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PROGRAM OF ABSTRACTS

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American Association of Blood Banks Annual Meeting

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LOCATION

Virtual Meeting

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Session: Meet The Poster Authors Event

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Optimizing US Platelet Supply by Shifting Minimum Platelet Dose

Travis Berry, Meredith Lummer

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BACKGROUND/CASE STUDIES: Following publication of final FDA guidance on bacterial safety, blood centers (BC) are evaluating methods to balance safety and sustainability of their platelet (PLT) supply while implementing strategies such as Pathogen Reduction (PR) and Large Volume Delayed Sampling (LVDS). BC and hospitals are assessing the potential impact of allowing routine use of doses <$3.0x10^{11}$ in order to maximize PLT availability and split rate (SR) without impacting patient outcomes. Current FDA and AABB standards allow for a subset of products <$3.0x10^{11}$. Analysis was done to determine the operational impact associated with implementation of FDA's bacterial safety guidance and inclusion of a lower minimum dose.

STUDY DESIGN/METHODS: Modeling was performed using data collected from 5 BC with varying SRs. BC collections were analyzed per donation at current volume, concentration, and yield to determine baseline SR with LVDS only. 16mL samples per final component were deducted for LVDS. Collections were then analyzed to determine SR with a combination of PR and LVDS; and a combination of PR, LVDS, and low dose. Collections were analyzed for PR eligibility with or without pre-splitting or volume adjustment. Required yields post-processing were 3.0, 6.0, 9.0 and $12.0x10^{11}$ to result in 1-4 final products, respectively. When low dose collections were analyzed, minimum yield for a single dose was $2.2x10^{11}$.

RESULTS/FINDINGS: SRs were maintained or increased across all bacterial safety strategies (**Table 1**). PR compatibility ranged from 88-97%. Low dose ranged from 17-43%. Average dose remained >$3.0x10^{11}$ in all cases.

CONCLUSIONS: Allowing a subset of products with doses <$3.0x10^{11}$ enables BC to implement PR and LVDS while increasing their overall SR. Incorporating minimum doses <$3.0x10^{11}$ enables standardization of PLT products, minimizing dose and volume variation. Substantial increases to SR and PR compatibility were most pronounced in BC that had optimized collection settings. Additional optimization and collection analysis may further benefit SR and PLT availability.

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Table 1. Summary of Results

Site	A Trima 100% Plasma n=5621			B Amicus PAS n=1820			C Trima 100% Plasma n=680			D Trima 100% Plasma n=2671			E Trima 100% Plasma n=6617		
	LVDS	PR, LVDS	PR, LVDS, Low Dose	LVDS	PR, LVDS	PR, LVDS, Low Dose	LVDS	PR, LVDS	PR, LVDS, Low Dose	LVDS	PR, LVDS	PR, LVDS, Low Dose	LVDS	PR, LVDS	PR, LVDS, Low Dose
SR	1.99	1.99	1.99	2.26	2.26	2.44	1.92	1.92	2.02	1.5	1.51	1.7	2	2	2.13
% Singles*	28	28	28	14	14	11	22	22	17	54	54	36	17	18	11
% Doubles*	47	47	48	47	47	45	60	60	62	35	37	53	58	59	60
% Triples*	23	23	22	35	35	33	17	17	20	8	9	10	23	23	29
% Quads*	3	3	3	3	3	11	0	0	0	0	0	0	0	0	0
Avg. Dose	3.9	3.5	3.4	3.8	3.5	3.2	3.6	3.5	3.3	3.8	3.7	3.2	3.8	3.4	3.1
% <3.0	0	0	17	0	0	38	0	0	16	0	0	23	0	0	25
% PR	0	59	88	0	71	97	0	72	90	0	80	97	0	64	93
% Conv.	100	41	12	100	24	3	100	28	10	100	20	3	100	36	7

**Totals per column <100% due to collections outside apheresis manufacturer specification.*

Optimizing Platelet Availability and Access to a ~100% Pathogen Reduced Inventory

Tracy Collier[1], Vera Chrebtow[2], Patricia Schmidt[2]

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2. Cerus Corporation, Concord, CA, United States

BACKGROUND/CASE STUDIES: In light of eBDS culture obsolescence, the Community Blood Bank of Northwest Pennsylvania and Western New York (NWPA/WNY) needed to implement either the BacT/Alert® culture or INTERCEPT® pathogen reduction (PR) to maintain safety of its apheresis platelet products. NWPA/WNY opted to implement PR for all 3,000 apheresis products; implementation initiated in January 2018 and reached ~100% PR production in April 2018. The impact to product shelf-life, expiry and associated savings, hospital receptivity, and implementation of production optimization measures to attain a ~100% PR inventory are described.

