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PROGRAM OF ABSTRACTS

AABB 2023

PRESENTED AT

Association for the Advancement of Blood and Biotherapies Annual Meeting

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October 13 - 17, 2023

LOCATION

Nashville, Tennessee

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POSTER PRESENTATIONS

Meet the Poster Authors: Sunday, October 15th, 12:00 pm - 1:00 pm

Impact of Amotosalen/UVA Treatment for Pathogen Reduction in Platelet Concentrates on Transfusion Efficacy in Cardiac Surgery

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BACKGROUND: One of the most recent advances to improve blood safety and lower the risk of transfusion-transmitted diseases is the pathogen reduction treatment (PRT) of platelet concentrates (PCs). The characteristics of PR-treated PCs slightly differ from those of untreated PCs, and may affect transfusion outcome. This clinical research project aims to see how effective amotosalen/UVA (INTERCEPT™ Blood System) PCs are when transfused to a group of cardiac surgery patients.

STUDY DESIGN: This study examined the influence of the PRT using amotosalen-HCl and UVA light in a population of cardiac surgery patients. We analyzed the bleeding and platelet drop post-operatively in cardiac surgery with cardiopulmonary bypass (CPB). Apheresis Platelet Concentrate (APC) or Buffy Coat Platelet Concentrate (BC-PC) with Platelet Additive Solution (PAS) stored at 22°C ± 2°C with gentle rotation and agitation for a maximum of 7 days before being released for transfusion. We selected 73 PCs after taking into account the medical exclusion criteria: 46 PCs without PRT versus 27 PCs with PRT.

RESULTS: The decrease of patient platelet count between pre-operative and H0 (Intensive Care Unit (ICU) admission), pre-operative and H6 (6 hours after ICU admission) did not differ significantly with or without PRT. The volume of post-operative bleeding after cardiac surgery under CPB did not differ significantly regardless of whether the patient was transfused with PRT-PC or untreated PC. No difference was found in the post-operative pulmonary infections rate (*pneumonia*) between the groups. Moreover, independently of the use of PRT for platelets, we observed an inverse correlation between preoperative fibrinogen and bleeding at 24 hours (post-surgery). A 1 mg/L increase in fibrinogen (preoperative) is associated with a 159 mL decrease in bleeding 24 hours after the start of the surgery.

CONCLUSION: In post-operative cardiac surgery, the use of platelets treated with amotosalen/UVA (INTERCEPT) for pathogen reduction does not appear to affect transfusion efficacy and post-operative bleeding.

