Support-e

SUPPORTing high quality evaluation of covid-19 convalescent plasma throughout EUROPE

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A message to all Support-ers

As the SUPPORT-E project draws to a close or to major milestone, it is clear it is successfully contributing assessing the value of plasma donated by persons recovered from SARS-CoV-2 infection for the treatment of patients with COVID-19. The project has further delineated how, when and which COVID-19 Convalescent Plasma (CCP) should be used in COVID-19 patients and confirms the importance of mobilizing all relevant stakeholders in responding to global challenges such as the pandemic. The extension of the project will provide more clinical evidence that will improve the strength of its conclusions and recommendations. Although it is very difficult to give closing words when not entirely clear whether the duration of Support-e will be extended or not, we believe that the findings the project will help combat the current pandemic and provide possible ways of responding to similar challenges in the future. Therefore, we thank all the participants of SUPPORT-E and other collaborators for their hard work and for the important results (already) achieved as well as the European Commission for financing it.

Dragoslav Domanović
Pierre Tiberghien

About CCP

CCP stands for Covid-19 Convalescent Plasma, plasma collected from Covid-19 recovered patients. CCP contains antibodies that could neutralize SARS-CoV-2 and thus may improve disease course in patients with SARS-CoV-2.

WP 7 MANAGE AND COORDINATE PROJECT AND PROJECT FINANCES

WP 6 DISSEMINATE PROJECT RESULTS

WP 1

ASSESS AND MONITOR THE ONGOING AND UPCOMING CLINICAL TRIALS

- Produce preliminary clinical trials guidelines and assessment criteria.
- Produce preliminary monitored access programmes guidelines.

WP 2

INCLUDE SELECTED CLINICAL TRIALS AND MONITORED ACCESS PROGRAMMES IN SUPPORT-E AND PROVIDE FUNDINGS

- Elaborate a new kind of clinical trials to evaluate CCP.
- Ensure high quality data set accrual in EU CCP Database.
- Contact stakeholders to promote the new generation clinical trials.

WP 3

MANAGE THE EU CCP DATABASE AND COLLECT THE DATA

WP 2 - 3

Analyse data collected in EU CCP Database.

WP 4

MAP THE USE OF ANTIBODY ASSAYS FOR THE CCP DONORS SELECTION

- Provide access to neutralisation assays.
- Develop, calibrate and standardise novel neutralisation assays.
- Establish a connection between antibody characteristics and clinical outcomes.

WP 5

INTEGRATE ALL THE INFORMATION GENERATED BY THE PROJECT

- Perform SWOT assessment to support future SoHO development.
- Create a mathematical model that will assist EU countries to financially manage the activities that are required to provide CCP as therapy during future pandemics.
- Formulate recommendations on therapeutical use of CCP.

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WP1 - Assessing CCP, conducting clinical evaluation and defining best practices

Team Leader – IRCCS OSM, Italy
Vice Leader – ASST di Mantova, Italy

The main objective of WP1 was to assess the state of the art relating the collection, characterization and efficacy of COVID-19 Convalescent Plasma (CCP) in the treatment of patients with COVID-19 through an analysis of published and ongoing studies, for the entire project period. An electronic literature search of the PubMed, Embase, Cinahl, WHO COVID-19 Global Research Database, ClinicalTrials.gov, Cochrane COVID-19 study Register (include EudraCt), WHO ICTRP, Transfusion Evidence Library, MedXriv, databases was performed (latest search May 31, 2022) to identify the studies on the use of CCP in COVID-19 patients. From the bibliographic research, a total of 10.460 articles and 3.825 trails were collected. Through the definition of inclusion criteria, **314 articles** and **277 trials** were selected. Simultaneously, the team built a database in REdCap in order to extract and to enter the data and, eventually, to draft the preliminary Report of EU and International ongoing/upcoming clinical trials as annex to the **Guidance Document** with assessment criteria for clinical trials. The criteria regards the three main issues of CCP use, i.e. donors selection, CCP collection, processing, biological qualification and storage and CCP treatment protocol.

At the end of these two years, WP1 were able to:

- Get an overview of the international current state of the art relating to the collection, characterization and use of CCP;
- Define the selection criteria for the enrolment of convalescent donors, CCP production and patients treatment;
- Select and identify eligible high quality clinical trials on the basis of the defined criteria. The data from the clinical trials were shared with Wp2 for selection;
- Identify best practice “monitored access” of plasma;
- Define a preliminary Guidance document for both clinical trials and monitored access use, that was later finalized by WP2.

