Questions and answers 2020 05 12

PLASMA

How do I know if plasma is available ?

Check website : https://www.plasma-covid19.be/

A login (1 combination of e-mail and password) will be sent to the sites

Alternatively you can go to https://dawnplasma.be/ , select 'plasma' tab and you will be directed to the above website.

If the website not available call Tel Croix Rouge 081 564120 , Tel Rode Kruis 015 443906

If there is no plasma available should I delay randomisations?

This could be an issue in the beginning of the study when there is not enough plasma available, in that case call Rode Kruis or Croix Rouge, there may be transport of plasma between both of them.

The plasma administration protocol states that the plasma must be transported frozen to the covid-19 department in order to be thawed there. With us at the hospital, this is not the procedure. Only in the lab do we have a plasma thawer at our disposal. Is this allowed?

The plasma may be thawed in the lab but must be administered within 2 – 6 hours

If one can be assured that the plasma is transported quickly enough and correctly into the COVID unit, then this is also OK: the internal procedure of 'standard plasma' may be followed.

First unit is "décongelé" (30 minutes in machine) and dispensed to yard
Patient administration starts and parameters are taken :start-15 minutes – end
Patient could make an AE
Which delay do you suggest to maintain before "décongelé the second plasma?
Do we have to wait until first is completely administered before "décongeler" the second ?
If the second is already décongelé , and if for any reason the patient can't get the plasma , Plasma can only be stored at 2-8°C for 24h at laboratory before administration , this would mean that the plasma is lost for another patient?

It is better to wait until the first unit has been infused before starting the thawing of the second unit. It is never known that, towards the end of the infusion of plasma 1, there would be a reaction which would delay second unit administration.

Indeed, that's the reason why it is better to wait a little bit to start thawing the second unit.

If a patient finally not gets the convalescent plasma, can we use it for another patient?

No, if it has not been used you should contact the Rode Kruis or Croix Rouge. It may not be used for another patient. Once the plasma has been on the Covid Unit it must be used on that unit or discarded on that unit if not used for any reason. To be noted on the Plasma accountability log (see website)

INCLUSION CRITERIA - RANDOMISATION

Can patients who are not mechanically ventilated but receive high-flow nasal oxygen through optiflow be included?

We do not consider optiflow as mechanical ventilation, so these patients can be included. Only invasive (requiring mechanical ventilation), or non-invasive mechanical ventilation is an exclusion criterion.

Should the patient be randomized within 60 hours after PCR, suppose plasma is not immediately available?
Preferably yes, to be discussed case by case. The main reason is that the administration of Plasma should start as soon as possible before the patient is getting worse and needs mechanical ventilation.

Suppose a patient is admitted to the hospital at 17h, can we wait until the next day for randomization?
If the patient is stable, you can wait. If the patient is not stable, you better randomize the patient.

Which is the maximum delay between screening and baseline: in case if plasma not available, 1 day , 2 days , 60hours ?
60 hours preferably. As screening is a simple procedure in the Dawn-plasma, wouldn't it be better to repeat screening once plasma is available in that case.

Should we do 2 blood typings before randomization?
1 blood typing is sufficient before randomizing the patient in Redcap and ordering the plasma, 2 blood typings MUST be done before the plasma can be released.
(the blood bank will never release the plasma if there are no two ABO D typings, taken at a different moment and showing an identical result).

What happens in case that second typage doesn't match and that third typage match with second
Indeed, this is called a 'near miss' adverse event in transfusion medicine. The whole procedure of ABO D typing will be started from scratch because an error occurred before (wrong sample, sample taken from wrong patient, wrong labelling of the sample etc are possible causes of error)

Can we use historical blood typing?
If two identical ABO D typings of the patient exist in the system of the local bloodbank, than it's OK.
If ABO D is copied from a 'blood group card' (bloedgroepkaartje) than it should be checked.
One exception: if a patient underwent a bone marrow transplantation, the BG should be checked twice also (BG can change).

Can we use a central venous line for plasma infusion?
Please follow the same procedure as for standard plasma at your hospital, remember to give it slowly. the administration of blood components via a central line is accepted, provided that good flushing of the line and aseptic work.

Can we use CT from 2 weeks ago?
There is no timeline in the protocol for CT but remember that the optimal study candidates are patients with a recent COVID-infection. If doubts are rising, a case by case discussion with one of the PI's in Leuven is always possible.

Patient is already 2-3 weeks in hospital, can he/she be included?
Not considered as an ideal candidate

Patient at emergency department with typical CT, do we have to wait for PCR result?

If you did the PCR test, then you should wait. If the swab is negative but you estimate the patient is covid+ (CT scan, signs, …) randomization can be performed.
If you have not done the test, you can include the patient based on CT and if you are clinically certain. (cfr inclusion criteria).

Who receives the randomization confirmation? Can all users of our site receive the confirmation?
Currently the confirmation is sent to the person who randomized the patient and to Rode Kruis/Croix Rouge. Next week the PI of the site will also receive the randomization mail. It is not possible to send it to all the users.

PBMC ISOLATIONS

The protocol for pbmc isolations is very summary and contains no information on what isolation medium and freezing medium should be used.
We also do not currently have the proposed tubes available in the lab. Is Ficoll separation an alternative?
If we do not perform PBMC isolations, how should the samples (for PBMC isolation) be stored?
A ficoll separation is certainly just as good. The tubes we have are actually prefilled tubes with ficoll with a filter.
Any protocol for pbmc isolation is good though. Buffer or freezing medium may also be what one is used to use.
If one can't do pbmc insulation, which I certainly understand, one can possibly take plasma and then the buffy-coat and just freeze it.

FINANCIAL ISSUES

Transport of plasma: who will finance urgent transport?
The fee is for transport from hospital to laboratory (D1,D6) for blood probe
Can you please check if this fee includes an eventual urgent adhoc transport of plasma from red cross to hospital?
Or will this fee be supported by red cross?
The fee for plasma and for the transport of the plasma will be financed by the sponsor.
For the Plasma of Rode Kruis the transport will be organized by IHCT – see procedure on the website.
For Croix Rouge it will be organized by Croix Rouge.

Is there a budget for sending blood samples (samples of day 6)
For the transport of the serum tubes (immunoparesis), a fee of 40 euro is foreseen for the study centres (per patient fee). Thus, it is logical that the study sites will organize the transport of this samples to the reference lab.

LABS

is the 'q' of qPCR qualitative (which is Standard of Care), or quantitative (not SOC – how should this be stored, until processing or 'shipment' to you) ?
cfr lab manual

Do which lab do I have to send samples for immunoparesis testing?
See website

QUESTIONNAIRES

What is the VAS-score?

This is a pain score. It is not yet in use at this moment.
When we revise the protocol we will add the VAS score and we will provide you with the questionnaire.

INVESTIGATOR STUDY FILE

contact list for the study: on the trial website the form is blank
Can you please send us a completed version
Will be provided by Klara Vlassak, the Monitor

Quality of life scoring :

on source data type is mentioned:
QoL questionary : completed by patient : → in practice orally by patient , noted by nurse
The VAS-pain score (when in use): will be orally asked to patient and completed by nurse
The EQ-5D-5L : idem : orally by patient and completed by nurse (COVID)

Drug accountability log :

I think this log is more adapted for orally given IMP

- **→ Will you create another drug accountabilityn log?**

The log is already adapted now.
This is only a dispensing and discarding log.
All the other information must be noted in the medical file of the patient. You can check the e-CRF for all the requested information and this information must be reported in the medical file.