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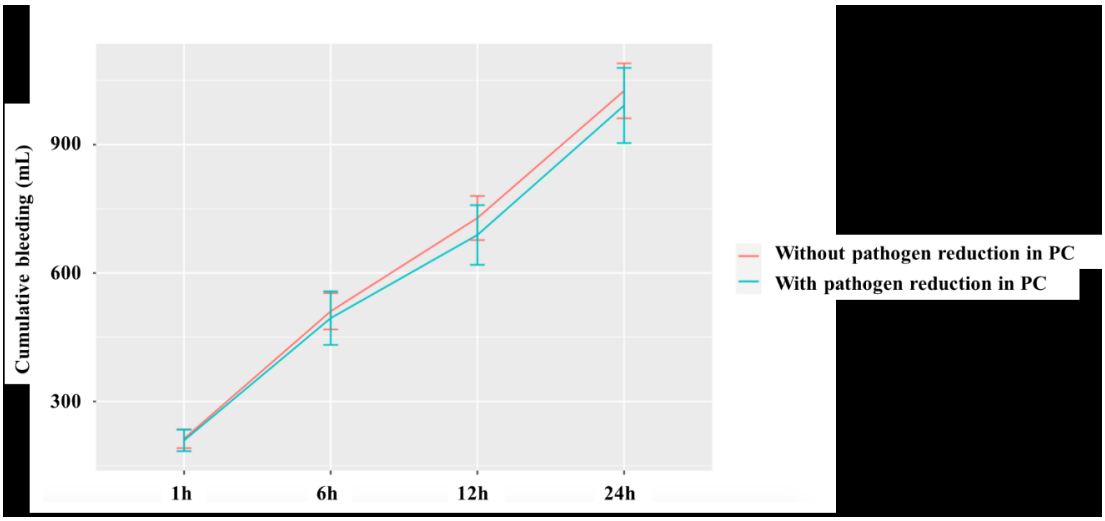
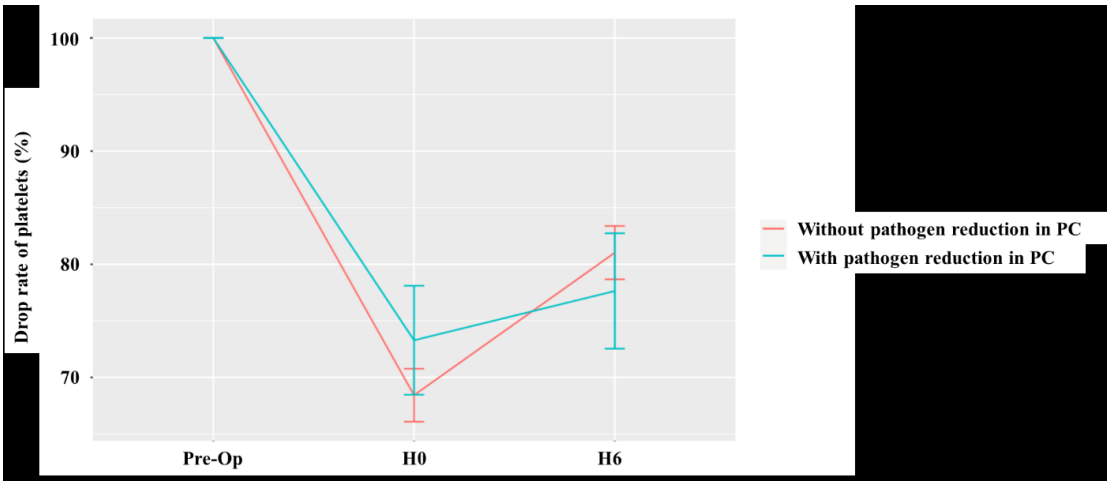
Figure 1: The Cumulative Bleeding and Drop Rate of Platelets. Cumulative Bleeding (A) and Drop Rate of Platelets (B) Between Pre-Operative and H0 (Start of Surgery) and Pre-Operative and H6 W (N=27) Or W/O (N=46) Amotosalen/UVA Treatment of PC Transfused





Safety and Efficacy of Amotosalen-UVA Pathogen Reduced Platelet Components Transfused to Mature and Premature Neonates

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BACKGROUND/CASE STUDIES: Neonates with immature organ systems who require platelet transfusion are at risk for infection and transfusion-associated graft-versus-host disease (TA-GVHD); and many require concurrent phototherapy (PT) for jaundice. Pathogen reduction (PR) of platelet components (PC) with amotosalen-UVA is indicated to reduce transfusion infection and TA-GVHD risk, but clinical data for neonates are limited.

STUDY DESIGN/METHODS: We evaluated the safety and efficacy of PRPC in premature and term neonates at the Insel Spitel, Bern, Switzerland by retrospective review of medical records for all premature and term neonates (0-28 days old) transfused with conventional PC (CPC) 72 months before (2005-2010) and PRPC 57 months after (2011-2015) PRPC adoption. Transfusion thresholds for premature and term non-bleeding neonates were < 50 x 10^9/L and < 30 x 10^9/L, respectively. Both cohorts were transfused with 5 mL PC/kg. PC platelet content was not measured at transfusion. Pre and post transfusion (1-4 hour) patient platelet counts were measured. CPC were stored for up to 5 days and gamma irradiated. PRPC were not gamma irradiated and were stored up to 7 days. Hospital records were audited for: gestation age, birth weight, PC use, pre and post transfusion platelet counts and increments, PT exposure, and PC transfusion-associated adverse events. P-values for treatment differences are based on Fisher's Exact test and a 1-way ANOVA model, respectively, for categorical and continuous variables.

RESULTS/FINDINGS: 100 neonates received 234 PRPC and 91 received 171 CPC. Similar proportions of patients in each cohort had bleeding (central nervous system 18% vs 19%, lung 3% vs 3.3%) as an indication for transfusion. All other PC transfusions were for thrombocytopenia prophylaxis. The average gestational ages and birth weights were similar between cohorts (**Table**). There were no substantial differences in the numbers of PC transfusions. The proportions of neonates with PT were similar (51%) but the PRPC cohort had more PT events. Mean platelet count increments were within therapeutic ranges in both cohorts. No PC transfusion related adverse events, including TA-GVHD, with and without concurrent phototherapy, were reported for either cohort.