STUDY DESIGN/METHODS: Analyses were completed to determine compatibility with PR input specifications via assessment of dose, volume, and concentration for each collection. Production measures were adopted to increase compatibility; these included: Trima collection optimization (adjustment of targets on collection devices), pre-splitting (splitting of double collections to meet PR specifications), and volume adjustment (removal of small volume quantities from units with excess volume to accommodate PR specifications). Subsequently, analyses were performed to compare the platelet effective shelf-life, expiry rates and financial impact before and after PR implementation.

RESULTS/FINDINGS: Approximately 30% of products underwent production optimization measures to meet PR specifications; the remainder fell within PR specifications. Ninety-nine percent of products (3,135) were treated with PR in 2019 (**Table**). Twelve percent of products were outdated in 2017 (pre-PR implementation), which decreased to 5 and 3% post-PR implementation in subsequent years. This translated to a net loss of $194,731, $106,659, and $70,139 in 2017, 2018, 2019, respectively, or a savings of ~$120,000 upon treating ~100% of products with PR.

Measures Implemented and PR Compatibility

Year	# Total Products	Average Split Rate	# PR treated Products** (%)	# of PR Ineligible Products** (%)	Average # Volume Reductions** (%)	Average # Pre-splitting** (%)	Average # Products Manipulated to Fit PR Specs** (%)
2017*	2331	1.82	NA	NA	NA	NA	NA
2018	2768	1.53	2059 (74)	68 (2.4)	72 (4)	720 (29)	816 (33)
2019	3155	1.58	3135 (99)	20 (0.6)	276 (10)	696 (26)	972 (36)

**Pre-PR implementation; ceased triple collections in December 2017*

***Annualized*

CONCLUSIONS: Blood centers today can adopt PR for a significant percent of their current supply. NWPA/WNY was able to attain a ~100% PR apheresis platelet inventory through optimized collection parameters, pre-splitting, and volume reduction. Individual analysis is warranted for each blood center. The elimination of the post culture inoculation hold period and PR implementation enabled increased platelet availability through early product release on day 1, resulting in a 75% decrease in expiry rate. This corresponded to ~$120,000 in savings per year.

In Vitro Quality of Trima Platelets in 35% Plasma/65% PAS-3 Treated with INTERCEPT After 7-Days Storage

Jamie Genthe[1], Crystal Stanley[2], Kathleen Kelly[2], Larry Dumont[2], Nina Mufti[1], Anna Erickson[1]

1. Cerus Corporation, Concord, CA, USA; 2. Vitalant Blood Center, Denver, CO, USA

BACKGROUND/CASE STUDIES: The INTERCEPT® Blood System for platelets is FDA approved for the *ex vivo* preparation of pathogen-reduced Amicus apheresis platelet components (PC) in PAS-3 to reduce the risk of transfusion-transmitted infection (TTI) and as an alternative to gamma irradiation for prevention of transfusion-associated graft versus host disease (TA-GVHD). Cerus is conducting studies to extend INTERCEPT treatment of PCs in PAS-3 in the US to include products collected on other apheresis platforms. The objective of this study was to evaluate *in vitro* function of platelets suspended in 35% plasma/65% PAS-3 (PAS), collected using the Trima® platform, after treatment with the INTERCEPT Blood System for platelets. The INTERCEPT process is currently not approved for Trima PAS or 7-day storage.

STUDY DESIGN/METHODS: 6 single or double dose apheresis PC were collected on the Trima apheresis platform in PAS and received INTERCEPT treatment in the dual storage (DS) set within 24 hours of donation. Input PCs were 3.8-7.4x10^{11} platelets in 278-419mL. All PC were evaluated on Day 0/1, Day 5, and Day 7 for physical/metabolic characteristics. Day 7 results were compared to previous Cerus data obtained with INTERCEPT treated PC collected on the Amicus® platform.

RESULTS/FINDINGS: Following INTERCEPT treatment the dose recovery was 93±1% and volume recovery was 98±3%. Units stored for 7 days retained platelet dose >3.0x10^{11} (Table 1). On Days 5 and 7 all units had pH22°C >6.2. *In vitro* platelet quality at Day 7 post-donation on Trima was consistent with INTERCEPT-treated Amicus platelet units in PAS (Table 1) and similar to the Trima Day 7 values.

