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PROGRAM OF ABSTRACTS

AABB 2024

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Association for the Advancement of Blood and Biotherapies Annual Meeting

DATE

October 19 - 22, 2024

LOCATION

Houston, Texas

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ORAL PRESENTATIONS

POSTER PRESENTATIONS

Meet the Poster Authors: Sunday, October 20, 12:00 pm – 1:00 pm

Acute Kidney Injury to Evaluate Amustaline/Glutathione Pathogen Reduced Red Cells in Cardiac Surgery: Outcomes of the ReCePI Phase III Clinical Trial

Michael E Sekela[1], Edward L Snyder[2], Ian J Welsby[3], Yoshiya Toyoda[4], Neel R. Sodha[5], Thomas M Beaver[6], Kathy Liu[7], Laurence Corash[7], Nina Mufti[7], Richard J Benjamin[7]

1. Gill Heart Institute University of Kentucky, Lexington, KY; 2. Yale University School of Medicine, New Haven, CT; 3. Duke University Medical Center, Durham, NC; 4. Temple University Hospital, Philadelphia, PA; 5. Rhode Island Hospital, Providence, Rhode Island; 6. University of Florida, Gainesville, Florida; 7. Cerus Corporation, Concord, CA, USA

BACKGROUND/CASE STUDIES: The Red Cell Pathogen Inactivation (ReCePI) study utilized acute kidney injury (AKI) as an indicator of tissue oxygenation to evaluate amustaline/glutathione pathogen-reduced (PR) RBCs.

STUDY DESIGN/METHODS: A Phase III, double-blinded, non-inferiority study randomized cardiac or thoracic aorta surgery patients at a high risk of RBC transfusion to receive PR (Test) or conventional (Control) RBCs during and for 7 days post-surgery. The primary endpoint was AKI within 48 hours of surgery. The study had 80% power to prove non-inferiority assuming 30% AKI incidence with conventional RBCs and a non-inferiority margin of half the conventional rate. Adverse events and treatment-emergent RBC antibodies were assessed through 28 and 75 days, respectively. A clinical stop was required if one subject had increased RBC clearance or hemolysis associated with a PR RBC-specific antibody.

RESULTS/FINDINGS: 581 subjects were randomized and 321 (55%) transfused with study RBCs, comprising the modified intention-to-treat (mITT) population. AKI within 48 hours of surgery correlated with death or the need for renal replacement therapy by day 30 post-surgery (OR 7.2, 95% C.I. 2.9, 18.1). The PR arm received fewer total RBCs within 48 hours of surgery (median 2.0 [range 1-16] Test; 3.0 [range 1-21] Control, P=0.048), had comparable total surgical blood loss (median 420 mL [range 10-3,135 mL] Test; 415 mL [range 20-4,045 mL] Control) and maintained similar hemoglobin levels (**Figure**). Forty six of 157 (29.3%) evaluable Test subjects versus 45 of 161 Control subjects (28.0%) met the AKI endpoint (treatment difference 0.74%, 95%C.I. -8.9%, 10.4%, non-inferiority margin 14.0%, P= 0.001 for non-inferiority). Non-study RBCs were transfused in 17.6% Test and 22.8% Control mITT subjects within 48 hours of surgery. In subjects receiving only study RBCs, 31 of 129 (24.0%) Test and 33 of 123 (26.8%) Control met the AKI endpoint (treatment difference -2.62%, 95%C.I. -13.0%, 7.8%, non-inferiority margin 13.4%, P=0.032 for non-inferiority). Adverse events and transfusion reactions were comparable between populations. Four Test and 4 Control subjects developed regular RBC alloantibodies. Five of 159 (3.1%) Test subjects developed low-titer antibodies with specificity for PR RBCs without clinical hemolysis. The DSMB reviewed each case and allowed the study to continue enrollment.

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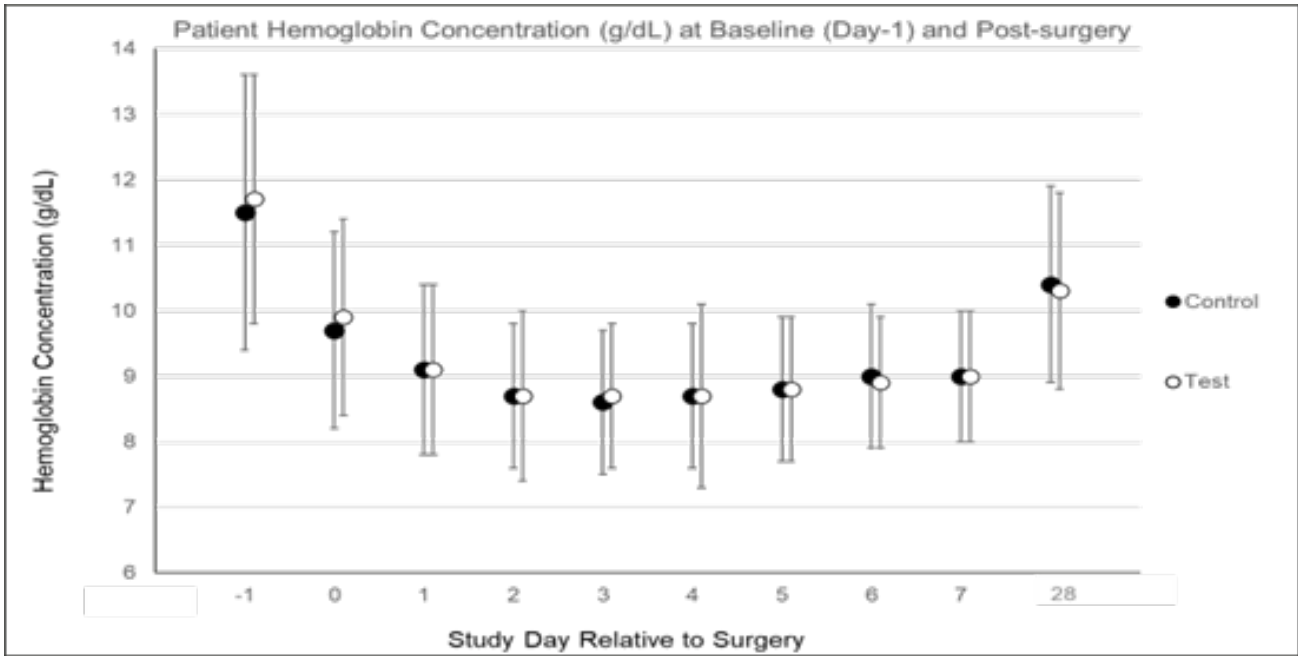
The INTERCEPT Blood System for Red Blood Cells is under regulatory review in Europe, and in late-stage clinical development in the US.

CONCLUSIONS: PR RBCs met the predefined non-inferiority criteria for AKI compared with conventional RBCs, with a similar adverse event profile. Treatment-emergent antibodies with specificity for PR RBCs were uncommonand not clinically significant. (Funded by the Biomedical Advanced Research Development Authority(BARDA), DHHS; ClinicalTrials.gov, NCT03459287).



The INTERCEPT Blood System for Red Blood Cells is under regulatory review in Europe, and in late-stage clinical development in the US.

Utilizing Sankey Diagrams to Quantify Laboratory Efficiency of INTERCEPT Fibrinogen Complex vs Traditional Cryoprecipitate

Dennis Chen, Melissa Cushing, Alexandra Jimenez, Priscilla Parra, Sidney Ong, Sabrina Racine-Brzostek, Denden Benabdessedek, Jaclyn Spinelli, Robert DeSimone, Tobias Cohen

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BACKGROUND/CASE STUDIES: INTERCEPT Fibrinogen Complex (IFC) (Cerus Corp. Concord, CA) has a thawed shelf-life of 5 days while traditional cryoprecipitate (TC) has a thawed shelf-life of 6 hours. Pathogen inactivation technology facilitates this longer shelf-life. Due to this, IFC may promote more flexibility for thawing, returning and reissuing products and may require less overall lab technologist labor and time compared to TC. Sankey diagrams are a data visualization tool to map the flow from one state to another. We demonstrate here how Sankey diagrams provide easy quantification of tech time saved with IFC vs TC.

STUDY DESIGN/METHODS: As part of a year long clinical trial, the blood bank was randomized by month to use IFC or TC for all orders for cryoprecipitate transfusion in one hospital site. Our standard practice is to thaw TC on demand per order with a pre-thaw phone call for non-operating room orders. This phone call reduces TC wastage by preventing premature thawing. However, on IFC months, a standing set of 4 thawed IFC was always maintained in the blood bank and pre-thaw phone calls were not needed. Using data extracted from the laboratory information system and analysis in Microsoft Excel, the number of unique [source] [target] pairs (e.g. "[issue] to [transfuse]" vs. "[issue] to [return]") were calculated and data were entered into Sankeymatic (www.sankeymatic.com) to generate a Sankey diagram (**Figure 1**) that reflects the various steps of the blood ordering and distribution process. Utilizing the Sankey diagram, we determined the total number of times various processes occurred and controlled for orders with multiple units, where the addition of a 2 simultaneous unit does not meaningfully increase tech time.

RESULTS/FINDINGS: IFC reissuing avoided 140 new thaw cycles whereas TC could only be reissued 34 times. Therefore, given an estimate of 10 minutes of tech time for a full thaw cycle, IFC saved 848 minutes during its 6 months of use vs TC. Similarly, IFC eliminates the need for calling bedside teams to confirm the patient is ready before thawing. This saves an additional 1,476 minutes (5 minutes per call) over 6 months. Finally, since fewer products are wasted, an additional 131 minutes of LIS product disposition entry (2 minutes per transacti on) were avoided during the 6 months. In total, and annualized for a year, switching to IFC would free up about 82 hours of techtime which represents 4% of one technologist's working hours and $4,428 in salary.

