Use of Convalescent Plasma Collected From EVD Survivors Treated With INTERCEPT Blood System for Pathogen Inactivation (PI) To Facilitate Passive Immune Therapy

Elan Weiner, MS, MPH, MT, SBB
(speaking in place of Jessica Hanover)
Cerus Corp.

Disclosures:
Employee of Cerus Corp
Shareholder: Cerus, Fresenius SE & Co KGaA
Committee: AABB BB/TS Standards Program Unit (Standards Committee)
Topics

• Introduction to the INTERCEPT system, mechanism of action and use around the world

• Overview of IDE for the treatment of EVD patients with INTERCEPT treated ECP

• Formation of the ECP Bank at Emory University

• The Convalescent Plasma Bank Model
INTERCEPT: Mechanism of Action

Amotosalen

Targeting

Helical region of single- or double-stranded DNA or RNA

Intercalation

Crosslinking

UVA Illumination

Amotosalen

Amotosalen is an optimized natural product

- PI by specific mechanism: cross-linking (not ROS)
- Minimize side reactions
- Optimized hemocompatibility
- Maximize safety margins
INTERCEPT Treatment Process: Efficient, Robust, Scalable Technology

1. **Add**
2. **Inactivate**
3. **Remove**
4. **Ready to Use/Store**

(A similar treatment set is used for platelets.)
Robust, Broad Spectrum Inactivation
Achieve >4 logs of inactivation for most pathogens

<table>
<thead>
<tr>
<th>Viruses</th>
<th>Log Reduction (pfu/mL)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1, cell-associated</td>
<td>5.4</td>
</tr>
<tr>
<td>DHBV (model virus for HBV)</td>
<td>≥4.8</td>
</tr>
<tr>
<td>BVDV (model virus for HCV)</td>
<td>≥4.4</td>
</tr>
<tr>
<td>HTLV-I</td>
<td>4.7</td>
</tr>
<tr>
<td>HTLV-II</td>
<td>≥5.1</td>
</tr>
<tr>
<td>West Nile Virus</td>
<td>≥5.7</td>
</tr>
<tr>
<td>Chikungunya virus (CHIKV)</td>
<td>≥5.7</td>
</tr>
<tr>
<td>Dengue virus</td>
<td>≥4.3</td>
</tr>
<tr>
<td>Cytomegalovirus (CMV), cell-associated</td>
<td>≥4.9</td>
</tr>
<tr>
<td>Influenza A virus</td>
<td>≥5.9</td>
</tr>
<tr>
<td>Bluetongue virus</td>
<td>4.4</td>
</tr>
<tr>
<td>Adenovirus 5</td>
<td>≥4.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protozoan Parasites</th>
<th>Log Reduction (pfu or cfu/mL)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmodium falciparum</td>
<td>≥5.6</td>
</tr>
<tr>
<td>Babesia microti</td>
<td>≥4.9</td>
</tr>
<tr>
<td>Trypanosoma cruzi</td>
<td>≥5.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Log Reduction (cfu/mL)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>≥6.3</td>
</tr>
<tr>
<td>Yersinia enterocolitica</td>
<td>≥5.9</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>5.8</td>
</tr>
<tr>
<td>Serratia marcescens⁴</td>
<td>≥6.7</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>≥6.1</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>≥5.4</td>
</tr>
<tr>
<td>Streptococcus pyogenes³</td>
<td>≥6.8</td>
</tr>
<tr>
<td>Bacillus cereus (vegetative)</td>
<td>≥5.5</td>
</tr>
<tr>
<td>Clostridium perfringens (vegetative)</td>
<td>≥6.5</td>
</tr>
<tr>
<td>Propionibacterium acnes</td>
<td>≥6.5</td>
</tr>
<tr>
<td>Treponema pallidum (syphilis)</td>
<td>≥6.4</td>
</tr>
<tr>
<td>Borrelia burgdorferi (lyme disease)</td>
<td>≥6.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Leukocytes</th>
<th>Log Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human T-Cells</td>
<td>4.0</td>
</tr>
</tbody>
</table>

2. Based on input titer and post-treatment titer in 1 mL. For a full list of pathogens, see Package Insert.
3. Based on culture of full platelet unit (300 mL).
Scalability demonstrated in a variety of countries, large and small

- Routine use at over 100 centers in 25 countries
- Kits sold to produce >3 million units of INTERCEPT platelets & plasma
- INTERCEPT safety and efficacy established in routine use
- FDA approved
Study on the preparation and use of ECP in the treatment of individuals with active EVD

• A Prospective, Open Label, Observational Phase I Safety Study of Passive Immune Therapy During Active Ebola Virus Disease using Transfusion of INTERCEPT Plasma Prepared from Volunteer Donors who have Recovered from Ebola Virus Disease.