CONCLUSION: The data support the efficacy and safety of PRPC in neonates who require platelet transfusion and phototherapy.

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n = Patients: Mean ± SD	PRPC (100)	CPC (91)	P-value
Gestation age (weeks)	32.8 ±5.3 n = 93	32.5 ± 5.0 n = 84	0.699
Birth weight (Kg)	1.8 ± 1.1 n = 100	1.8 ± 1.1 n = 91	0.649
Number of phototherapies	3.8 ± 3.0 n = 51	2.3 ± 1.3 n = 46	0.002
Bleeding prior to PC transfusion (%)	21%	22%	0.901
Number of PC transfusions / patient	2.3 ± 2.9 n = 100	1.9 ± 1.2 n= 91	0.162
Pre transfusion platelet count (10^9/L)	53.2 ± 48.9 n = 100	42.5 ± 30.1 n = 91	0.074
Post transfusion platelet count (10^9/L)	130.4 ± 45.5 n = 100	137.8 ± 58.8 n = 91	0.330
Platelet count increment (10^9/L)	82.5 ± 45.0 n = 100	96.4 ±53.0 n = 91	0.052

INTERCEPT Treatment of Contaminant Bacteria *Enterobacter soli*, *Leclercia adecarboxylata*, and *Staphylococcus saprophyticus* in Human Apheresis Platelets

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BACKGROUND: The INTERCEPT® Blood System for Platelets is a pathogen reduction 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 whole-blood derived platelets.

Enterobacter soli, Leclercia adecarboxylata, and *Staphylococcus saprophyticus* were isolated from an INTERCEPT-treated apheresis platelet unit that was involved in a transfusion-transmitted infection in a clinic in the United States. Whether the unit was contaminated post-pathogen reduction was unclear as the bag was discarded before analysis could be performed. However, previous data have shown that both *L. adecarboxylata* and *S. saprophyticus* are inactivated by the INTERCEPT Blood System for Platelets (Fadeyi *et al*., 2020). There are no inactivation data for *E. soli* and no *E. soli* transfusion-transmitted infections have been previously reported.

AIMS: The aim of this study was to assess the inactivation of *E. soli* alone and in combination with *L. adecarboxylata* and *S. saprophyticus* in apheresis platelets using the INTERCEPT Blood System for Platelets.

METHODS: To measure pathogen inactivation, 3.4 mL of an overnight culture of *E. soli* or a 1:1:1 (volume) mixture of *E. soli, L. adecarboxylata*, and *S. saprophyticus* were inoculated into an apheresis platelet unit (35% plasma/65% platelets) and treated using the INTERCEPT Dual Storage Platelet Processing Set by amotosalen and UVA light. The unit was incubated in the compound adsorption device (CAD) container for 16 h at 22°C and then transferred into storage bags for incubation at 22°C with shaking. Bacterial titer was determined pre-treatment and post-treatment on day 5- and 7-post collection. On day 7, residual bacterial titer was determined by combining the remaining unit with LB broth and incubating in a flask overnight at 37°C.

RESULTS: INTERCEPT treatment inactivated 7.5 ± 0.1 log CFU/mL of *E. soli* alone and 7.2 ± 0.1 log CFU/mL of the combination of *E. soli, L. adecarboxylata*, and *S. saprophyticus*. No detectable bacteria were observed post-treatment, at 5- and 7-days post-collection in either case.

SUMMARY/CONCLUSIONS: We show in this study that INTERCEPT treatment can inactivate *E. soli, L. adecarboxylata*, and *S. saprophyticus* achieving sterility throughout the 7-day storage period. Previous reports of TTIs involving an INTERCEPT-treated unit have shown defects in the storage containers that presumably allowed contamination during storage (Fadeyi *et al*., 2020). Further studies are required to understand how units can be contaminated during the storage period.

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

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BACKGROUND: The INTERCEPT® Blood Systems for platelets and plasma utilize amotosalen and UVA light to efficiently inactivate a wide range of pathogens and leukocytes in platelet concentrates (PC) and plasma. The World Health Organization (WHO) Expert Committee on Biological Standardization (ECBS) in association with the Paul-Ehrlich-Institut (PEI) approved an extended panel of bacterial strains to evaluate methods for improving the microbial safety of blood components in 2015 (Spindler-Raffel *et al*, 2015).