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Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

CONCLUSIONS: Switching to IFC reduces tech time required to thaw and issue TC. Eliminating pre-thaw phone calls account for 60% of time savings. Even more time would be saved if accounting for the bedside team's time spent receiving these calls. Any cost analysis of new blood products should also include labor costs and Sankey diagrams facilitate this calculation.

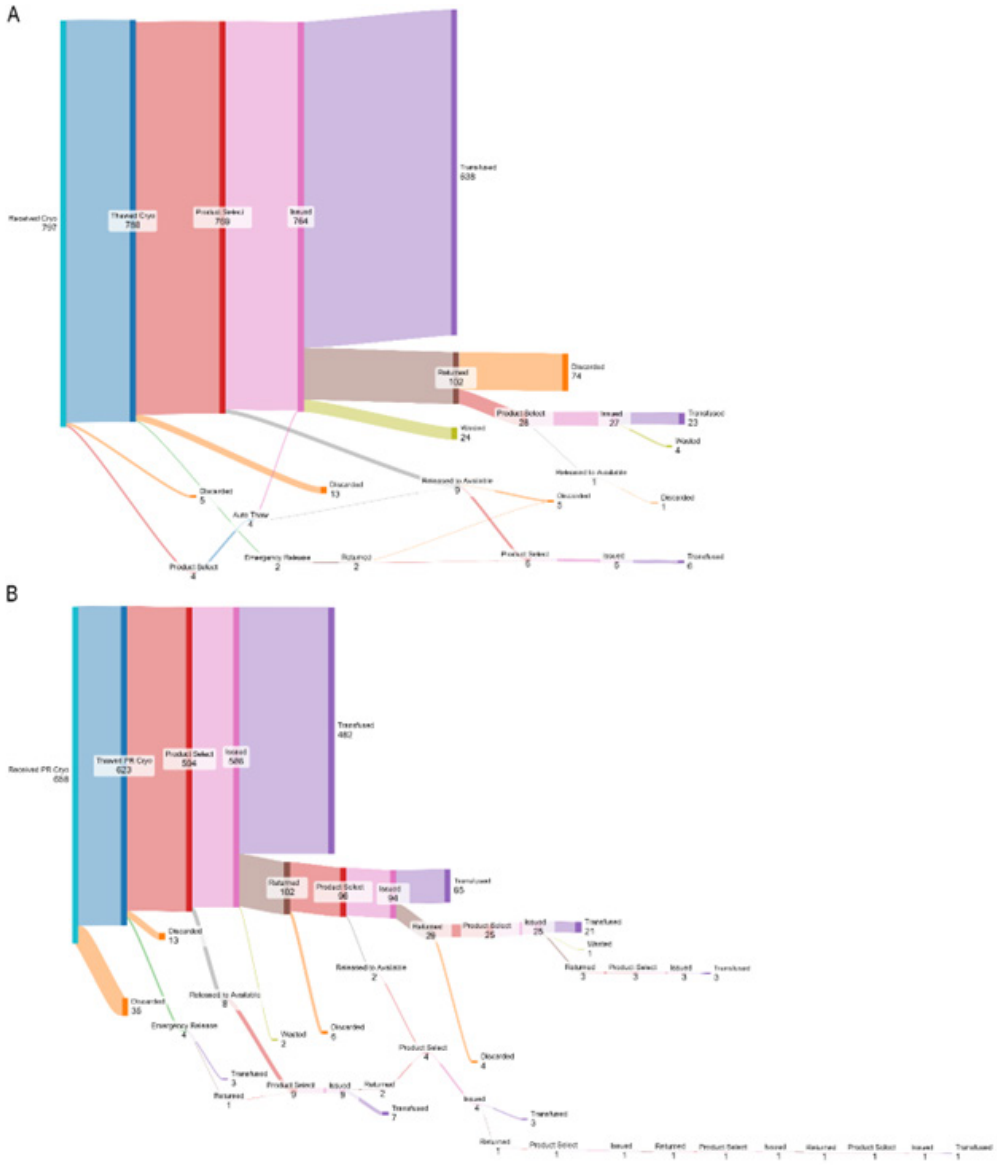

Figure 1. Sankey Diagrams showing the movement of (A) traditional cryoprecipitate (Trad Cryo) products and (B) INTERCEPT fibrinogen complex (PR Cryo) products through the issuing process for order fulfillment. Numbers represent the total number of units for each step over 6 months. Discarded products expired while in the blood bank. Product select is the assignment of a product to a patient. Wasted products expired outside the blood bank or were returned in unacceptable condition. Released to Available is unassigning a product from a patient back to available inventory. Auto thaw are products that the LIS assigned thaw status to since a downstream process was performed without modifying the product in the LIS.

Phase IV Trial of Pathogen-reduced Cryoprecipitate vs. Cryoprecipitated AHF to Lower Operative Transfusions (TOP-CLOT) in Cardiac Surgery

Melissa M. Cushing[1], Tobias Cohen[1], Sophie Rand[1], Abraham Sinfort[1], Sidney Ong[2], Priscilla Parra[2], Meghann M. Fitzgerald[1], Christopher Lau[1], Natalia Girardi[1], Robert A. DeSimone[1]

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BACKGROUND/CASE STUDIES: Low perioperative levels of fibrinogen are associated with severity of hemorrhage and increased transfusion of blood components in cardiac surgery. The ability to supplement fibrinogen during hemorrhage is often delayed >45 minutes because CryoAHF (Cryo) is stored frozen, due to a short post-thaw shelf life. Pathogen Reduced Cryoprecipitated Fibrinogen Complex, INTERCEPT Fibrinogen Complex (IFC) can be kept thawed at room temperature for up to 5 days, and thus immediately available for hemorrhaging patients. This single center, prospective, cluster randomized clinical trial compared IFC to Cryo in bleeding cardiac surgery patients with hypofibrinogenemia with the hypothesis that the earlier availability of IFC might lead to earlier hemostasis and reduced transfusions overall.

STUDY DESIGN/METHODS: During the trial, all hospital cryoprecipitate orders were cluster randomized by month to be fulfilled with either IFC or Cryo. Bleeding cardiac surgery patients were enrolled if either component was transfused intraoperatively for acquired hypofibrinogenemia (indication FIBTEM A10≤ 10 mm). The primary outcome was the total number of allogeneic blood products (red blood cells, plasma, and platelets) transfused within 30 days of surgery. Fisher's exact test, Pearson's Chi-squared test, and Wilcoxon rank sum test were used to evaluate baseline characteristics and outcomes between the groups. Multivariable linear and logistic regression models were used to assess the association of IFC use with each outcome, adjusting for the effects of patient baseline characteristics.

RESULTS/FINDINGS: The trial enrolled 173 subjects: 86 in the IFC and 87 in the Cryo arms. Median FIBTEM A10 prior to first cryo transfusion was 7 mm and all patients were bleeding. There were no significant differences in baseline patient characteristics between groups. There were no significant differences in the primary outcome or any of the secondary clinical outcomes (**Table 1**). Time from order to issue and order to start of transfusion, were 19 and 11 minutes shorter ($p< 0.001$), respectively, with IFC. Fibrinogen levels measured immediately after surgery showed no difference, indicating that both performed similarly in terms of fibrinogen replacement. Transfusion related adverse events did not differ between the products.

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Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

CONCLUSIONS: This is the first trial of IFC in humans and demonstrates its safety for treating acute bleeding in cardiac surgery, with earlier availability of IFC in the OR. Cryo and IFC showed similar post transfusion fibrinogen levels and blood component utilization. Pre-ordering cryoprecipitate before active bleeding was seen in both groups and thus IFC was not transfused earlier during surgery. This hindered our ability to test our hypothesis. Having IFC available at the bedside rather than in the blood bank may demonstrate further benefit in reducing blood transfusion.

Baseline Characteristics

Characteristic	PR Cryo, N=86[1]	Traditional Cryo, N=87[1]	p-value[2]
Race			0.6
American Indian or Alaska Native	1 (2.0%)	0 (0%)	
Asian	9 (18%)	6 (12%)	
Black or African American	8 (16%)	7 (14%)	
White	33 (65%)	38 (75%)	
Unknown	35	36	
Sex			0.7
Female	33 (38%)	31 (36%)	
Male	53 (62%)	56 (64%)	
Age at surgery	64 (54, 73)	68 (56, 72)	0.6
Ethnicity			0.5
Hispanic or Latino	4 (8.0%)	7 (12%)	
Not Hispanic or Latino	46 (92%)	52 (88%)	
Unknown	36	28	
Procedure subtypes			0.5
REPAIR, ANEURYSM	28 (33%)	36 (41%)	
REPAIR, AORTIC ARCH	9 (10%)	10 (11%)	
REPAIR, VENTRICULAR SEPTAL DEFECT	1 (1.2%)	0 (0%)	
VENTRICULAR ASSIST DEVICE IMPLANTATION OR REVISION	1 (1.2%)	0 (0%)	
VALVE REPAIR OR REPLACEMENT/ CORONARY ARTERY BYPASS GRAFTING	47 (55%)	41 (47%)	
ASA Score			0.5
2	0 (0%)	1 (1.1%)	
3	17 (20%)	18 (21%)	
4	68 (79%)	64 (74%)	
5	1 (1.2%)	4 (4.6%)	

