COVID 19 Convalescent Plasma: Guidance for Mayo Expanded Access Program or an eIND for Special Circumstances

Purpose

To describe the clinical processes needed to request and administer therapeutic convalescent plasma to COVID-19 eligible patients under the umbrella of either the Mayo Expanded Access Program or the Investigational New Drug request process.

- All patients eligible for convalescent plasma will be enrolled via the Mayo Expanded Access Program
- Pediatric patients will be covered under the eIND process (special circumstance)

Rationale

Beyond providing supportive care, there currently exist no proven treatment options for coronavirus disease (COVID-19) and the related pneumonia, the infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).

Experience from prior outbreaks with other coronaviruses, such as SARS-CoV-1 shows that such convalescent plasma contains neutralizing antibodies to the relevant virus (1). In the case of SARS-CoV-2, the anticipated mechanism of action by which passive antibody therapy would mediate protection is viral neutralization. It is hoped this therapeutic effect will decrease the chance of further deterioration and the need for intensive care and/or assisted ventilation.

The only antibody type that is currently available for immediate use is that found in human convalescent plasma. This document is intended to support physicians and patients making the decision to transfuse convalescent plasma as it becomes available.

On March 23, 2020 the FDA provided guidance on how individual physicians can request convalescent plasma for an emergency IND for compassionate use or via the Mayo Expanded Use Program (2).

Indications

- Patient must be hospitalized with COVID-19 respiratory symptoms and confirmation via COVID-19 SARS-CoV-2 RT-PCR testing. Patient or their legal representative is willing and able to provide written informed consent.
- Must have severe or immediately life-threatening COVID-19, defined as follows: Severe disease is defined as one or more of the following:
  - Dyspnea
  - Respiratory rate greater than or equal to 30/min
  - Blood oxygen saturation less than or equal to 93%
  - Partial pressure of arterial oxygen to fraction of inspired oxygen ratio less than 300 and/or Lung infiltrates greater than 50% within 24-48 hours
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Life threatening disease is defined as one or more of the following:
- Respiratory failure
- Septic shock and/or
- Multiple organ dysfunction or failure

Contraindications
1. Receipt of pooled immunoglobulin in past 30 days
2. Other clinical contraindication to transfusion or history of prior reactions to transfusion blood products.

Requesting and Obtaining Convalescent Plasma
The ordering physician should contact the Regulatory Coordinator for your state to initiate the appropriate process for requesting convalescent plasma. They will provide guidance in completing the necessary documentation to allow for the release of the product for transfusion.

a. In Illinois: Sherri Velez Email: sherri.velez@advocatehealth.com
b. In Wisconsin: ASLMC-CCP.Request-WI@aah.org

Patient Preparation and Monitoring
A. Informed consent obtained
B. Baseline evaluation to document in the medical record:
   1. Demographics (age, sex, ethnicity, race)
   2. Medical history (timing of exposure to COVID-19 source patient, acute and chronic medical condition, medications, allergies)
   3. COVID-19 symptom screen (fevers, cough, shortness of breath), onset of symptoms, source of contagion
   4. Vital signs
   5. COVID-19 testing (RT-PCR) from nasopharyngeal, throat, tracheal aspirate or bronchoalveolar lavage and stool (optional) samples
   6. Blood typing, CBC, comprehensive metabolic panel (consider labs within 24 hours of beginning therapy) – or if older than 72 hours
   7. Serological testing: anti-SARS CoV-2 titers when available
   8. Urine or serum pregnancy test for females of childbearing potential (results from laboratory tests obtained up to 7 days before enrollment may be used for the pregnancy test, however serum pregnancy tests recommended)
   9. Determination of eligibility as per inclusion/exclusion criteria, consent for treatment, positive for COVID-19, respiratory symptoms
   10. Any medical condition arising after consent should be recorded as an adverse event
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Dosing

- If no titers are available:
  - Based on the available evidence, the recommended dose is 2 units; ~200 - 500 mL
    (Start with one unit, repeat a second unit within 12 hours after the completion of the first unit)
  - Recommend initiating therapy before the patient progresses to the need for mechanical ventilation support

- (Updated dosing based on titers will be provided when available)
- Additional units beyond two is not recommended
- For other transfusion scenarios (such as those listed below), physicians may pursue eIND applications:
  - Transfusing more than two units of convalescent plasma
  - Transfusing a second unit more than 12 hours after the initial unit is transfused

Administration

- Rate of transfusion:
  - Physicians should transfuse each unit of convalescent plasma at an infusion rate that adheres to Advocate Aurora guidelines and best clinical practice.
- Pretreatment to minimize transfusion reactions (e.g. acetaminophen, diphenhydramine) may be given per physician’s discretion
- If a reaction develops during infusion, the infusion may be slowed or stopped as per the physician’s decision.

Monitoring During Treatment

- Nursing care and monitoring should align with Advocate Aurora Health Care’s policy and procedure for the Administration of Blood and Blood Products

Post Therapy Monitoring

Day 1-7 (or for duration of hospitalization)

1. Vital signs daily or as ordered by the physician, or per unit standard
2. COVID-19 symptom assessment (fevers, cough, shortness of breath).
3. New medical conditions or adverse events – these must be reported via the Mayo eAP website and to the transfusion service (blood bank)
4. Physical examination.
5. CBC, comprehensive metabolic panel, CRP (day 1 and 7) – repeat if changes from baseline.
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References


(2) Investigational COVID-19 Convalescent Plasma Emergency INDs / FDA

(3) Convalescent Plasma to Limit Coronavirus Associated Complications: An Open label, Phase 2A Study of High-Titer Anti-SARS-CoV-2 plasma in hospitalized patients with COVID-19
   Short title: CSSC-002
   Clinical Phase: 2A Open Label
   IND Sponsor: Johns Hopkins via a national IND:
   Conducted by: Mayo Clinic in collaboration with Johns Hopkins University, Washington University in St. Louis and other interested parties. – March 2020


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