g. shorter delays to setting up new trial sites. Projects are strongly encouraged to further explore options for collaboration in this perspective.

The trial sponsors of the adaptive platform trials emphasised that the selection of suitability of new compounds for uptake by the existing adaptive platform trials is done through the JAAM. This implies that the developer presents their compound to an independent panel of experts, followed by a discussion between the sponsors for coordination purposes. An important aspect for the successful integration of a new compound in one of the adaptive platform trials is the possibility of co-sponsorship for the developer of that compound. The recently launched new clinical trial regulation (CTR) provides a legal option to allow for such co-sponsorship and could thereby provide a solution to advance concrete collaborations between clinical trials[2]. The assessment of combination therapy is of increasing interest, and options for such treatment arms in the adaptive platform trials would be interesting to explore. Also, treatment for specific target groups, such as the immunosuppressed, provide opportunities for future trials with public health relevance.

The different multi-country adaptive platform trials highlighted that a number of hurdles related to regulatory, ethics or legal-administrative aspects have and are being encountered. The new CTR is aimed at increased harmonisation in the EU for the assessment of multi-country trial protocols by the national competent authorities, and the related clinical trials information system (CTIS) is anticipated to also accommodate complex trials. Timely engagement of the trial sponsors with the competent authorities on the trial protocols is expected to further smoothen the process. Moreover, ECRIN is working on the creation of a master template for site contracts. While there were several reminders of the commonly experienced hurdles for the implementation of multi-country trials in Europe, it was recognised that efforts are being made to overcome these, albeit in a complex environment. It is important for (academic) sponsors to be acquainted with the landscape of initiatives that exist to support addressing such barriers. Further bilateral discussions can be set up between the sponsors of the European adaptive platform trials and project coordinators of the newly funded clinical trials, to provide input in the design of the later-stage clinical trials.

All the three new research projects receiving funding for the early clinical development of different types of therapeutics against SARS-CoV-2 and its variants of concern are featured on the COVend project website. This is the very first step from the COVend consortium to promote networking and collaboration with other players. Given the volatility of the COVID-19 cases, patient recruitment can become a major challenge. A close dialogue has been maintained with the Project Officer and future contacts with other consortia in similar situations will potentially be established.

[2] Clinical Trials Regulation | European Medicines Agency (europa.eu)

4 Annex

6 April 2022, 9h30 – 13h00 CET
Virtual Meeting

Agenda:

TIME	PROJECT/ACTIVITY	PRESENTERS
09:30 – 09:45	Welcome & Objectives of the meeting	**Evelyn Depoortere** Policy Officer, European Commission, DG Research & Innovation
09:45 – 10:00	REMAP-CAP	**Marc Bonten** University Medical Center Utrecht, Netherlands
10:00 – 10:20	EU-SolidAct and DisCoVeRy	**Florence Ader** Lyon University Hospital, France **Marius Troseid** Oslo University Hospital, Norway **Yazdan Yazdanpanah** National Agency for Research on AIDS and Viral Hepatitis, Emerging Infectious Diseases, France
10:20 – 10:35	Coordination of European Network for COVID-19 therapeutic trials	**Jacques Demotes** European Clinical Research Infrastructure Network, France
10:35 – 10:45	ECRAID-PRIME	**Christopher Butler** University of Oxford, United Kingdom
10:45 – 10:55	Ecraid	**Marc Bonten** University Medical Center Utrecht, Netherlands
10:55 – 11:10	Coffee Break	
11:10 – 11:20	COVend	**Benjamin Friedrichson** University Hospital Frankfurt, Germany
11:20 – 11:30	iMPact	**Wolfgang Brysch** MetrioPharm AG, Switzerland
11:30 – 11:40	EPIC-CROWN-2	**Pauline Radreau** Fab'entech, France
11:40 – 11:50	XVR011-Phase 2	**Maarten van den Boer** ExeVir, Belgium
11:50 – 12:50	Discussion on potential collaborations	Moderators: **Evelyn Depoortere and Stefanie Sowinski** European Commission, DG Research & Innovation
12:50 – 13:00	Summary of discussion & Next steps	**Evelyn Depoortere** Policy Officer, European Commission, DG Research & Innovation