METHODS: Apheresis PC collected in 100% plasma or 65% PAS-3/35% plasma (65%/35%) were pooled into individual units of 420 mL with platelet doses of 4.0 to 5.0 × 10^{11} and 4.0 to 7.9 × 10^{11} respectively. Human plasma donations were collected and pooled to yield individual units of ~650 mL. Four replicates per platelet matrix were performed for each PEI strain of transfusion-relevant bacteria, including *K. pneumoniae* and *S. aureus* in plasma, with each replicate consisting of one unit spiked with a single PEI strain. The contaminated PC and plasma units were then treated with amotosalen and UVA light in the INTERCEPT Blood System for platelets and plasma, respectively. 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).

RESULTS: Platelet and plasma units contaminated with PEI bacterial strains (**Table 1**) were treated with amotosalen and UVA in the INTERCEPT Blood System for platelets and plasma, respectively. Robust bacterial inactivation was observed post-treatment (**Table 1**).

SUMMARY/CONCLUSIONS: The INTERCEPT Blood System for Plasma consistently inactivated high titers of *K. pneumoniae* and *S. aureus*. The INTERCEPT Blood System for Platelets efficiently inactivated *K. pneumoniae, S. aureus, E. coli, S. epidermidis, S. marcescens* and *S. pyogenes*. The data demonstrate that that the INTERCEPT Blood System for platelets and plasma robustly inactivate the tested WHO standardized bacteria strains associated with TTBI.

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Table 1: Bacterial Inactivation Using Amotosalen/UVA Treatment for Human Plasma and Platelet Concentrates in 100% Plasma and 65% PAS-3/35% Plasma

Bacteria (Strain)	Matrix	Log Reduction (Log cfu/mL)
K. pneumoniae PEI-B-P-08	PC In 100%plasma	4.7 ± 0.4
	PC In 65%/35%	5.6 ± 0.2
	Plasma	4.5 ± 0.5
S. aureus PEI-B-P-63	PC In 100%Plasma	6.7 ± 0.0*
	PC In 65%/35%	7.6 ± 0.1*
	Plasma	6.5 ± 0.1*
E. coli PEI-B-P-19	PC In 100%Plasma	7.4 ± 0.2*
	PC In 65%/35%	7.2 ± 0.1*
S. epidermidis PEI-B-P-06	PC In 100%Plasma	7.7 ± 0.1*
	PC In 65%/35%	7.8 ± 0.0*
S. marcescens PEI-B-P-56	PC In 100%Plasma	6.8 ± 0.1
	PC In 65%/35%	6.3 ± 0.3
S. pyogenes PEI-B-P-20	PC In 100%Plasma	6.0 ± 0.2*
	PC In 65%/35%	6.4 ± 0.1*
* No residual bacteria were detected post-UVA treatment		

Pilot Study of ABO-isogroup or Universal Plasma Pools with or without Pathogen Reduction Treatment

F Cognasse[1,2]

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BACKGROUND: The procedure of pooling 5 units of plasma derived from whole blood (about 1.3 liter), divided into 2 equal volumes for pathogen reduction treatment (PRT) with 2 disposable sets and UVA light (amotosalen/UVA (A/UVA)- INTERCEPT™ Blood System) has been introduced in France. The main benefits of this technique are the obtaining of 6 PFCM-IA from 5 native plasmas with potential savings in treatment time and disposable set costs, a standardization of products (volume, coagulation factors) and a potential reduction of recipient adverse events by dilution of allergens, cytokines, anti HLA or HNA antibodies.

STUDY DESIGN: The aim of this study was i) to compare the concentration of Factor VIII, fibrinogen and soluble inflammatory factors level in fresh frozen plasma with or without A/UVA PRT and ii) to compare the profile and standardization of plasma units, in mini-pools (5 units) and maxi-pools (10 units) with universal mixing method (combination of A, B and AB blood group samples). We analyzed 3 types of parameters: i) soluble inflammatory biomarkers: sCD40L, IFN-alpha, IFN-beta, IFN-gamma, IL-1 beta, IL-6, IL-8, IL-10, IL-18, IL-12 and TNF-alpha); ii) Fibrinogen and Factor VIII (as indicators of clotting factor content used in regular QC) and iii) circulating immune complexes. The pilot study used samples (tube segments) from untreated and INTERCEPT-treated apheresis plasma units.