CONCLUSIONS: Trima PC in PAS treated with the INTERCEPT Blood System for platelets using the DS set and stored for 7 days retained *in vitro* metabolic and functional properties consistent with *in vivo* functionality. These results demonstrate platform and storage medium compatibility of the INTERCEPT system even with 7-day storage.

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US. Clinical trials are in progress: ClinicalTrials.gov Identifier: NCT04022889.

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Table 1: Day 5 and 7 *In Vitro* Summary (Mean±SD)

	Day 5	Day 7	
	INTERCEPT Trima (N=6)	INTERCEPT Trima (N=6)	INTERCEPT Amicus (N=72)
Platelet count ($x10^3$ platelets/L)	1356±238	1350±239	1359±242
Platelet dose ($\times10^{11}$ cells/unit)	4.5±1.4	4.3±1.5	3.7±0.6
Mean platelet volume (fL)	7.4±0.6	7.6±0.6	7.9 ±0.8
pH (22°C)	6.8±0.1	6.8±0.1	7.0±0.1
pO_2 (mm Hg)	64±28	76±31	141±23
pCO_2 (mm Hg)	18.5 ±3.8	16.7±4.4	16.3±4.3
HCO_3^- (mmol/L)	2.9±0.9	2.6±1.0	2.7±0.9
Supernatant glucose (mmol/L)	1.8±0.8	0.7±0.1	0.4±0.6
Supernatant lactate (mmol/L)	9.0±2.19	11.07±1.13	12.7±1.5
Total ATP (nmol/10^8 platelets)	3.4±0.6	3.0±0.8	3.1±1.2
Morphology score	186±11	186±14	265±27
Extent of Shape Change (%)	18.0±5.2	15.6±5.4	14.8±5.4
Hypotonic Shock Response (%)	48.7±7.2	41.3±11.0	34.5±10.7
Normalized Supernatant LDH (U/10^{12} cells)	67±20	75±23	131±61
Total LDH (U/L)	2143±487	2109±458	2818±514
P-selectin (CD62, %)	42.7±11.9	46.8±12.8	44.6±12.4
Lactadherin (%)	0.08±0.05	0.10±0.05	ND

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US. Clinical trials are in progress: ClinicalTrials.gov Identifier: NCT04022889.

In Vitro Evaluation of Platelets Stored for 7 Days Prepared with INTERCEPT Blood System

Jamie R. Genthe[1], Waseem Anani[2], Jose A. Cancelas[3], Kadi Schroeder[4], Zbigniew M. Szczepiorkowski[5], Beth Shaz[6], Margaret Hennig[1], Nina Mufti[1], Anna Erickson[1]

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BACKGROUND/CASE STUDIES: The INTERCEPT® Blood System for platelets is FDA approved for *ex vivo* preparation of pathogen-reduced apheresis platelet components (PC). Two studies were preformed to evaluate the post-storage (up to 7 days) *in vitro* platelet function of apheresis platelets in either 100% plasma (PL) or 35% plasma/65% PAS-3 (PAS) prepared with the INTERCEPT Blood System for platelets (T) compared to paired untreated control platelet components (C).

STUDY DESIGN/METHODS: PC were collected on the Trima® (PL) or Amicus® (PAS) platforms. T were treated using the Small Volume, Large Volume, or Dual Storage INTERCEPT sets. 72 single-dose and double-dose PAS containing 2.9-8.0×10^{11} platelets and 68 single-dose and double-dose PL containing 3.2-7.9×10^{11} platelets were collected. The primary analysis was post-INTERCEPT platelet yield retention (≥85% PAS and ≥80% PL), Day 7 platelet dose (≥3.0x10^{11}), and Day 7 $pH_{22°C}$ ≥6.2. Indices exceeding ±20% difference from C were compared to reference ranges for conventional platelets stored for 7 days.

RESULTS/FINDINGS: The average dose recovery after INTERCEPT treatment was 87.3% (85.7%-89.0%) for PAS and 84.9% (83.8%-86.0%) for PL. T stored for 7 days retained therapeutically effective platelet doses (PL 3.7 and PAS 3.6x10^{11}). On Day 7 100% T had $pH_{22°C}$ ≥6.2 with retention of adequate *in vitro* metabolic and functional properties (**Table 1**). *In vitro* INTERCEPT platelet quality at Day 7 was within ± 20% of C or within the reference range (**Table 1**).

CONCLUSIONS: Platelet components in PL or PAS treated with INTERCEPT Blood System for platelets and stored for 7 days retained *in vitro* metabolic and functional properties.

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US. Clinical trials are in progress: ClinicalTrials.gov Identifier: NCT04022889.