Patient Level Outcomes: Univariate analysis

Characteristic	PR Cryo, N=86[1]	Traditional Cryo, N=87[1]	p-value[2]
Number RBC units transfused: within 30 days after surgery	3.0 (1.3, 6.8)	4.0 (1.0, 7.0)	0.7
Number PLT units transfused: within 30 days after surgery	2.00 (1.00, 2.00)	1.00 (1.00, 3.00)	>0.9
Number PLASMA units transfused: within 30 days after surgery	1.00 (0.00, 2.00)	1.00 (0.00, 2.00)	0.8
Total number of units transfused: within 30 days after surgery	6 (3, 12)	6 (3, 12)	0.9
Number of doses cryo or fibrinogen concentrate products used perioperatively (3 days)	2.00 (1.00, 2.00)	2.00 (1.00, 2.00)	0.9
Number of RBC products used perioperatively (3 days)	3.0 (1.0, 6.0)	2.0 (1.0, 5.0)	0.3
Number of platelet products used perioperatively (3 days)	2.00 (1.00, 2.00)	1.00 (1.00, 3.00)	0.9
Number of plasma products used perioperatively (3 days)	1.00 (0.00, 2.00)	1.00 (0.00, 2.00)	>0.9
Most proximal fibrinogen to end of surgery	199 (177, 219)	196 (164, 228)	0.3
Length of stay OR	480 (438, 560)	474 (409, 548)	0.3
Length of stay of ICU after surgery	5 (4, 7)	6 (4, 8)	0.5

Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

HLA Alloimmunization in ReCePI, a Phase III Study of Amustaline/Glutathione Pathogen Reduced RBCs

Philip J. Norris[1,2,3], Mars Stone[1,2], Clara Di Germanio[1,2], Brendan Balasko[1], Zhanna Kaidarova[1], Henry Friend[4], Kathy Liu[4], Larry Corash[4], Nina Mufti[4], Richard J. Benjamin[4]

1. Vitalant Research Institute, San Francisco, CA; 2. University of California, San Francisco, Department of Laboratory Medicine; 3. University of California, San Francisco, Department of Medicine; 4. Cerus Corporation, Concord, CA

BACKGROUND: Alloimmunization to human leukocyte antigens (HLA) is a known side-effect of transfusion, which can complicate subsequent platelet transfusion or organ transplantation. The risk in recipients of amustaline/glutathione (GSH) PR red blood cells (RBCs) has not been reported.

METHODS: In the ReCePI Phase III clinical study (funded by the Biomedical Advanced Research Development Authority, DHHS; ClinicalTrials.gov, NCT03459287), complex cardiac or thoracic aorta surgery patients were transfused with PR vs. control, leukoreduced RBCs during and for 7 days post-surgery. Samples were collected pre-transfusion and on day 28 and tested for HLA antibodies using a fluorescent bead-based screening assay. Antibody levels were examined at low, medium, and high cutoff values, using 3 SD and 5 SD above the mean values previously reported in non-transfused males.

RESULTS: The study included 114 participants (51% female) in the PR and 113 (53% female) in the control arms who had pre- and post- study transfusion samples available, a subset of the 321 ReCePI evaluable subjects. In the PR arm 80 participants received exclusively PR RBC units, and 34 also received non-study RBC units. In a modified intention to treat analysis, there was no signal that PR RBCs affected the rate of HLA Class I or II antibody formation (**Table 1**). Similar results were seen in a study RBC only analysis, with OR 1.4 (95% CI 0.59 – 3.2) for new HLA Class I and OR 0.88 (95% CI 0.31 – 3.0) for new HLA Class II antibodies at the high cutoff. Female transfusion recipients had higher risk of developing new high-level HLA Class I antibodies, OR 9.0 (95% CI 2.8 – 29), and HLA Class II antibodies, OR 5.0 (95% CI 1.4 – 17). The mean number of RBC transfusions (5.5 vs. 3.6 units, p=0.016) and concurrent platelet transfusions (1.8 vs. 1.1 units, p=0.037) was higher in those who developed new high-level HLA Class II antibodies. Intensity of transfusion did not correlate with risk of HLA Class I alloimmunization, and plasma transfusion exposure intensity did not affect HLA Class I or II alloimmunization risk.

CONCLUSION: Receipt of amustaline/GSH PR RBC units did not affect HLA alloimmunization risk. Female sex was a risk factor for development of new high-level HLA Class I and II antibodies. Risk of new high-level HLA Class II antibodies correlated with the number of platelet and RBC but not plasma transfusions, potentially due to higher levels of passenger WBCs in the two cellular products, despite leukoreduction.

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Table 1: HLA Alloimmunization Rate in Control vs. PR RBC Recipients

		Control RBCs N=113	PR RBCs N=114	Odds Ratio	(95% CI)
New HLA Class I Ab	Low	22	23	1.02	0.50 - 2.1
	Med	17	16	0.97	0.45 - 2.1
	High	13	17	1.3	0.62 - 2.9
New HLA Class II Ab	Low	15	17	1.2	0.55 - 2.5
	Med	10	14	1.4	0.59 - 3.3
	High	8	8	0.99	0.35 - 2.8

The INTERCEPT Blood System for Red Blood Cells is under regulatory review in Europe, and in late-stage clinical development in the US.

Treatment-Emergent Antibodies to Amustaline/Glutathione Pathogen-Reduced Red Blood Cells in the ReCePI Phase III Clinical Trial

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1. Stanford University Medical Center, Stanford, CA; 2. University of Florida, Gainesville, FL; 3. Rhode Island Hospital, Providence, RI; 4. U Colorado Hospital, Denver, CO; 5. Mayo Clinic, Rochester, MN; 6. Cerus Corporation, Concord, CA

BACKGROUND: The ReCePI Phase III randomized, controlled clinical study compared amustaline (S-303)/glutathione pathogen-reduced (PR)RBCs (Test) with conventional RBCs (Control). The incidence and clinical significance of treatment emergent antibodies with specificity for PRRBCs was assessed.

METHODS: Subjects received study RBCs during and for 7 days after complex cardiac surgery and were screened using an indirect antiglobulin test (IAT) for PRRBC-specific antibodies at baseline, when a routine IAT test was performed, and at 28- and 75-days post-surgery. Subjects with positive antibody screens were followed at ~2-week intervals and investigated for clinical evidence of increased RBC clearance. Serological confirmation was performed at Versiti Blood Center (Milwaukee, WI) and monocyte monolayer (MMA) assays at American Red Cross (Pomona, CA).

RESULTS: One screened subject was excluded with a natural antibody specific for PRRBCs. 159 Test and 162 Control subjects received 456 Test and 524 Control (P=0.049) study RBCs. Four Test and 4 Control subjects developed RBC alloantibodies. Five Test (3.1%,) and 0 Control subjects (P=0.015) developed PRRBC-specific antibodies, first detected on Days 26-80 after surgery after receipt of 1-3 study units. Antibody titers were low (titer ≤8) and decreased over time (**Table**). A MMA for clinically relevant antibodies was either non-reactive (3/5) or indeterminate (2/5) and the DAT was negative in 4 of 5 subjects. One subject had a weak positive DAT and an eluate specific for PRRBCs. Of four tested, three antibodies could be inhibited by free acridine (a component of S-303) and one could not, suggesting two epitope specificities. The protocol required the DSMB to advise a clinical stop if one subject showed evidence of hemolysis; none was observed and the study proceeded. Flow cytometry of RBC samples frozen during the investigations revealed circulating acridine-positive PRRBCs at levels consistent with the expected post transfusion levels (**Table**) considering RBC dose, hemorrhagic loss, RBC survival and hematopoietic recovery after surgery. RBC acridine surface density on transfused PRRBCs *in vivo* was substantially lower (200-300 acridine/cell) than on PRRBCs before transfusion (~8,500 acridine/cell) suggesting acridine loss in the presence of antibodies.

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CONCLUSION: PRRBC specific antibodies occurred in 3.1% of Test subjects. There was no evidence of hemolysis or *in vitro* properties indicative of clinical significance. Circulating PRRBCs could be enumerated by flow cytometry with a loss of RBC surface acridine expression, which is a potential escape mechanism from destruction. (Funded by the Biomedical Advanced Research and Development Authority, DHHS; ClinicalTrials.gov, NCT03459287).

Table: Characteristics of Treatment Emergent Antibodies Specific for Pathogen Reduced RBCs

Study Subject	Underlying Condition	Study RBC Exposure	Study Day of Discovery	Highest Titer	DAT MMA	Clinical Evidence of Hemolysis[1]	Antibody Characteristic	Flow Cytometry % Positive Surface Acridine (Study Day)	Predicted % Positive
08-014	73 yo, WF, AVR	I unit on Day 1	43	8	Neg. Non-reactive	No hemolysis	Inhibited by free acridine	1.3% (Day 55)	1.9%
016-012	72 yo, WF, MVR	I unit on Day 2	80	Neat	Neg. Indeterminate	No hemolysis	Inhibited by free acridine	0.2% (Day 91)	0.3%
011-011	57 yo, WF, MVR, TVR	3 units on Days 0, 0, 4	32	Titer not Done	Pos. Eluate Pos.	No hemolysis	Not Done	9.7% (Day 42)	8.7%
02-029	75 yo, WF, Multiple CABGs	1 unite on Day 0	26	Titer not Done	Neg. Indeterminate	No hemolysis	Not inhibited by free acridine	2.6% (Day 32)	3.8%
010-049	61 yo, WM, AVR	3 units on Days 0, 2, 3	30	2	Neg. Non-reactive	No hemolysis	Inhibited by free acridine	3.0% (Day 39)[2]	8.4%

yo = years old; WF = white female; WM = white male; AVR = aortic valve replacement; MVR - mitral valve replacement; TVR = tricuspid valve replacement; CABG = coronary artertery by pass graft.

[1] *Investigators assessed subjects for clinical evidence of intravascular or extravascular hemolysis, including change in hemoglobin concentration over time, DAT, RBC eluates, IAT, lactate dehydrogenase, serum bilrubin, serum haptoglobin and urinalysis. Plasma samples were submitted to reference laboratories to confirm antibody specificity, titer, MMA and inhibition by free acridine.*

[2] *Possible alloantibody noted by reference laboratory.*

The INTERCEPT Blood System for Red Blood Cells is under regulatory review in Europe, and in late-stage clinical development in the US.