RESULTS: Contrary to Factor VIII found stable (decrease of 8.5%, non-significant), there was a significant decrease (11%) in the concentration of fibrinogen contained in plasma treated with PRT (while being on average >2 g/L). We noted that sCD40L and IL-12 were significantly increased in individual plasma with PRT, whereas the IL-18 concentration was similar. This pilot study allowed us to identify a strong inter-individual variation of the inflammatory molecules of interest (sCD40L, IL-18 and IL-12) measured in the plasmas and an importance of the blood group on the variation of the molecules of interest. A significant reduction of the variation of the molecules of interest was observed in universal plasmas. There were no measurable circulating immune complexes.

CONCLUSION: The perspectives of the proposed pilot study were to explore the extension of the pooling concept to larger volume mixtures (10 units to obtain 12 PFCM-IA) with plasma of combined groups (e.g. 4A, 4B, 2AB) to obtain universal plasma. The distribution of blood groups seems important to define. Several reports show that together with IL-18, IL-12 induces anti-CD40 activated B cells to produce IFN-gamma, which inhibits IL-4 dependent IgE production. Also, our study suggests one hypothesis for a decrease in post-transfusion allergic reactions with PRT treated plasma. Further research, including a careful post- transfusion follow-up of plasma-treated patients, will be required to thoroughly define the clinical relevance of these findings.

Reduced Blood Bank Product Preparation Time and Waste with Implementation of Pathogen Reduced Cryoprecipitate

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BACKGROUND/CASE STUDIES: Kaiser-Permanente Los Angeles Medical Center (LAMC) is a 560 licensed bed facility, providing regional cardiovascular services, including 1,200 open heart surgeries annually. The LAMC blood bank was purposely located next to CV OR, separate from other laboratories, to minimize transport time. Due to availability constraints LAMC experienced treating bleeding patients with cryo AHF, an alternative solution, Pathogen Reduced Cryoprecipitated Fibrinogen Complex (PR Cryo, Cerus Corporation) was implemented. PR-cryo has the same benefits in treating coagulopathy as cryo AHF, but minimizes order to ready time as it can be stored, thawed, at room temperature, for 5 days and reduces the risk of transfusion transmitted infection because it is pathogen reduced. The increased shelf life also minimizes wastage risk and enhances supply stability. On July 1, 2021, LAMC incorporated PR Cryo into the blood bank inventory, and on August 16, 2021, LAMC transfused their first patient with the product. 20 months post-implementation, after 576 patients were transfused with 949 PR Cryo 4-pool units, the institution reviewed a portion of the product experience and found that PR Cryo reduces waste, provides supply stability, and reduces order to dispense time. Additionally, all previous issues with supply stability due to the pandemic blood shortages and general national seasonal product shortages are no longer occurring.

STUDY DESIGN/METHODS: LAMC Blood Bank reviewed records for the cryoprecipitated AHF units issued from September 2019 through February 2020, just prior to the pandemic, and separately Blood Bank reviewed PR Cryo and cryo AHF orders from September 2022 through February 2023, to provide an analogous time of year segment as close to the end of the pandemic as possible. Wastage and time from order to ready for pick up at blood bank data were recorded.

RESULTS/FINDINGS: Before implementation of IFC, and potential pandemic influence (Sept 2019 – Feb 2020), cryo AHF wastage was 6.1%. After IFC implementation, during the analogous months post-pandemic (Sept 2022-Feb 2023), the wastage rate of cryo AHF and IFC (dual inventory, PR Cryo ~60%) dropped to 1.6%, a 74% reduction in waste. Order to ready time dropped 70%, from a median of 30 minutes to 9 minutes.

CONCLUSION: The reduction preparation time, reduction in waste, and reduction risk of transfusion transmitted infection, and supply stability that PR cryo has provided LAMC align with LAMC's goals for excellence in patient care.

