NEWSLETTER OCT-2020

Dear DAWN-plasma investigators,
Dear friends and colleagues,

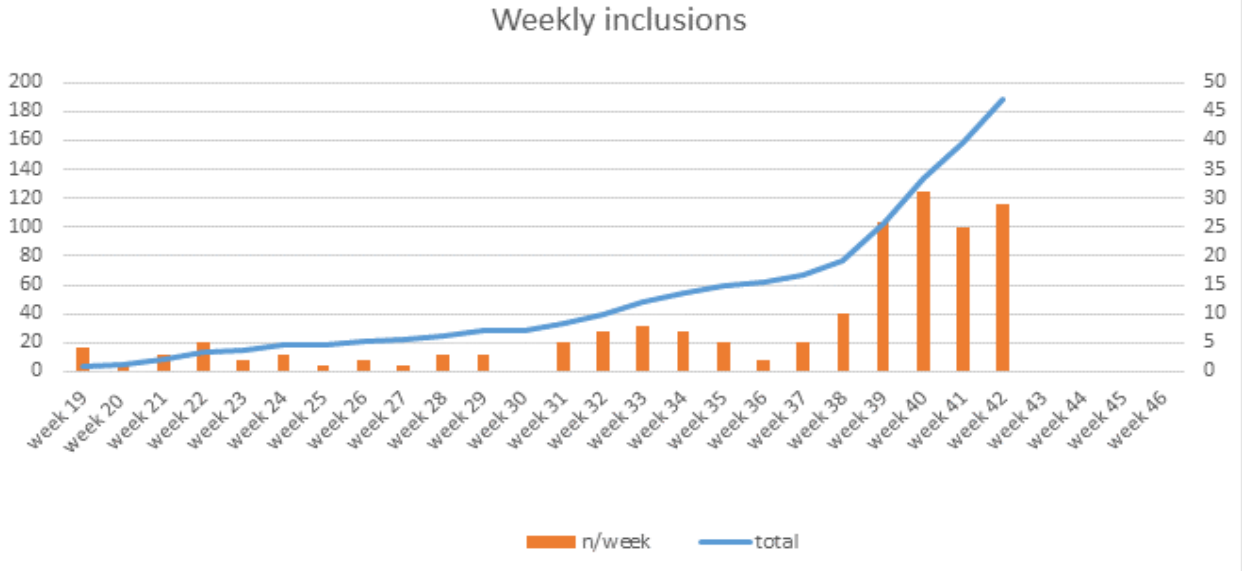
It can no longer be denied: we are in the middle of the Autumn COVID peak. Hospitals and clinicians are working hard to manage the large inflow of patients, labs are at full capacity to process the screening and diagnostic COVID tests, and Rode Kruis Vlaanderen – Croix Rouge are doing major efforts to ensure the availability of convalescent plasma.
Thanks to all your hard work, and dedication to clinical research, today, October 15th, we have included our 188th patient in the DAWN-plasma trial. We value and foster the large and broad Belgian collaboration of so many clinicians and partners. The DAWN-plasma group can be very proud of this major endeavor.
This newsletter intends to update you on the status of the trial. We have been able to expand the group of centers to 22, and 19 of these centers have already actively recruited patients. A protocol amendment has been approved. The protocol of the DAWN-plasma trial will soon be published in Trials, and is already available online.
We remain available for all your questions and practical concerns regarding the trial, so do not hesitate to contact us should practical or other problems arise.
Most importantly, we hope you and your families remain healthy, and that amidst all this hard work, there is still some time to spend with your loved ones.
COVID-19 is not a sprint, but a long marathon.
Take care!

Thank you!