Evaluation of Pathogen Reduction Efficacy in Platelet Concentrates Until End of Shelf-Life With Two Different Automated Bacterial Detection Systems

Reem El Gendy[1], Afnan Al Hawsawi[1], Khawla Al Hawsawi[1], Fatemah Bahmadin[1], Sara Al Sawat[1], Mamdouh Al Motairi[1], Marcus Picard-Maureau[2], Ali Al Buhairy[1]

1. East Jeddah General Hospital, Jeddah, Saudi Arabia; 2. Cerus Europe B.V., Amersfoort, The Netherlands

INTRODUCTION: The storage condition of platelet components (PCs) (20-24°C under continuous agitation) bears an increased risk for bacterial growth to clinically relevant levels in case of contamination. The incidence of septic transfusion reactions (STRs) is globally often underreported in routine treatment. Active hemovigilance studies revealed an STR incidence of approx.1:10.000 (Hong H *et al*., 2016. *Blood* 127: 496-502), despite interventions to increase safety. Pathogen reduction (PR) was shown to inactivate bacteria effectively. However, most experiments were conducted assessing bacterial growth pre-and post-treatment. The aim of our study was the assessment of bacterial safety with transfusion-relevant species, post PR-treatment, until end of shelf-life (5 days) and the maximum shelf life according to product specifications (7-days) using two different bacterial detection technologies, minimizing the risk of false-negative results.

METHODS: Single-donor platelet concentrates (PCs) in 100% plasma were prepared from individual 450 mL whole blood donations within 8 h post collection by the PRP method. Five ABO-identical single-donor PCs were pooled to obtain an adult transfusion dose (ATD), containing ≥$3x10^{11}$ platelets. ATDs were inoculated with a bacterial load of $5x10^4$/mL with different bacterial species (identity confirmed by biochemical analysis with a Phoenix device (Becton-Dickinson)), respectively. ATDs were incubated for 3 h at 20-24°C under continuous agitation followed by PR-treatment with amotosalen/UVA (AS) (INTERCEPT Blood System, Cerus Corporation). ATDs were further incubated until day 7. Samples (15 mL) were taken from each unit pre-inoculation, pre-treatment, post-treatment, at day 5, and day 7, under sterile conditions using a satellite bag. Samples were analyzed for bacterial growth with two automated bacterial detection systems, BacT/Alert (Biomerieux, 10 mL, 5 days incubation until negativity) and eBDS (Haemonetics, 5 mL).

RESULTS: The average pre-treatment volume of ATDs (n=8) was 289.1 ± 33.4 mL, the average post-treatment volume 272.2 ± 34 mL (5.8% processing loss). The average pre-treatment platelet count was 3.5×10^{11} ± 0.5, the post-treatment platelet count was 3.1×10^{11} ± 0.4 (11.4% processing loss). Four ATDs were inoculated with *S. aureus*, 2 with *E. coli* and 2 with *P. aeruginosa*. All units were negative pre-inoculation using both bacterial detection systems, positive pre-PR-treatment, and negative directly post PR-treatment as well as at day 5 and 7 of storage.

CONCLUSION: *AS*-treatment reliably inactivated clinical relevant bacterial loads of 3 species with effectively until end of shelf-life (terminal sterility) at day 5 and maximum shelf life according to product specifications at day 7.

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US.

Amotosalen/UVA Treatment of Human Apheresis Platelets Contaminated with *Bacillus mobilis, Acinetobacter seifertii, Staphylococcus saprophyticus*, and *Leclercia adecarboxylata*

Mary Krath, Pallavi Nahata, Melissa McCormack, Aja Johnson, Bianca Stafford, Thea Lu

Cerus Corporation, Concord, CA, USA

BACKGROUND/CASE STUDIES: The INTERCEPT Blood System for Platelets is a PR technology that inactivates pathogens and leukocytes using amotosalen and UVA light. The system is used in the United States and Europe to treat apheresis- and/or whole-blood derived platelets. *BM, AS, SS*, and *LA* were isolated from an INTERCEPT-treated apheresis platelet unit from a TTI case in Ohio, USA. As previously reported, a leak was identified near the platelet unit port, suggesting environmental contamination after PR (Gammon *et al*., 2022). Prior data show that *AS, LA*, and *SS* are inactivated by amotosalen and UVA light. PR was not assessed previously for *BM*.

STUDY DESIGN/METHODS: To measure the effectivity of PR treatment, 3.4 mL of a vegetative culture of *BM* alone or a 1:1:1:1 (volume) mixture of *BM, AS, SS*, and *LA* were inoculated into an apheresis platelet unit (35% plasma/65% Platelet Additive Solution) and treated using amotosalen and UVA light. Bacterial titer was determined pre- and post-treatment and on days 5- and 7-post collection.

RESULTS/FINDINGS: Amotosalen and UVA light treatment inactivated 3.6 ± 0.1 log cfu/mL of *BM* alone and 7.0 ± 0.0 log cfu/mL of the mixture of *BM, AS, SS*, and *LA* (calculated input titer of 3.0 ± 0.0, 7.5 ± 0.0, 7.4 ± 0.1, and 6.5 ± 0.1 log cfu/mL of *BM, AS, SS*, and *LA*, respectively). No bacteria were observed post-treatment, at 5- and 7-days post-collection in either case.

CONCLUSIONS: We show that amotosalen and UVA light treatment inactivates *BM* alone and in combination with *AS, SS*, and *LA* in platelet components, achieving sterility throughout the 7-day storage period.

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US.

Development of a Next Generation Illuminator for Photochemical Inactivation of a Broad Spectrum of Pathogens in Platelet Concentrates

Gurvani B. Singh, Laarni Batin, Kelsey Goldbeck, Maria Silva Gomez, Dennis Hicks, Aja Johnson, Mary Krath, Thea Lu, Felicia Santa Maria, Melissa McCormack, Pallavi Nahata, Bianca Stafford, Natalie Stoker, Peter Bringmann

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BACKGROUND: The INTERCEPT® Blood System for Platelets uses amotosalen and ultraviolet A (UVA) light to inactivate a broad spectrum of pathogens and leukocytes in donor platelet concentrates (PC). The current commercial illuminator (INT100) uses fluorescent bulbs to deliver a controlled dose of UVA light. In recent years, Cerus has developed a new LED-based illuminator (INT200) as a planned replacement for the INT100. There is no change to the intended use of the Illuminator.

AIM: The objective of these studies was to compare the performance of the INT200 Illuminator to the INT100 Illuminator through the evaluation of pathogen inactivation levels achieved in PC.

METHODS: Two-arm pool and split studies were performed with apheresis PC (35% plasma/65% PAS-3 and 100% plasma). Pooled PC were spiked with the pathogen of interest and split into two identical units. The contaminated PC were treated with the INTERCEPT processing sets for platelets. One unit was illuminated using the INT100 Illuminator and the second unit was illuminated using the INT200 Illuminator.

RESULTS: **Table 1** shows the inactivation levels achieved with amotosalen using the INT100 and INT200 Illuminators, as indicated by the log reduction factors (LRFs). The efficacy of inactivation was tested and compared for a wide spectrum of pathogens in PC.

CONCLUSION: Equivalent levels of inactivation (LRF difference ≤ 0.5 log) could be achieved for all pathogens in PC at the UVA light doses tested for INT200. Overall, these results demonstrate that the INT200 illuminator can provide similar performance compared to the INT100 for inactivating pathogens in donor PC.

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Table 1: Pathogen Inactivation using the INT100 and INT200 Illuminators

Pathogen	PC in 35% plasma/65% PAS-3 LRF (log cfu/mL or log pfu/mL or log $TCID_{50}$/mL)		PC in 100% plasma LRF (log cfu/mL or log pfu/mL or log $TCID_{50}$/mL)	
	INT100 Illuminator	INT200 Illuminator	INT100 Illuminator	INT200 Illuminator
BVDV	>4.7	>4.7	>4.6	>4.6
DENV	>6.3	>6.3	>5.8	>5.8
Ad5	>6.5	>6.5	≥5.7	≥5.4
BTV	≥4.4	≥4.4	5.2	5.0
*Klebsiella pneumoniae**	≥5.6	≥5.7	3.4	3.6
*Serratia marcescens**	≥6.3	≥6.4	6.8	6.9
Clostridium perfringens	>6.6	>6.7	>6.7	>6.7
*Staphylococcus aureus**	>7.6	>7.6	≥7.7	≥7.7

**WHO approved bacterial reference strains provided by PEI were used.*

Amotosalen/UVA Treatment of Plasma Components to Inactivate WHO Reference Bacterial Strains Using the INTERCEPT Blood System

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BACKGROUND: The INTERCEPT® Blood System for Plasma utilizes amotosalen and UVA light to inactivate a wide range of pathogens in plasma and is available both in Europe and the US. The World Health Organization (WHO) Expert Committee on Biological Standardization (ECBS) in association with the Paul-Ehrlich-Institut (PEI) approved an extended panel of platelet transfusion-relevant bacterial reference strains to evaluate methods for improving the microbial safety of blood components (Spindler-Raffel *et al*, 2017).

METHODS: Human plasma donations were collected and pooled to yield individual units of ~650 mL. A minimum of three replicates were performed for each PEI strain of transfusion-relevant bacteria, including *S. aureus*, *P. fluorescens*, *E. cloacae*, *B. thuringiensis*, *K. pneumoniae*, *E. coli* and *S. marcescens*, with each replicate consisting of one unit spiked with a single PEI strain. The contaminated plasma units were then treated with amotosalen and UVA light. Samples were taken pre- and post-UVA treatment (5 mL and 50 mL, respectively) and were analyzed for bacterial titer by plating on appropriate media (100µL–10mL/plate).

Treatment of the contaminated plasma units with amotosalen and UVA resulted in robust bacterial inactivation (**Table 1**).