In this project, the formulation of recommendations based on scientific and clinical insights from newly developed standardized assays and the evaluation of donor and recipient CCP data revealed to be of paramount importance for this Pandemic and for the future one.

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WP2 - Supporting high quality clinical evaluation and producing data-sets for inclusion in the database

Team Leader – DRK-BSD, Germany

WP2 team conducted and analysis on the data on the EU CCP *Database*. A quantitative overview on datasets related to SUPPORT-E was carried out by assessing the completeness of datasets and quality of the data. This was coupled with a descriptive review of some key characteristics of donations, transfusions and recipients. A more detailed statistical analysis will be performed by WP3 members in the coming month. A total of 155.893 CCP donations were registered in the EU CCP database as of Oct.22, 2021. Of these, 142.227 datasets were reported by institutions related to the SUPPORT-E project (91%). Descriptive statistics in the analysis included are gender, body mass index (BMI), age, collection method, interval from symptom to donation, donor adverse reactions, plasma volume.

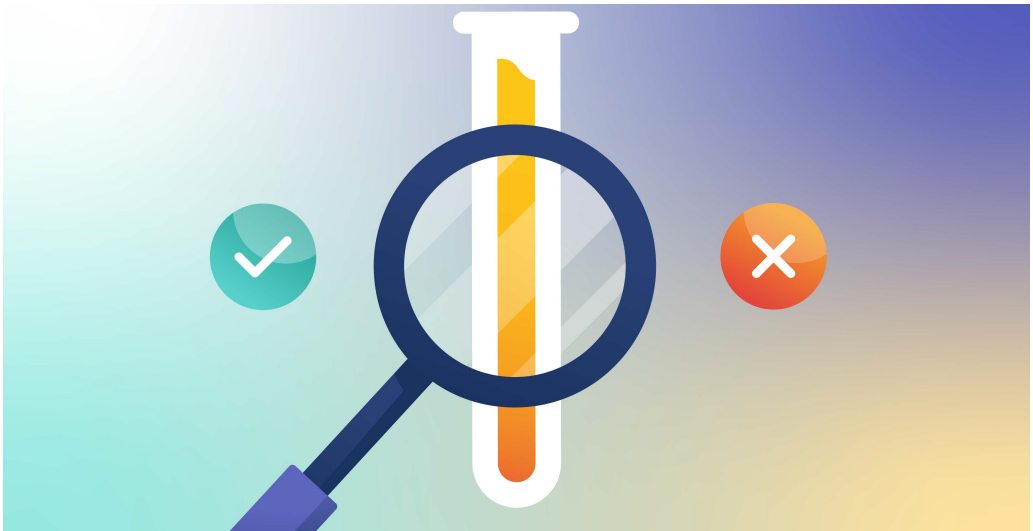
Additionally, a key component of the work carried out by WP2 was the support of the COVID-19 clinical trial. A detailed clinical trial protocol for COVID-19 has been developed and was submitted and approved for regulatory approval for Germany, who has been granted funding for the entire duration of the trial (just for Germany). The COVID-19 trial has been initiated in Germany and is actively including patients. It is planned that substantial part of the WP2 budget will be allocated to this trial and additionally that the COVID-19 trial will be conducted in France, United Kingdom and Germany while we are also in discussion with North Macedonia and Switzerland if they will also be interested in taking part. The launch of this trial has been a priority, primarily for France and the UK, whereas Germany has focused on the commencement of the trail.

WP3 - Collecting, monitoring and analysing EU-CCP Database data

Team Leader – EFS, France
Co-leader – AUH, Denmark

Besides to supporting the registration on the EU CCP DB, WP3 has mainly been focused on carrying out analyses of the data on the Database (in addition to those done by WP2). Entered data was assessed for quality, data safety and curated in function of analysis purposes, generating repositories and reports. Initial analyses are ongoing, mainly on donations data, where numbers allow statistical analysis.

Before June 2022, additional efforts are focusing on carrying out a second analysis of the data received so far on donors, plasma donations and patients.



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WP4 - Improving plasma potency assessment

Team Leader – Sanquin, Netherlands
Vice Leader – Rode Kruis, Belgium; NHSBT, United Kingdom

A questionnaire was sent out to 26 Blood Establishments within Europe to investigate which serological assays were used to test convalescent plasma to treat COVID-19 patients. Meanwhile, a novel competition ELISA to determine neutralizing capacity of CCP was developed (*Wouters et al, Transfusion, 2021;61:2981-90*). In order to standardize COVID-19 serology assays we have distributed a standard plasmapool that can be converted to international BAU/ml units. A quality control of COVID-19 serology tests has been performed in 26 Blood Establishments within Europe.