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Table 1: Wastage Rates and Order to Ready Time in Minutes of Cryoprecipitate Products Before (Sept 2019-Feb 2020) and After (Sept 2022-Feb 2023) Implementation of PR Cryo

	Sept 2019 to Feb 2020	Sept 2022 to Feb 2023
% Waste	6.1%	1.6%
Order to ready time (mins) (Mean, Median, SD, N)	30, 30, ± 9, 100	13, 9, ± 12, 233

Implementation of Pathogen Reduced Cryoprecipitated Fibrinogen Complex in a Pediatric Level II Trauma Center

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BACKGROUND/CASE STUDIES: Due to the 4-6 hour shelf life to evade potential infectious transmission, the wastage rates for Cryo AHF were consistently exceeding our targets of less than 10% waste per quarter and contributing to increased costs. The FDA has approved Pathogen Reduced Cryoprecipitated Fibrinogen Complex (PRCFC) for the treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency. The local blood center initiated the manufacture of PRCFC from amotosalen/UVA-treated plasma to mitigate transfusion transmission risk with a post thaw shelf life of 5-days. Opportunities for increasing patient safety and decreasing CryoAHF waste were identified.

STUDY DESIGN/METHODS: Implementation of PRCFC began in November 2021 of the first fiscal quarter of FY2022 (Oct-Dec 2021). Increasing patient safety while decreasing CryoAHF waste was managed as a process improvement project. A retrospective analysis of wastage for CryoAHF vs. PRCFC transfusion was performed for orders placed between 1QFY2021 (October 2020) and 2QFY2023 (March 2023).

RESULTS/FINDINGS: Steps identified in the project plan included product review, acceptance from physician stakeholders, blood utilization committee approval, IT, and procedure updates. The Transfusion Service determines if CryoAHF or PRCFC is used to fill an order based on clinical diagnosis, age, weight, ABO capability, and inventory. The quarterly wastage rate for CryoAHF ranged from 11.3% to 25.8% with an annual average wastage rate of 16.3%. Following the implementation of PRCFC, the annual average wastage rate has decreased to 5.64%. (**Table 1**).

CONCLUSION: This process improvement project was successful as evidenced by progress and completion reports submitted to change management leadership and positive results on a six-month post implementation survey with physician stakeholders. The ability to store PRCFC thawed for the extended expiration of 5 days for PRCFC compared with 6 hours for CryoAHF has also contributed to a 65% decrease in wastage of this critical blood component. Implementation of a CryoAHF equivalent with an FDA approved level of risk reduction of infectious transmission has allowed our transfusion service to provide a safer source of fibrinogen and other clotting key factors and facilitate a more rapid hemostasis in bleeding patients.

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	1Q FY2021	2Q FY2021	3Q FY2021	4Q FY2021
100% CryoAHF use - % wastage	11.3%	25.8%	14.5%	13.4%
	1Q FY2022	**2Q FY2022**	**3Q FY2022**	**4Q FY2022**
75% Cryo AHF/25% PRCFC use - % wastage	16.5%			
50% Cryo AHF/50% PRCFC use - % wastage		6.1%	3.9%	11.2%*
	1Q FY2023	**2Q FY2023**		
50% Cryo AHF/50% PRCFC use - % wastage	3.6%	3.4%		

*increased number of MTPs activated, which led to an increase in wastage rates.

Improved Operational Efficiencies with Pathogen Reduced Cryoprecipitated Fibrinogen Complex vs. CryoAHF

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BACKGROUND/CASE STUDIES: Due to the potential risk of infectious transmission, the 4–6 hour shelf-life of CryoAHF prevents thawed storage, often delaying fibrinogen supplementation during major surgical bleeding. The FDA has approved Pathogen Reduced Cryoprecipitated Fibrinogen Complex (PRCFC) manufactured from amotosalen/UVA-treated plasma that can be kept at room temperature for up to 5 days for the treatment/control of bleeding associated with fibrinogen deficiency. Opportunities for rapid dispensing of PRCFC & decreasing CryoAHF wastage were identified.

STUDY DESIGN/METHODS: PRCFC was implemented in Jan '22. The ordering process was not modified to indicate Cryo AHF or PRCFC. Two units of PRCFC were kept thawed at 20-24°C in a labeled box. Turnaround time (TAT) to prepare/allocate & issue cryoprecipitate orders were documented. A retrospective analysis of TATs for CryoAHF vs. PRCFC was performed for orders between Jan '22 & Feb '23. Outliers, including all orders taking >60 minutes for issue, were excluded from analysis (these reflected non-urgent orders or cryo released as part of massive transfusion protocols that were not released until later shipments).