SUMMARY/CONCLUSIONS: The INTERCEPT Blood System for Plasma consistently inactivated high titers of *S. aureus* and *P. fluorescens*, *E. cloacae*, *B. thuringiensis*, *K. pneumoniae*, *E. coli* and *S. marcescens*. The data demonstrate robust inactivation of the WHO standardized platelet transfusion-relevant bacterial reference strains.

REFERENCES: Spindler-Raffel *et al*,. 2017 Enlargement of the WHO international repository for platelet transfusion-relevant bacteria reference strains. *Vox Sang*, 112: 713-722.

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Table 1: Bacterial Inactivation Using Amotosalen/UVA Treatment for Human Plasma

Bacteria (Strain)	Log cfu/mL		
	Input Titer	Post-UVA Treatment Titer	Log Reduction
Staphylococcus aureus PEI-B-P-63	6.5±0.1	0.0±0.0	6.5±0.1*
Pseudomonas fluorescens PEI-B-P-77	7.8±0.1	0.6±0.8	7.2±0.8
Enterobacter cloacae PEI-B-P-43	6.7±0.2	0.2±0.3	6.5±0.2
Bacillus thuringiensis PEI-B-P-07	5.5±0.2	0.0±0.0	5.5±0.2*
Klebsiella pneumoniae PEI-B-P-08	6.2±0.4	1.7±0.4	4.5±0.5
Escherichia coli PEI-B-P-19	7.0±0.1	0.0±0.0	7.0±0.1*
S. marcescens PEI-B-P-56	6.9±0.0	0.2±0.3	6.7±0.3

* *No residual bacteria were detected post-treatment.*

Accelerating Treatment Delivery and Reducing Waste with Implementation of Pathogen Reduced Cryoprecipitated Fibrinogen Complex

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BACKGROUND/CASE STUDIES: UCSF Health operates three blood banks, one at each of its medical centers: Parnassus Heights, Mission Bay, and Mount Zion. Collectively, these banks transfuse over 60,000 blood products annually, including 2,300 cryoprecipitated (cryo) AHF pools. The breakdown of cryo orders is 91% at Parnassus Heights, 9% at Mission Bay, and less than 1% at Mount Zion. UCSF Health routinely implements processes and products that improve blood stewardship, efficiency, access, reduce waste, and enhance patient safety. UCSF Health can store red blood cells, plasma, and platelets ready for immediate use, but cryo AHF must be stored frozen due to its short 4-6 post-thaw shelf life, partly due to the risk of transfusion-transmitted infections.

To address long turnaround times and high cryo AHF waste, UCSF Health implemented Pathogen Reduced Cryoprecipitated Fibrinogen Complex (IFC), a cryoprecipitate product made from pathogen-reduced plasma that can be stored thawed at room temperature for up to five days for treating and controlling bleeding associated with fibrinogen deficiency. UCSF Health onboarded IFC in October 2022. By July 2023, 99% of cryo orders were filled using IFC. Based on historical transfusion data, UCSF Health initiated maintaining two units of prethawed IFC at its Parnassus Heights campus at all times starting in October 2023, which was increased to four units in March 2024. The turnaround time (TAT) data presented here represents all orders across the entire UCSF Health system.

STUDY DESIGN/METHODS: From October 2022 through March 2024, 2,844 IFC units (FC15) were transfused. Turnaround time (TAT) from order receipt to product allocation (ready and assigned to the patient) and wastage were obtained from Crystal Reports. A retrospective analysis of TAT for cryo AHF versus IFC was performed for orders prior to IFC implementation (January-October 2022) and post implementation of IFC (July 2023 - March 2024). Outliers, including all orders taking more than 60 minutes to issue, were considered non-urgent orders.

RESULTS/FINDINGS: Between January and October 2022, 909 cryo AHF orders were processed. During this period, 6% of orders had a 0-19 minute TAT, and 49% had a 20-39 minute TAT. Post-IFC implementation, between July 2023 and March 2024, 1,638 IFC orders were processed. Of these, 53% of IFC orders had a 0-19 minute TAT, with 41% in 0-4 minutes, and 22% had a 20-39 minute TAT (**Table 1**). Prior to IFC implementation, cryo AHF had the highest rate of blood component wastage at 15% system-wide. Post-IFC implementation, wastage was nearly eliminated (<1%).

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Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

CONCLUSIONS: The implementation of IFC has significantly reduced TAT and accelerated the delivery of a critical source of fibrinogen for hemorrhaging patients. Additionally, IFC has dramatically reduced wastage and improved productivity, efficiency, and blood stewardship.

Table 1: Comparison of IFC vs. Cryo AHF Turnaround Times (TATs)

Pre-IFC turnaround times (minutes): January 2022 - October 2022 (909 cryo AHF orders)													
TAT (minutes)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-60	>60
Percentage	4%	1%	0%	2%	7%	13%	17%	12%	7%	6%	4%	4%	24%
Post-IFC turnaround times (minutes): July 2023 - March 2024 (1,638 IFC orders)													
TAT (minutes)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-60	>60
Percentage	41%	7%	3%	2%	3%	5%	8%	6%	5%	3%	2%	2%	12%
Accelerating Treatment Delivery and Reducing Waste with Implementation of Pathogen Reduced Cryoprecipitated Fibrinogen Complex													

Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

Wastage and Cost Analysis for INTERCEPT Fibrinogen Complex

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BACKGROUND/CASE STUDIES: Transfusion of INTERCEPT Fibrinogen Complex (IFC) is designed to decrease product wastage vs a 5-pool of conventional cryoprecipitated AHF (cryoAHF) due to the 5-day vs 6-hour expiration at room temperature. Wastage costs may be markedly reduced by using IFC. This study compared product acquisition costs for transfused and wasted products during a one-year clinical trial when the blood bank was randomized monthly to use of either cryoAHF or IFC20 (IFC with ~2.2 g fibrinogen) at a large quaternary care academic medical center (~115,000 type & screens and 25,000 RBCs, 10,000 Platelets, 4,000 Plasma and 1,200 cryoAHF transfused per year).

STUDY DESIGN/METHODS: Total number of transfused and wasted products were collected from the blood bank LIS, including reasons for wastage for the 482 adult patients who received cryoAHF or IFC from April 1, 2023 to March 31, 2024. Reasons for wastage were categorized as clinical trial related wastage, supplier-related reimbursed wastage (e.g., breakage while thawing or failed visual inspection), and clinical wastage (i.e., expired on the floor or in the blood bank). Only clinical wastage was analyzed.

RESULTS/FINDINGS: During the six cryoAHF months, 6715-pools (annualized 1342 pools) were transfused to 238 patients and during the six IFC months, 5866-pools (annualized 1172 pools) were transfused to 244 patients. During the cryoAHF months, 139 units (17% of total units thawed) were attributed to clinical wastage. There were 12.7% less IFC units transfused to slightly more patients (244 vs 238) during the cluster-randomized study periods, indicating less doses administered to patients receiving IFC (2.4 vs 2.8). Only eight IFC units (1% of total units thawed) were attributed to clinical wastage. As pathogen-reduced blood products cost more to manufacture, we estimated different price points based on our experience with the increased costs of such components. **Table 1** compares the total cost of both products at various hypothetical price points for IFC and assumes a fixed $350 cost for a five-pool of cryoAHF. At $500 per unit, IFC, would cost the institution an additional $71,650 annually ($149 per patient). At $1,000 per unit IFC, it would cost the institution an additional $661,650 ($1,373 per patient) (**Table 1**).

CONCLUSIONS: There was a 94% reduction in clinical wastage during the IFC study period. In this study, based only on wastage, an IFC price of $439.28 would be cost neutral. However, other benefits of IFC should be considered in the value proposition including: reduced time to fulfill urgent orders, increased sense of security with readily available cryoprecipitate, decreased infectious risk due to pathogen reduction, and more standardized fibrinogen content.

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Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

Table 1: Cost Models based on 3 hypothetical costs for IFC20 ($1000, $500, $439.28)

Total Pools Transfused annualized over 1 year	Cost/Pool	Pools Transfused x Cost	Pools Wasted	Pools Wasted x Cost	Annual Cost of Transfused Cryo and Clinical Wastage
CryoAHF (5 pool)					
1342	350	$ 469, 700.00	139	$ 48, 650.00	$ 518, 350.00
IFC20 (6 pool)					
1172	**1000**	$ 1, 172, 000.00	8	$ 8, 000.00	$ 1, 180, 000.00
		Difference between IFC20 and CryoAHF			**$ 661, 650.00**
CryoAHF (5 pool)					
1342	350	$ 469, 700.00	139	$ 48, 650.00	$ 518, 350.00
IFC20 (6 pool)					
1172	**500**	$ 586, 000.00	8	$ 4, 000.00	$ 590, 000.00
		Difference between IFC20 and CryoAHF			**$ 71, 650.00**
CryoAHF (5 pool)					
1342	350	$ 469, 700.00	139	$ 48, 650.00	$ 518, 350.00
IFC20 (6 pool)					
1172	**439.28**	$ 514, 836.16	8	$ 3, 514.24	$ 518, 350.40
		Difference between IFC20 and CryoAHF			**$ 0.40**

Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

Comparative Analysis of ABO Titers and Reverse Hemolysis Risk in Cryoprecipitate-AHF and Pathogen Reduced Cryoprecipitate Fibrinogen Complex

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BACKGROUND/CASE STUDIES: Transfusing ABO-incompatible cryoprecipitate is a well-established practice and supported by literature. The recent implementation of Pathogen Reduced Fibrinogen Complex (IFC, INTERCEPT, Cerus, Concord, CA) at our institution prompted a reassessment of this practice's safety. This is the first study to compare ABO titers in cryoprecipitate-AHF (Cryo-AHF) and IFC.