Geert Meyfroidt
Myriam Cleeren
Timothy Devos
Katleen Vandenberghe
Peter Verhamme
Anne Luyten

188 patients

target: 483 patients



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Recruitment overview

Trial site	City	# patients
3209 CHC Liège Mont Légia	Liège	43
3202 CHU Brugmann	Brussels	26
3212 AZ Groeninge	Kortrijk	25
3201 UZ Leuven	Leuven	16
3205 UMC Sint-Pieter Brussel	Brussels	15
3204 UZ Brussel	Brussels	13
3211 ZNA Stuivenberg	Antwerpen	11
3207 CHU de Liège	Liège	9
3203 ULB Erasmus ziekenhuis	Brussels	7
3219 AZ Maria Middelares Gent	Gent	5
3221 AZ Sint Lucas	Gent	4
3217 Imelda	Bonheiden	3
3215 Sint-Trudo Ziekenhuis	Sint-Truiden	3
3214 CHR Citadelle Liège	Liège	2
3208 Cliniques Univ. St-Luc	Brussels	2
3213 CHR Jolimont	Mons	1
3210 Institut Jules Bordet	Brussels	1
3216 CHU Ambroise Paré	Mons	1
3220 AZ Sint-Vincentius Deinze	Deinze	1
TOTAL # patients		**188**
CH de Wallonie Picarde	Tournai	0
AZ Delta	Roeselare	0
AZ West Veurne	Veurne	0

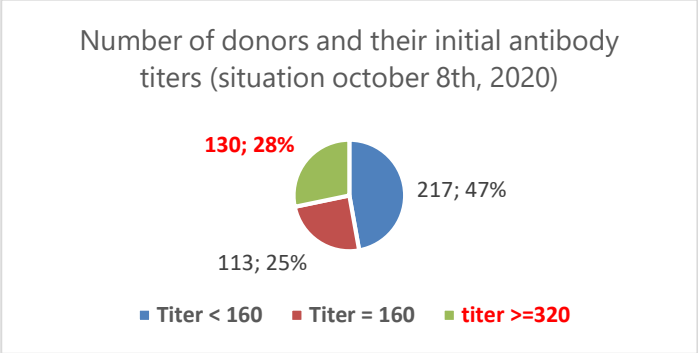
KCE is using EDGE, an online Clinical Trial Management System (CTMS), to follow-up on recruitment of all sites in DAWN study. Recruitment by site is publicly available on KCE's dynamic dashboards (https://kce.fgov.be/en/cov201003-donated-antibodies-working-against-ncov-dawn-plasma), updated every Friday. As a site participating in a KCE Trials funded study, you are entitled to have a full license to use this CTMS in your hospital to manage your own clinical studies. Should you be interested to hear more about EDGE, do not hesitate to contact KCE Trials for more information (trials@kce.fgov.be).

Convalescent COVID 19 Plasma (CCP) – donor recruitment, selection and CCP donation

Rode Kruis:

Red Cross Flanders continues to recruit and collect convalescent COVID 19 plasma.
As the SARS-CovV-2 antibody titers are highest short after infection Red Cross Flanders reactivated donor recruitment in September. Organisations, in direct connection with care givers and patients are informed about the increased need of CCP. A new information campaign was started October 1st.

Hospitals, First line, tracing centers and pharmacists were contacted with a link to the Red Cross Flanders website https://www.rodekruis.be/nieuws-kalender/nieuws/oproep-aan-genezen-mannelijke-covid-19-patienten/. Social media are also included.
Since the start of the project 728 male donors registered to the website. 484 were eligible as potential donors; 470 showed up for an initial SARS-CoV-2 antibody test. 219 of them had at least one donation. We counted a mean of 2.74 CCP donations per donor.



Currently, October 8th, 2020, 176 units were delivered to the DAWN-plasma trial. 305 units are in stock. As expected at the beginning of the trial, the number of blood group B and/or AB donors and consequently also CCP product is very low. The clinical protocol allows the use of a lower titer than 320 in case of insufficient blood group compatible CCP. CCP of blood group B and blood group AB at titer 160 are available for these patients. Therefore patients with blood group B or AB don't risk to be excluded from the trial because of lack of compatible CCP.

Croix Rouge:

A total of 312 donors gave COVID plasma. We have presently available 46 plasmas with a titer of anti Sars Cov 2 neutralizing antibodies above 1/320 and 54 plasmas with a titer above or equal to 1/160 but lower than 1/320. We don't have anymore B and AB plasmas available in our stock. Irrespective of blood group, the stock is diminishing.
Consequently, the SFS is working on communication actions to motivate new convalescent donors to give COVID plasma. In parallel, the SFS started anti SARS Cov 2 antibody screening by ELISA to identify anti SARS Cov 2 immunized donors among regular B and AB plasma donors in order to solve the issue of the availability of B and AB Covid plasmas.