The outcome of the questionnaire was distributed among the SUPPORT-E partners. The standardization and quality control of the European Blood Establishment will be published and also presented at the international ISBT2022 conference. The novel competition ELISA was less selective for high titer CCP than other (commercially available) tests and therefore only used spuriously. WP4 published a *paper* on commentary on evaluation of SARS-CoV-2 antibody titers and potency for convalescent plasma donation. As viruses evolve and continuously compete with the (human) immune system, lab tests for determining the quality of CCP are outdating quickly. The inhibition of wild type RBD binding to ACE2 by CCP is only a proxy for the inhibition of mutant RBD binding to ACE2 by CCP is only a proxy for the inhibition of mutant RBD binding to ACE2. The plethora of tests has not helped interpretation of CCP quality over different trials/studies in the EU and worldwide.

WP5- Developing recommendations and preparing for the future

Team Leader – NHSBT, United Kingdom

We have used evidence based methods to provide recommendations for the use of CCP to treat infected patients in future outbreaks of COVID-19. The aim is to apply our findings to future pandemics. There is high certainty of evidence from our systematic review of randomised controlled trials (RCTs) conducted worldwide. This evidence does not support the use of CCP to treat moderate and severe disease in patients with pre-existing antibodies against SARS CoV2. Instead these trials suggest that CCP would benefit immune compromised patients that are unable to make their own antibodies against SARS CoV2. We therefore recommend further RCTs with sufficient participant numbers to examine the effectiveness of CCP in the immune compromised and for early or prophylactic treatment. CCP may not be harmful but the evidence for this requires increased certainty through careful reporting of adverse events in both treatment arms of future RCTs. Finally we have collected data from three blood establishments in Europe that detail the cost of collection, testing and distribution of CCP in 2020 and 2021. NHS Blood and transplant have provided health economists with data required for a model framework that, together with data from other blood establishments within Europe, will estimate the affordability and impact on healthcare resources of rolling out a CCP programme across Europe.

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WP6- Dissemination, exploitation and communication

Team Leader – CNS-ISS, Italy

Among other things, in the last year, the WP6 team produced the SUPPORT-E promotional video. The latter consisted of a short animated output that explained the objectives of the project, described the consortium behind it, gave information about the CCP database and, last but not least, launched a call to action to donate CCP. The video was shared on the SUPPORT-E Twitter account and was tweeted also by the official EU-DG Santé account, a feed followed by over 84k Twitter users. WP6 team also delivered the final version of the dissemination plan and produced the layman's version of the SUPPORT-E Interim Report. Moreover, the Team managed the dissemination of the Open Letter to WHO in response to their recommendation against the use of CCP for COVID-19 patients. The letter was published on two newsfeed platforms (EurekAlert and AlphaGalileo), which are dedicated to a key-target public of health sector journalists and stakeholders. WP6 also started to produce and disseminate a series of interviews to SUPPORT-E WP leaders. This last project proceeded accordingly to the WP leaders' availability. Two interviews were produced as of now. We also collaborated with WP7 to the organisation of the SUPPORT-E meeting that will be held in Rome the 17 th of June.

WP7- Project Management

Team Leader – EBA, Brussels

WP7's main goal has been to safeguard the effective execution of the proposed project and the delivery of quality results within time and budget. Furthermore, WP7 has ensured the appropriate liaison with the European Commission and with and between the external Advisory Board, the Database Management Board and the internal Project Management Board.

WP7 has coordinated the work and progress in all WPs, ensure communication flows among partners and manage common consortium activities in addition to overseeing all administrative, financial and contractual aspects of the project.

EBA, as WP7 Leaders, led in the project management and coordination of the project ensuring that project objectives and deliverables are achieved in full within time, cost and resource constraints. Since the start of the project, WP7 has set up the Scientific and Ethical Support-e Advisory Board, which has been kept informed of the progress of the project via regular meeting and review of output.

It also coordinated the SUPPORT-E team in reviewing and commenting the EU Commission Guidance on collection, testing, processing, storage, distribution and monitored use of CCP.

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Partners

eba Safe blood for Europe

midt Central Denmark Region
Aarhus University Hospital

Carlo Poma
Sistema Socio Sanitario Regione Lombardia
ASST Mantova

Belgian Red Cross

BLUTSPENDE SRK SCHWEIZ
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EFS Établissement Français du Sang
Du donneur aux patients

Fondazione IRCCS Policlinico San Matteo
Sistema Socio Sanitario Regione Lombardia

CENTRO NAZIONALE SANGUE
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