STUDY DESIGN/METHODS: The standard fibrinogen dose for adult recipients at our institution, approximately 2 grams, is supplied by either a 5-donor pool of Cryo-AHF or a 6-donor pool of IFC (FC20). A total of 45 cryoprecipitate pools were evaluated: 10 A, 6 B, and 10 O of Cryo-AHF and 5 A, 3 B, and 11 O of IFC. Three mL were sampled from each pool on or before the expiration date, frozen at -30 C, and titers were performed on the frozen specimen up to 19 days after freezing. Serial dilutions from 1 to 512 were tested using the manual gel-card method (Micro Typing System, Inc., Pompano Beach, FL). Additionally, patient (pt) records were examined over a 12-month period for any evidence of reverse hemolysis from incompatible cryo transfusions. Statistical analysis, using a two-tailed t-test with unequal variance assumption, was performed to compare titers between the products and a chi-square analysis for reverse hemolysis rate, with significance set at $p < 0.05$.

RESULTS/FINDINGS: The median anti-A titers in O pools were significantly lower in IFC than Cryo-AHF (64 vs. 128, $p < 0.01$). The median anti-B titers in O pools were 32 for IFC and 64 for Cryo-AHF ($p=0.09$). The anti-B titers for A pools were significantly lower in IFC, with a median of 4 for IFC and 8 for Cryo-AHF ($p=0.01$). The anti-A titers for B units were 8 for both IFC and Cryo-AHF; but the sample size for B pools was too small to make an inference from findings. None of the IFC pools tested had a titer exceeding 128 for group A, B, or O; however, 1/10 group O Cryo-AHF had a titer of 256 for anti-A (**Figure 1**). Among the pts who received incompatible transfusions, 5/55 (9%) who received Cryo-AHF and 6/85 (7%) who received IFC showed clinically insignificant but laboratory-detectable increases in indirect bilirubin (above the reference range and at least 1 mg/dL increase) ($p = 0.66$). Nine of these pts were transfused intraoperatively including 5/9 with out-of-group platelets.

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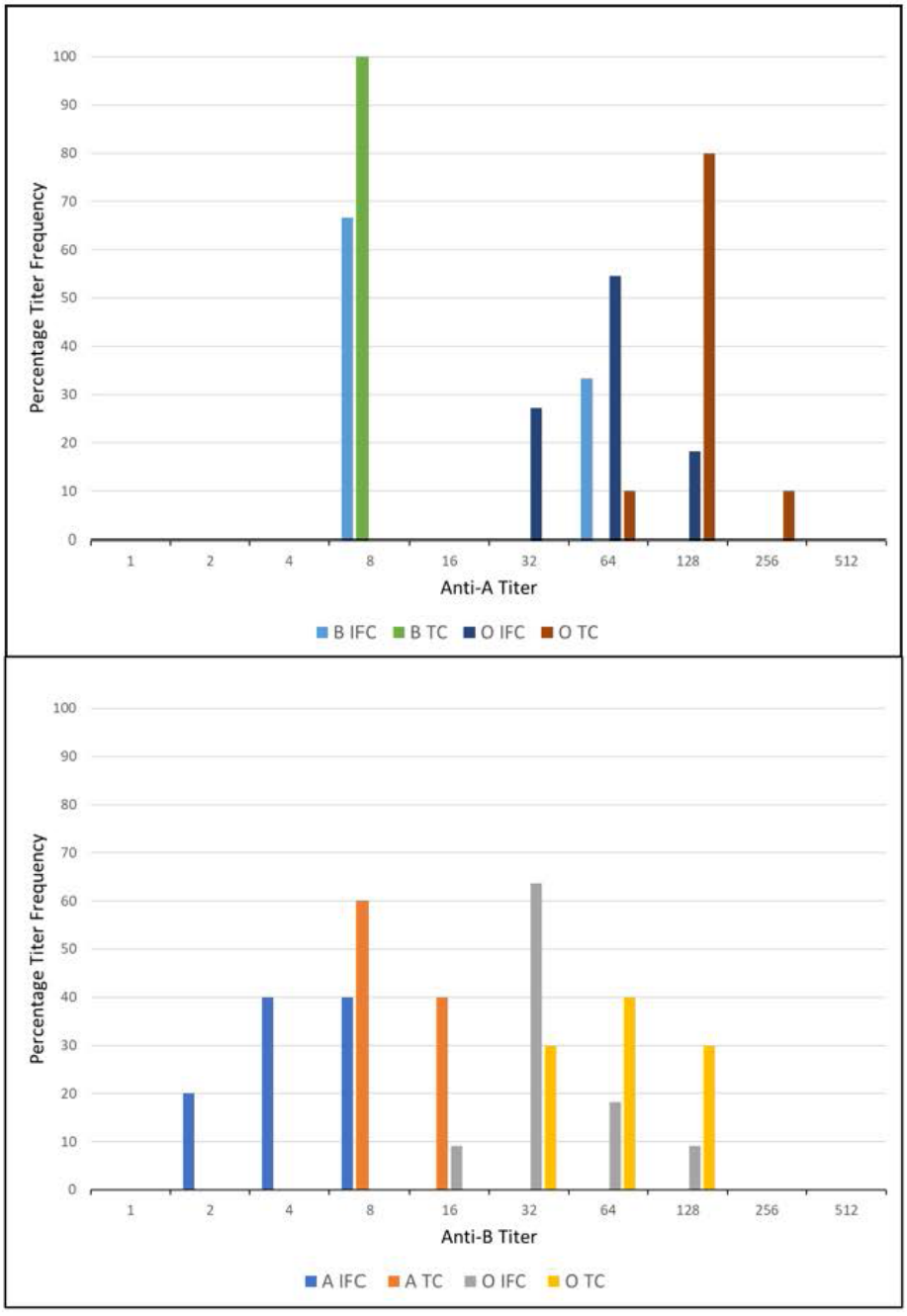
Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

CONCLUSIONS: ABO titers for IFC FC20 are lower than Cryo-AHF. This is likely due to differences in median (IQR) volume between FC20, 187 mL vs pooled Cryo-AHF 121ml; the difference in donor pool size (6 vs 5); and possible impact of the pathogen inactivation process. Based on our chart review, out-of-group IFC transfusion does not pose a higher risk of reverse hemolysis compared to the current standard of care. These data support the safety and acceptability of transfusing non-blood group matched IFC.

Figure 1: Anti-A (top) and anti-B (bottom) titer frequencies for IFC and Cryo-AHF units. Titers for group O units are split between the appropriate graphs



An Analysis of Anesthesiologist and Transfusion Service Staff Preferences Between Pathogen Reduced Cryoprecipitated Fibrinogen Complex and Conventional Cryoprecipitated AHF

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BACKGROUND/CASE STUDIES: Our center recently completed a clinical trial comparing Pathogen Reduced Cryoprecipitated Fibrinogen Complex, Intercept Fibrinogen Complex (IFC) to conventional Cryoprecipitated AHF (Cryo-AHF) to reduce overall operative transfusions. During the trial, all hospital cryoprecipitate orders were cluster randomized by month to be fulfilled with either IFC or Cryo-AHF. For IFC months, units were kept thawed in the blood bank at all times to fulfill orders due to its longer expiration compared to Cryo-AHF (5 days vs. 6 hours). This study was designed to analyze anesthesiologist and transfusion service staff preferences between IFC and Cryo-AHF.

STUDY DESIGN/METHODS: Two surveys, one for transfusion service staff and one for anesthesiologists, were sent to 80 individuals experienced with both components. At the conclusion of the trial, surveys were distributed by e-mail and analyzed using a web-based platform (Qualtrics).

RESULTS/FINDINGS: The anesthesiology and transfusion service staff surveys had response rates of 88% (21/24) and 79% (44/56), respectively. Most anesthesiologists (86%) and transfusion staff (82%) preferred IFC over Cryo-AHF. Some had no preference between IFC and Cryo-AHF (14% for anesthesiologists and 11% for transfusion staff). No anesthesiologists and 7% of transfusion staff preferred Cryo-AHF over IFC. Most anesthesiologists felt that IFC and Cryo-AHF demonstrated comparable clinical efficacy (81%), and the remainder (19%) felt that IFC showed superior efficacy. The most common reasons anesthesiologists preferred IFC included less wastage due to product expiration (89%), reduced time to fulfill orders (89%), increased sense of clinical security by having cryoprecipitate readily available (78%), decreased infectious risk (72%) and a more standardized fibrinogen content (61%). The most common reasons transfusion service staff preferred IFC included less wastage (89%), immediate availability to fulfill emergency orders (89%), less time for the blood bank to fulfill orders (72%), less stress to complete orders (69%) and decreased infectious risk (67%). Most transfusion service staff believed that IFC saved time (96%) and arrived sooner to patients (98%) compared to Cryo-AHF.

CONCLUSIONS: Anesthesiologists and transfusion service staff preferred IFC over Cryo-AHF and perceived that use of IFC was associated with less wastage due to product expiration. The availability of pre-thawed IFC in the transfusion service resulted in an increased sense of clinical security in the operating room. Likewise, transfusion service staff felt less stress completing IFC orders and believed that use of IFC saved time and arrived sooner to patients compared to Cryo-AHF.

Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

Analysis of Wastage, Savings, and Maternal and Pediatric Outcomes for Pooled Pathogen Reduced Cryoprecipitate versus Conventional Cryoprecipitate

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BACKGROUND: Hypofibrinogenenmia is a significant cause of mortality in bleeding pediatric and obstetric patients. Cryoprecipitate is commonly used for replacement for fibrinogen in these patients. Conventional cryoprecipitate (CRYO, 5-unit pool) wastage is a common issue in hospitals due to its 6-hour shelf life. Pathogen-reduced cryoprecipitate (PRC, 4-unit pool), with a 5-day shelf-life, may reduce waste. The aim of this study was to evaluate wastage, safety, and efficacy in our pediatric and obstetric populations.