RESULTS/FINDINGS: A total of 2014 cryoprecipitate orders were included in the analysis. Of these, 398 (19.7%) were PRCFC. Reduction in TAT between PRCFC & CryoAHF was most significant for orders placed from the OR and Labor & Delivery (L&D), with a 48.7% reduction in time from order to prepare ($p<0.001$) and 41.3% reduction in time from order to issue ($p<0.001$). When adding ICU orders to the analysis, similar reductions in TATs were achieved. When all orders regardless of location were included, time to prepare & issue were reduced by 39.2% & 38.6%, respectively ($p<0.001$). (**Table 1**).

After implementing PRCFC, there was a 100% reduction in wastage in the blood bank and a 17.20% reduction in wastage in the patient care areas, with overall cost savings of 30.8% ($19,800).

CONCLUSION: PRCFC is ready to dispense & provides an immediate source of fibrinogen in critically bleeding patients with significant reductions in TAT. There is an added benefit of reduced wastage and thus, cost saving.

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Table 1: Comparison of TATs for PRCFC vs. CryoAHF*

OR, L&D	PRCFC (n=326)	CryoAHF (n=1029)	% diff	p-value
Order to prepare (min)	13.8 (±11.9)	26.9 (±9.0)	-48.7	<0.001
Order to issue (min)	16.5 (±12.2)	28.1 (±9.5)	-41.3	<0.001
OR, L&D, ICU	**PRCFC (n=343)**	**CryoAHF (n=1288)**	**% diff**	**p-value**
Order to prepare (min)	14.2 (±12.5)	26.3 (±9.6)	-46.0	<0.001
Order to issue (min)	17.1 (±12.9)	30.2 (±11.1)	-43.4	<0.001
ALL LOCATIONS	**PRCFC (n=398)**	**CryoAHF (n=1616)**	**% diff**	**p-value**
Order to prepare (min)	16.0 (±14.0)	26.3 (±10.2)	-39.2	<0.001
Order to issue (min)	19.1 (±14.5)	31.1 (±11.9)	-38.6	<0.001

*Values expressed as a % or mean (±std. deviation). Non-normal continuous data analyzed by Mann-Whitney test.

Design of ReCePI, a Randomized, Double-Blinded, Phase III Study to Evaluate the Efficacy and Safety of Pathogen Reduced RBCs in Complex Cardiac Surgery

Richard J. Benjamin, John Pitman, Laurence Corash, Jeanne Varrone, Nina Mufti for the ReCePI Investigators

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BACKGROUND: Pathogen reduction of RBCs (PR-RBCs) treated with amustaline/glutathione is an investigational process designed to reduce transfusion-transmitted infection and TA-GVHD. The Red Cell Pathogen Inactivation (ReCePI) study aims to evaluate the efficacy and safety of PR-RBC transfusions for support of acute anemia. An acute kidney injury (AKI) endpoint in cardiovascular surgery (CVS) was selected based on the hypothesis that RBC transfusions protect against tissue hypoxia and reduce the incidence of AKI, an outcome directly-related to 30-day mortality in CVS surgery (Lassnigg *et al*. J Am Soc Nephrol 2004; Crit Care Med 2008).

DESIGN: ReCePI is a prospective, multicenter, randomized, double-blinded, controlled, parallel, non-inferiority study (ClinicalTrials.gov: NCT03459287). The study population includes subjects ≥ 11 years of age undergoing complex CVS with a high (≥3) TRUST score risk of transfusion. Test components are leukocyte reduced RBCs treated with amustaline and glutathione suspended in SAG-M (PR- RBCs). Control components are leukoreduced RBC components in an FDA approved additive solution. Both are stored at 1-6°C for up to 35 days. Subjects with confirmed positive baseline antibody to PR-RBCs are excluded.

Primary efficacy outcome is the proportion of patients who have received at least one study transfusion with renal impairment (AKI) defined as any increased serum creatinine (sCr) (≥0.3 mg/dL or 26.5 µmol/L) from the pre-surgery baseline sCr, within 48 ±4 hours of the end of surgery. Safety outcomes are the proportion of patients with any treatment-emergent adverse events related to study RBC transfusion through 28 days; and the proportion of patients with treatment-emergent antibodies with confirmed specificity to PR-RBCs. Assuming an AKI event rate of 30% in the Control group with no more than a 50% increase from the Control rate as the non-inferiority margin, a sample size of >292 patients (146 per arm) will provide approximately 80% power to declare non-inferiority at the two-sided 0.05 alpha level, assuming the true treatment difference is zero.