Quantification of neutralising antibodies for the DAWN-plasma trial

For the DAWN-plasma trial, circulating antibodies able to neutralize SARS-CoV-2 infection are measured by virus-neutralizing assays (VNA) in different samples and by different participating laboratories.
The principle of this assay is to pre-incubate defined dilutions of inactivated plasma/serum samples with a defined quantity of SARS-CoV-2, to add these to an infection-permissive cell-line in microplates and to quantify percentage of infected wells at a given sample dilution. Different read-outs (such as microscopic analysis of cytopathic effect or immunostaining of viral particles) are applied to score infected wells and to determine titres of neutralizing antibodies (NAb) in the sample. These are expressed as 50% neutralization titres (NT50), which correspond to the titre that reduced the number of infected wells by 50%.

For the DAWN trial, blood samples from potentially eligible convalescent COVID19 plasma (CCP) donors recruited through the Rode Kruis or the Croix Rouge are respectively screened for SARS-CoV-2 neutralizing

antibody levels in the laboratory of Piet Maes (REGA Institute Leuven) or of Daniel Desmecht (University of Liège). Only CCP from donors with a NT50≥320 are eligible for the DAWN trial.
In addition, evolution of levels of circulating SARS-CoV-2 neutralizing antibodies in participating patients is also addressed in the DAWN trial as an exploratory outcome. For that purpose, patient's serum samples are taken at randomization before administration of CCP (day 0) and at day +6 after randomization. Based on geographical localization of the clinical site, these samples are sent to four different laboratories in Belgium for determination of NT50 titres. Namely, the laboratory of Piet Maes (REGA Institute Leuven) or of Daniel Desmecht (University of Liège) or of Kevin Arïen (Institute of Tropical Medicine Antwerp) or of Cyril Barbezange (Sciensano Brussels).

Important clarifications

Blood plasma availability

Always check the plasma availability on the website (https://www.plasma-covid19.be) before randomization. In case there is insufficient plasma available (especially B and AB), make a phone call to Rode Kruis (015 443906) or Croix Rouge (081 564120) to ask if there is plasma with lower titer (1/160) available, this is allowed by the protocol in these exceptional circumstances.

Screening and randomization

Always complete the 'screening and eligibility' section before completing the 'randomisation' section. Once the data is entered in the randomisation section, don't forget to set the form status to 'complete' before saving. The study arm will then appear on the screen and a randomisation confirmation will be sent to you and to Rode Kruis or Croix Rouge.

Informed consent form

Make sure you are using the latest approved informed consent form (v2.3 in Dutch and French, v1.2 in English). Ask patients to resign this new version if they are still in follow-up.

Serum 10 ml tubes for COVID-19 NEUTRALIZING ANTIBODY DETECTION (baseline and day 6), described in the protocol as immunoparesis testing

Collected samples should be transferred in batch to one of the reference laboratories for neutralization antibody detection. Please organise the transport of the samples (on dry ice, indicate patient number and day 0 or day 6) to your reference lab (fee is foreseen) and inform your lab that samples will be sent.
Transfer of samples will be organized at the latest every four weeks as samples cannot stay longer than 4 weeks stored locally. Transport will be done on dry ice, please indicate the patient study number on the samples and also 'Day 0' or 'Day 6'. Make sure the labels stick well to the tube!
The labs will send you the neutralizing ab results, please enter the NT50 results in the eCRF upon receipt of the results (NT90 is not required in the eCRF; some labs even do not report NT90 results).

Updates to the eCRF (will soon be implemented)

VAS pain score: check the VAS Pain Score daily until discharge.
Specific treatment used other than plasma**:** steroids and anticoagulants (type and dose)

SAE form

The SAE form should always be signed by the investigator, there is a new SAE form on the dawn plasma website with a section for the PI to sign

More questions?

Check the Q&A on the Dawn plasma website. If you do not find the answer, please mail to dawn-plasma@uzleuven.be

Remember all study documentation can be found on https://dawnplasma.be/