METHODS: The blood bank LIS was reviewed to identify transfusion and wastage data for cryoprecipitate. Baseline wastage data was collected from January 2022 to September 2022. The study period, in which both CRYO and PRC were in use, was from October 2022 to December 2023. For CRYO wastage, all pools were reviewed to determine likelihood of usage if shelf-life had been 5 days. We determined pools were "highly likely" to have been used if >3 pools were issued in 5 days and "likely" to be used if 1-2 pools were issued in 5 days. We retrospectively reviewed the electronic medical record to collect age, weight, number of units, fibrinogen increment, and presence of tranfusion reactions for pediatric (<18 years) and obstetric patients receiving CRYO and PRC. Statistical analysis was performed using SPSS version 27 (IBM, NY).

RESULTS: Baseline wastage was 13.3%. For the study period, total waste for CRYO and PRC was 10.2%. When separated, there was 13% wastage for CRYO and 3.0% wastage for PRC. The total cost of wasted units was $24,096 (CRYO: $19,096; PRC: $5,000). For CRYO pools, 40 were "highly likely" and 11 were "likely" to have been transfused with 5-day outdating similar to PRC, resulting in a possible savings of $13,640-$17,391 and yielding an adjusted total wastage 1.6-4.5%. The efficacy and safety data for pediatric and obstetric patients are listed in **Table 1**. There were no significant differences identified in patient demographics or fibrinogen response between the CRYO and PRC patients. One transfusion reaction occurred in the CRYO group.

CONCLUSION: Use of a dual inventory of cryoprecipitate did not result in reduced wastage as compared to institutional baseline. However, utilization of PRC is associated with decreased waste as compared to CRYO in our tertiary pediatric and obstetric hospital. No significant differences were identified regarding safety or efficacy in our pediatric or obstetric populations.

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Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

Table 1: Efficacy and Safety Data for Pediatric and Obstetric Patients

Pediatric Patients	CRYO	PRC	p-value
	n=160	n=44	
Age (years)	12 ± 4	11 ± 5	0.4
Weight (kg)	53 ± 24	48 ± 29	0.1
Starting Fibrinogen (g/dL)	152 ± 82	163 ± 84	0.2
Increment per pool	61 ± 57	74 ± 66	0.4
Increment per pool/ weight (kg)	1.6 ± 1.9	3.5 ± 7	0.2
Transfusion Reactions	0	0	
Obstetric Patients	**n=115**	**n=53**	
Age (years)	32 ± 6.6	31 ± 6	0.07
Weight (kg)	80 ± 16	83 ± 19	0.7
Starting Fibrinogen (g/dL)	262 ± 61	251 ± 53	0.3
Increment per pool	40 ± 48	40 ± 47	0.6
Increment per pool/ weight (kg)	0.5 ± 0.7	0.5 ± 0.7	0.5
Transfusion Reactions	1 (0.9%)	0	

Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

Pathogen Reduced Cryoprecipitate Implementation and Assessment of Its Impact in a Large Academic Medical Center

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BACKGROUND: Cryoprecipitate anti-hemophilic factor (AHF), also known as cryoprecipitate, is a blood product prepared from Fresh Frozen Plasma (FFP) by precipitation and is enriched for fibrinogen, von Willebrand Factor (vWF), factor VIII, factor XIII, and fibronectin. Cryoprecipitate is thawed on demand and once thawed it expires after storage 4-6 hours at 20-24ºC. INTERCEPT® fibrinogen concentrate (IFC) is approved by the Food and Drug Administration (FDA) and contains fibrinogen, factor XIII and vWF, has similar clinical indications as cryoprecipitate and has a shelf life of 5 days after thawing. The goal of this study is to evaluate effect of IFC implementation on provision turnaround time (TAT) and product wastage compared to cryoprecipitate at a large academic medical center.

METHOD: Preparations for implementations included inventory build of six units thawed and stored at 20-24°C at any given time, order set modifications and education. FC15 was selected because a pooled dose of 4 units can be used interchangeably with pooled doses of 5 cryoprecipitate units, allowing for flexibility in inventory if needed. IFC implementation and provision to clinicians began April 18, 2024. A retrospective review of TAT for cryoprecipitate was performed for orders from operating rooms from 1/1/2023 to 12/31/2023, and for wastage from 1/2/2022 to 12/31/2023. TAT is defined as cryoprecipitate or IFC order to issue time in the blood bank. Data on TAT and wastage was collection for IFC from 4/18/24 to 5/13/2024 from the electronic medical record and laboratory information system.

RESULTS: The total of 997 cryoprecipitate and 97 IFC orders were included. Mean TAT for cryoprecipitate was 44.7 minutes (range 35-82.2 minutes) and for IFC was 12.2 minutes (range 2.2.-25.4 minutes). Cryoprecipitate wastage rate was 16 of 1677 units (0.6%) for 2022 and 3 of 2663 units (0.1%) for 2023. No IFC products were wasted units for the given period (0 of 181 units wasted for April 18, 2024, and May 13, 2024).

CONCLUSION: IFC decreases TAT over 3-fold compared to cryoprecipitate from ordering to issue in the blood bank , which can impact situations that require quick provision of blood products to patients, such as massive transfusions or cardiac surgeries. Although wastage is low with cryoprecipitate, it was reduced to zero using IFC in the timeframe studied. Further study will be helpful to elucidate if shorter TATs, lower wastage, and inventory are sustained over time as well as overall cost effectiveness.

Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

Implementation of INTERCEPT Fibrinogen Complex (IFC) for Postpartum Hemorrhage

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BACKGROUND: In postpartum hemorrhage (PPH), fibrinogen <200 mg/dL predicts worsening morbidity and mortality, as well as progression to severe hemorrhage. Fibrinogen replacement is therefore very important in PPH. On January 17, 2024, we implemented INTERCEPT Fibrinogen Complex (IFC, Cerus, Concord, CA) as an adjunct to conventional cryoprecipitate (CRYO) to increase availability and improve turnaround time (TAT) of fibrinogen replacement in PPH patients. Prior to implementation, massive transfusion protocol (MTP) activation consisted of 6 red blood cells, 6 plasma, and 1 apheresis platelet, but did not include CRYO unless ordered by the clinician. Once ordered, frozen CRYO was then thawed, leading to a >30 minute TAT. IFC is pathogen-inactivated cryoprecipitate and has a thawed shelf life of 5 days at room temperature, as compared to 4 hours with CRYO. The long shelf life of IFC allowed us to keep 1 pre-thawed IFC available at all times at each of our two hospital sites, and provide it automatically upon MTP activation for PPH. Herein we describe the implementation process and observed TATs before and after implementation.

METHODS: Meeting notes for IFC implementation were reviewed to report key aspects of the process and challenges. TAT and number issued of CRYO/IFC were reviewed for PPH patients before and after implementation.

RESULTS: Implementation of IFC took approximately 6 months. Key logistics included adding and validating the new IFC product to the laboratory information system (SafeTrace, Haemonetics, Salt Lake, UT), building a new billing code for IFC in the hospital information system (HIS, EPIC, Verona, WI), and communicating the new product and protocols to hospital providers. Also, a new proces was needed for blood bank (BB) identification for PPH patients. Typically, BB recognizes these patients from the labor and delivery location on the MTP order, but patients could be moved to the critical care unit or operating room where they would not be easily identifiable. A patient flag exists in the HIS that is applied to pregnant or post-partum patients regardless of their location; we added it to our MTP order so that is automatically appears in the order comment for all PPH MTPs. Further, given the low frequency of PPH MTPs (1-2 per month), we protocolized issue of IFC to any patient with an adult dose of CRYO ordered on day of expiration to avoid IFC wastage.

CONCLUSIONS: Implementation was lengthy and challenging. After implementation of a pre-thawed IFC unit at each hospital site for PPH patients, we saw a 78% decrease in TAT for 1st fibrinogen replacement. Additionally, 100% of PPH patients are now issued IFC upon MTP activation, as opposed to 20% of PPH patients who were issued CRYO previously.

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Table 1: Change in PPH MTP TAT for 1st CRYO or IFC and % patients issued CRYO or IFC in 2023 (only CRYO available) versus 2024 (after implementation of IFC alternative)

	Average TAT 1st CRYO or IFC	Range	% of PPH Patients Issued CRYO or IFC
CRYO 2023	41.6 minutes	26 - 65 minutes	20%
IFC 2024	9.2 minutes	6 - 15 minutes	100%

PPH = postpartum hemorrhage, MTP = massive transfusion protocol, TAT = turnaround time, % = percentage, CRYO = conventional cryoprecipitate, IFC = INTERCEPT fibrinogen complex

Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex) is only approved for use in the US.

Evaluation of INTERCEPT RBC Pathogen Reduction in Combination with Irradiation

Susanne Marschner[1], Caroline Leite[1], Brian Wolfe[1], David Buesing[1], Erika Allen[1], Aderemi Adebayo[2], Kathleen Leung[2], Katie Waldhaus[2], Jamie Genthe[2], Anna Erickson[2]

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BACKGROUND/CASE STUDIES: The INTERCEPT® blood system for red blood cells (RBC), using amustaline and glutathione, is being developed for the inactivation of pathogens and leukocytes in AS-1 RBC. Amustaline forms adducts with nucleic acids and inhibits replication of contaminating pathogens and leukocytes. Although previous studies showed inactivation of leukocytes in INTERCEPT pathogen-reduced (PR) RBCs, institutional practices may further require irradiation (IR) of PR RBCs. This study characterized the *in vitro* function of AS-1 RBC with and without PR and IR on Day 7 through 35 days of storage.

STUDY DESIGN/METHODS: Leukocyte reduced AS-1 RBCs were prepared from CPD whole blood (WB) on the day of collection. For each replicate (n=6), four ABO matched AS-1 RBCs were pooled and divided into 2 PR input units and 2 Control (C) units. Within 19 hrs of WB collection, PR input AS-1 RBCs were treated with 20mM GSH/0.2mM S-303 and C were untreated and placed at 1-6°C. On Day 7 post donation one PR and one C unit from each replicate were IR using X-ray (25-50 Gray) radiation (PR-IR and C-IR). Sampling for analysis of *in vitro* parameters was performed throughout storage for 35 days. On D35 samples were removed and rejuvenated using PIPA.