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RESULTS: ReCePI opened for enrollment at 18 US sites and transfused the first subject in December 2019. Enrollment was impacted by the COVID-19 pandemic. DSMB review on three occasions has recommended continued enrollment. In view of robust patient blood management practices and despite stringent selection criteria, only 56% of enrolled subjects are transfused (site range: 18-82%). To date, no cases of increased RBC clearance or hemolysis associated with antibodies to PR-RBCs have been documented. Average AKI rates for all patients are 30% but vary by site. The study remains blinded. Enrollment is expected to be completed in 2023.

CONCLUSIONS: The ReCePI study utilizes changes in the incidence of AKI as a robust assessment of PR-RBC safety and efficacy in severely ill CVS subjects with surgical blood loss.

The INTERCEPT red blood cell system is under regulatory review in Europe, and in late-stage clinical development in the US.

Developing a Tool to Assess Red Blood Cell Clearance *in Vivo* Utilizing Pathogen-Reduced RBCs

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BACKGROUND/CASE STUDIES: A simple clinical method to assess clearance of transfused RBCs would help predict the physiologic activity of antibodies or drugs implicated in hemolytic reactions. Pathogen reduction of RBCs (PR-RBCs) with amustaline/glutathione is an investigational process to reduce transfusion-transmitted infections. We describe a novel tool to track PR-RBC survival *in vivo* by flow cytometry (FACS) using a monoclonal antibody specific for membrane-bound acridine, a byproduct of the PR process. Data were derived from Phase 2 RBC survival studies in a healthy volunteer and in sickle cell anemia (SCA) patients.

STUDY DESIGN/METHODS: A healthy volunteer received a 5 mL aliquot of autologous 35-day-stored 51Cr and biotin-labelled PR-RBCs during a RBC recovery and survival study (Clinicaltrials.gov NCT03384407). In a separate study of SCA using biotin-labelled RBCs, two patients received three ~7 mL aliquots of different biotin dose levels of labeled RBCs: Two aliquots from an RBC unit before and after PR treatment (Pre-PR RBCs, 2µg biotin; PR-RBCs, 6µg biotin), and one from a conventional RBC unit (Control, 18µg biotin). The remaining PR-RBC and Control RBC units were transfused concurrently. The proportion and antigen density of circulating acridine-labeled cells in recipient blood was determined by FACS using an acridine antibody (2S197-2MI).

RESULTS/FINDINGS: The healthy volunteer study demonstrated that after transfusion of 5 ml of PR-RBCs the acridine label could be detected by FACS at 24 hours (0.33% circulating RBCs) and up to 112 days post transfusion (0.06%circulating RBCs).

In the biotin study of SCA patients, the acridine assay detected 10.0-12.3% circulating PR-RBCs 24 hours after transfusion of the entire PR-RBC units. The density of acridine RBC surface antigen (**Table**) was equivalent to the 18µg biotin label 1-hour after transfusion and declined homogeneously ~50% at 24 hours post-transfusion and by >80% on day 7 but remained stable near the 2µg biotin label level through the 98-110-day observation period. Biotin and acridine labeling resulted in similar linear RBC survival curves.

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CONCLUSIONS: Circulating PR-RBC can be detected *in vivo* following transfusion of small RBC aliquots or entire RBC units using FACS for RBC surface acridine, with similar sensitivity as biotin labels and increased sensitivity compared to 51Cr labels. Transfusion of PR RBCs provides a potential method to rapidly assess the physiologic activity of antibodies and drugs, including therapeutic monoclonal antibodies, that may impact RBC clearance *in vivo*, without additional processing or use of radiolabels. A standardized method and criteria for defining rapid clearance are in development.

Table: FACS Results from a Representative Biotin Study Patient

Study Day	Acridine molecules/RBC	% Acridine positive RBCs
0	8,414	12.30
1	3,764	12.60
7	1,360	11.20
14	1,417	11.00
25	1,039	7.10
54	946	3.40
67	760	1.80
82	649	0.50
98	643	0.10

The INTERCEPT red blood cell system is under regulatory review in Europe, and in late-stage clinical development in the US.

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Consult package inserts[1,2] 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.