• 3 functional groups within the study:
  • Collection Sites
  • Processing/ Blood Banking Facility
  • Patient Treatment Sites
Study Rational

- Strong mechanistic argument for convalescent plasma therapy
  - Prior Ebola Convalescent Whole Blood indicated a reduction of mortality to 20% (Mupapa, Massamba et al. 1999).
    - Acute EVD treated with current standard therapy has a mortality of 45-60%
  - Studies have demonstrated the persistence of neutralizing antibodies to Ebola Virus up to 10 years after acute infection (Sobarzo, Groseth et al. 2013)
- Donors who have recovered from EVD are potentially exposed to other transfusion transmittable infectious agents that, in some cases, can’t be detected
  - Pathogen reduction could improve the safety of this treatment
Donor Eligibility

- **Donor Inclusion Criteria:**
  - Recovered from EVD
    - 28 days post discharge
    - 2 consecutive negative Ebola Virus nucleic acid tests
  - Plasma/serum tested for specified infectious agents (*not automatically excluded if positive*)
  - Standard donor criteria assessed but potentially waived
  - EBOV antibody titer, when feasible
  - Sign Informed Consent and cleared by treating physician

- **Donor Exclusion Criteria:** active EVD
Study Design: Pathogen Reduction Step

- Up to 1300mL of Plasma is collected from a EVD survivor/donor
  - If >~650mL, albumin replacement is generally administered.

- Product is split between two containers each ~650mL to conform to the INTERCEPT system

- Each container is sterile connected onto an INTERCEPT system set, mixed with amotosalen and treated with UV-A light for ~6 minutes

- The resulting pathogen-reduced products are stored as 6 doses of ~210mL (3 each per INTERCEPT set)

- Frozen for long-term storage
Starting the ECP Bank

• Cerus contacted FDA with offer to assist in the creation of a pathogen reduced ECP bank from Ebola Survivors

• FDA agreed to review IDE expediently, if submitted

• Emory chosen as partner to run bank due to high degree of expertise in dealing with EVD patients, including the administration of ECP that was not pathogen reduced

• Preliminary IDE approval was received and Dr. Winkler and 3 Emory staff began training on INTERCEPT system

• Emory used as site to train first team to deploy INTERCEPT system in West Africa

• Final protocol approved, 5 donor subjects enrolled in study, 36 units of ECP in inventory
Convalescent Plasma Bank Model

• Banking of Convalescent Plasma is not limited to EVD
  • Convalescent Plasma and Serum has been used in the prophylaxis and treatment of pathogens in humans and in animal models
  • H5N1, Spanish flu, SARS, Measles, Hepatitis A, South American Hemorrhagic Fevers (Junin/Muchapo), Diptheria, Orthopox (variola/vaccinia)

• INTERCEPT-treated Convalescent Plasma for EVD serves as a model for the management of pandemics
  • Broad spectrum of pathogen inactivation
  • Technology is widely available and rapidly scalable

Ebola survivors can donate up to potentially twice per week.

A custom blood mobile is outfitted for apheresis plasma collection, PI, testing, & freezing.

Each apheresis collection of 650mL yields 3 x 200mL doses.

Patients receive an average of 3 doses.

Convalescent patients enter donor pool if eligible.
In Just 12 Hours...

1 blood mobile... with 4 apheresis plasma collection devices... and 2 INTERCEPT Illuminators...

can support...

32 x 650mL plasma collections

96 x 200mL pathogen-inactivated therapeutic doses

32 patient treatments
Obtaining ECP for a patient in the US

• Contact the CDC
  • Investigators at Emory and UNMC are actively building an inventory of pathogen-reduced ECP

• In the case of any additional cases of EVD in the US, the CDC will organize daily management conference calls
  • Participants also include clinical consultants from Emory and UNMC

• If ECP is recommended for treatment, a request would be made to the ECP Bank from either the CDC or treating facility

• Cerus, the study sponsor, contacts the FDA to arrange the transfer of ECP to the patient’s treating institution under the IDE
Summary

- Convalescent Plasma is a time-honored treatment for rapidly emerging epidemics and pandemics
  - Passive immunity is well-proven for various infectious diseases with some data supporting use with EVD

- INTERCEPT-treated CP can address public health and national security needs in a public health emergency
  - Broad-spectrum pathogen reduction
  - Plasma collection is possible anywhere in the US and abroad
  - INTERCEPT is rapidly scalable with growing adoption in the US

- The EVD efforts in the US and East Africa demonstrates the feasibility of INTERCEPT-treated CP in both advanced and austere environs

- Remember to attend Dr. Winkler’s talk on genesis of the Emory ECP bank, treatment of EVD patients in the USA and utilization of ECP in the USA—Tomorrow at 10:45am, Lone Star B & C.