RESULTS/FINDINGS: Post-PR the Hb retention and volume recovery were 95±1%. Extracellular protein was significantly reduced from 267±16 mg in C to 44±6mg in PR units. On D35 hemolysis was significantly higher in C than PR units and higher in IR units compared to non-IR units. PR resulted in lower K+ and deformability and higher ATP, glucose and p50 than C. IR (PR and C) resulted in decreased ATP, increased extracellular K+, and similar p50 compared to non-IR units (PR and C). Compared to C-IR, PR-IR units had higher levels of ATP, glucose, morphology scores, and p50. Post-rejuvenation ATP and p50 levels were also significantly higher in PR-IR compared to C-IR units (**Table 1**).

CONCLUSIONS: Although IR is not expected to be required for routine use of PR RBCs, this study demonstrates that there are some differences *in vitro* parameters of PR-IR RBCs, including ATP and p50, however the parameters are conserved within physiologic ranges after irradiation.

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The INTERCEPT Blood System for Red Blood Cells is under regulatory review in Europe, and in late-stage clinical development in the US.

Table 1:

	Day 35			
	C	C-IR	PR	PR-IR
Hemolysis (%)	0.2±0.1[a,d]	0.5±0.2[c]	0.1±0.0[b]	0.3±0.1
pH (37°C)	6.3±0.0[a,d]	6.3±0.0[c]	6.2±0.0[b]	6.2±0.0
ATP (µmol/gHb)	4.0±0.3[a,d]	3.5±0.2[c]	4.7±0.5[b]	4.2±0.4
ATP[e] (µmol/gHb)	7.8±0.7[d]	7.7±0.4[c]	9.7±0.8	9.4±0.8
K+[f] (mmol/L)	14.6±0.6[a,d]	20.0±0.7	13.4±1.0[b]	20.1±0.9
Glucose[f] (mmol/L)	15.8±1.4[a,d]	15.0±1.4[c]	19.2±1.2	18.8±0.9
p50 (mmHg)	15.0±1.2[d]	14.7±0.9[c]	16.1±0.9	15.9±0.9
p50[e] (mmHg)	34.6±1.2[d]	34.6±1.3[c]	35.8±1.5	36.2±1.5
MCHC (g/dL)	29.3±0.5[a]	28.4±0.4[c]	29.0±0.2	29.2±0.4
Morphology Score	71.0±3.8	67.6±4.6	73.0±5.9	71.8±6.1
Deformability El Max	0.620±0.011[d]	0.615±0.013	0.605±0.011	0.607±0.008

$p<0.05$: [a]C vs C-IR; [b]PR vs PR-IR; [c]C-IR vs PR-IR; [d]C vs PR

[e] *Post-rejuvenation*

[f] *Corrected for Hematocrit*

The INTERCEPT Blood System for Red Blood Cells is under regulatory review in Europe, and in late-stage clinical development in the US.

Manufacturing Amustaline/Glutathione Pathogen-Reduced Red Cells to Support the ReCePI Phase III Clinical Study

Patrick Sadler[1], Rita Reik[2], Susanne Marschner[3], Bethany Brown[4], Alicia Pritchard[2], Richard R. Gammon[2], Teresa Hedrick[5], Katie Waldhaus[5], Anna Erickson[5], Richard J. Benjamin[5], for the ReCePI study group

1. Central California Blood Center, Fresno, CA; 2. OneBlood, Orlando, FL; 3. Vitalant Research Laboratories, Denver, CO; 4. American Red Cross, Rockville, MD; 5. Cerus Corporation, Concord, CA

BACKGROUND: The ReCePI Phase III randomized, double blinded clinical study compared amustaline (S-303)/glutathione (GSH) pathogen-reduced (PR) RBCs (Test) with conventional RBCs (Control) in subjects undergoing complex cardiac surgery. Study RBCs were provided from 2018 to 2023 by four US blood centers that manufactured sufficient Test and Control RBCs units with storage to 35 days to maintain an inventory at 18 hospital sites despite blood shortages related to the COVID pandemic.

METHODS: Test units were leukoreduced PRRBCs in SAG-M additive solution manufactured from packed RBCs in AS-5 storage solution that were treated with the S-303/GSH process and then resuspended in SAG-M storage solution after a final exchange step. Control units were leukoreduced RBCs in AS-1 or AS-5 storage solution. Blood centers validated bespoke manufacturing and whole blood collection processes to produce both Test and Control components that were labeled with a common ISBT-compatible label to maintain the blind. A computerized ordering system facilitated communication between the transfusion services and blood centers.

RESULTS: 4,755 Test and 4,856 Control RBC components were manufactured and 456 Test and 524 Control (P=0.049) were transfused to 321 subjects at 18 clinical sites (Overall 10.2% transfused). RBC units were ~33% ABO group A and ~67% group O and ~21% Rh negative, but this varied by blood center. On average, Test units were older than Control at the time of transfusion (Test 23.2 ±7.6 vs. Control 21.4 ±8.1 days, P=0.003). Test and Control RBCs (**Figure**) contained a range of total hemoglobin (40-85 g Hb/concentrate). On average, 2.7 g Hb (4.4%) was lost during the PR process, however, Test RBCs remained well within the Hb content range of Control RBCs. Despite the manufacturing losses, the ReCePI study showed that Test subjects received fewer total study RBCs within 48 hours of surgery (median 2 (range 1-16) Test versus 3, (range 1-21) Control, P=0.048) despite similar baseline Hb (11.7 ±1.9 g/dL Test, 11.5 ±2.1 g/dL Control) and surgical blood losses, and maintained comparable hemoglobin levels post-surgery for 7 days (Day 1 post surgery Hb 9.1 ±1.3 g/dL in both Test and Control).

CONCLUSION: Four US Blood Centers demonstrated the capacity to validate and implement a dedicated manufacturing process for S-303/GSH PRRBCS despite the COVID pandemic. The ~10.2% overall transfusion rate speaks to the difficulty in maintaining sufficient hospital inventories of both Test and Control RBCs, and the extraordinary effort of the blood center staff to minimize non-study RBC transfusions in this randomized, double-blinded study. (Funded by the Biomedical Advanced Research Development Authority, DHHS; ClinicalTrials.gov, NCT03459287).

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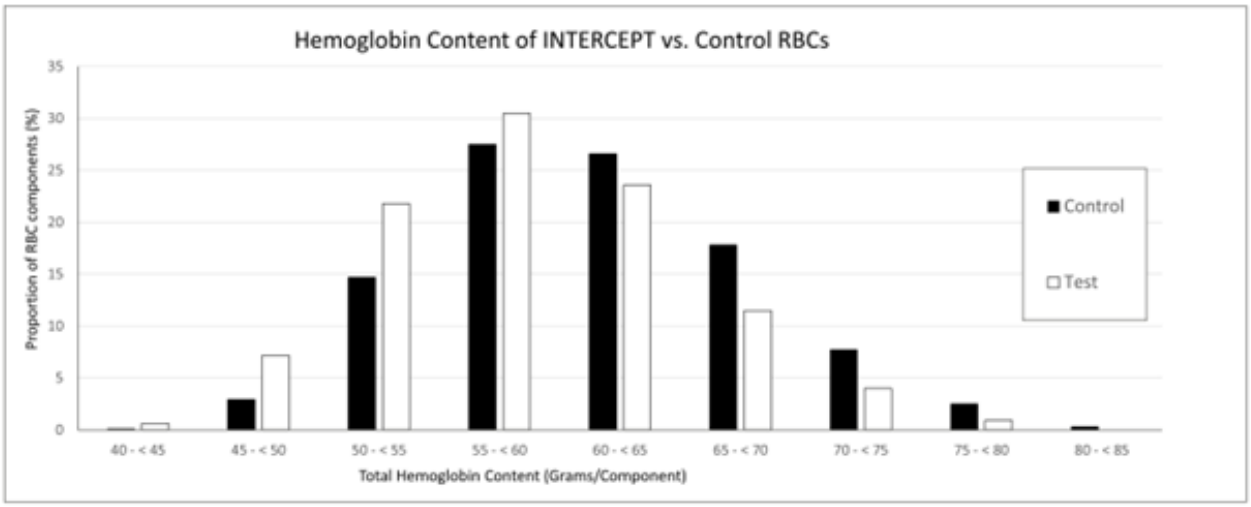

	Test	Control	P-value
Components Released into Inventory	4,755	4,856	0.002
Mean (SD) Hb Content (g/unit)	58.2 (6.4)	60.8 (6.7)	<0.001
Components Transfused	456	524	0.049
Mean (SD) Age at Transfusion (days)	23.1 (7.6)	21.4 (8.1)	0.003
Mean (SD) Hb Content (Transfused) (g/unit)	58.1 (6.5)	61.5 (6.8)	<0.001

The INTERCEPT Blood System for Red Blood Cells is under regulatory review in Europe, and in late-stage clinical development in the US.

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Use of INTERCEPT Plasma, Platelets, and Pathogen Reduced Cryoprecipitated Fibrinogen Complex are contraindicated in patients with a history of allergic response to amotosalen or psoralens.
Consult package inserts[1,2,3] for indications, contraindications, warnings, and precautions.

1. The INTERCEPT Blood System for Platelets Package Insert, Cerus Corporation. 2. The INTERCEPT Blood System for Cryoprecipitation for the manufacturing of Pathogen Reduced Cryoprecipitated Fibrinogen Complex Package Insert, Cerus Corporation. 3. The INTERCEPT Blood System for Plasma Package Insert, Cerus Corporation.

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