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Table 1: Day 7 Summary (Mean±SD)

	PL N=72		PAS N=68		
	T	C	T	C	W/in 20% or Ref Range #/N(%)
Component volume (mL)	290±55	279±64	271±50	275±48	140/140(100%)
Platelet count ($\times 10^3/\mu L$)	1286±252	1413±247	1359±242	1381±258	139/140(99.3%)
Platelet Dose ($x10^{11}$)	3.7±0.8	3.8±0.7	3.6±0.7	3.7±0.6	120/140(86%)
MPV (fL)	7.5±0.8	7.5±0.9	7.9 ±0.8*	7.8±0.9	135/135(100%)
pO_2 (mm Hg)	142±13*	133±21	141±23*	117±22	128/135(94.8%)
pCO_2 (mm Hg)	35.3±7.8*	29.8±7.1	16.3±4.3	23.4±3.8	136/136(100%)
HCO_3^- (mmol/L)	5.1±2.1	7.7±2.4	2.7±0.9	4.0±1.0	125/130(96.2%)
Supernatant glucose (mmol/L)	10.9±3.0	12.6±4.1	0.4±0.6	0.6±0.8	140/140(100%)
Supernatant lactate (mmol/L)	13.7±3.3	13.3±6.1	12.7±1.5	13.4±1.9	140/140(100%)
Total ATP ($nmol/10^8$plts)	3.6±1.3	3.7±1.4	3.1±1.2	3.0±1.2	135/140(96.4%)
Morphology (Kunicki score)	273±28	272±37	265±27*	255±32	140/140(100%)
Extent of shape change (%)	18.2±5.0	21.2±6.2	14.8±5.4	14.2±5.6	138/140(98.6%)
Hypotonic shock response (%)	51.8±15.6*	43.9±13.7	34.5±10.7	36.9±10.2	133/140(95%)
Proportional lysis (%)	9.1±2.8*	6.1±1.5	6.2±2.6	6.3±4.0	36/131(27.5%)
Membrane P-selectin (%)	30.6±11.7*	22.9±17.2	44.6±12.4	37.4±15.1	138/140(98.6%)

**95% CI for mean treatment difference (T-C) showed T to be significantly higher than C*

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US. Clinical trials are in progress: ClinicalTrials.gov Identifier: NCT04022889.

Operational Validation of Double Dose Buffy Coat Platelet Concentrates Prepared with the IPP Pooling and Leukodepletion Set

Hervé Isola[1], Sébastien Linossier[2], Nathalie Marais[2], Françoise Donnadieu[2], Beatrice Belcour[3], Delphine Haas[1], Floriane Rudwill[1], Dr Christian Gachet[1], Dr Jacques Chiaroni[2]

1. EFS Grand Est, Strasbourg, France; 2. EFS Paca Corse, Marseille, France; 3. EFS Grand East, Nancy, France

BACKGROUND: Double dose (DD) leukodepleted platelet concentrates (PC) can be obtained from pools of 8 buffy coats (BC) supplemented by a Platelet Additive Solution (PAS). An I-Platelet Pooling Set (IPP) has been developed by Kansuk (Turkey) with Cerus (Netherlands) to perform this preparation with a semi-automatic method using centrifuges and presses. The obtained DD-BC-PC are intended to be pathogen reduced (PR) with the INTERCEPT™ (Cerus) Dual Storage (DS) processing set including two platelet storage containers. The objective was to perform a routine operational validation of the process to support an application for regulatory approval by ANSM.

METHODS: 100 evaluable DD-BC-PC were prepared with IPP at each EFS site (EFS1=Strasbourg and EFS2=Marseille) at day 1. Eight BC and 280 ml of PAS InterSol (Fresenius Kabi, Germany) (EFS1) or 300 ml of PAS SSP+ (Macopharma, France) (EFS2) are sterile docked to the Octopus harness and combined into a 700 ml pooling bag. Pools are constituted so that the addition of the 8 donor pre-counts falls within a range of approximately 1800-2100 x 10^9/l. Each pool is centrifuged in a Cryofuge 6000i (Heraeus (Germany) (EFS1) at 2000 rpm / 8 min or in a Rotosilenta 630 RS (Hettich (Germany) (EFS2) at 1800 rpm / 10 min and the PC supernatant expressed through a Sepacell™ PLX-5 leukodepletion filter (Asahi Kasei, Japan) into a temporary platelet storage container. The obtained DD-BC-PC were tested within one hour of preparation for compliance with the INTERCEPT process entry (guard bands) and regulatory requirements for volume (300-420 mL), platelet content (2.5-8.0.10^{11}), residual leukocytes (WBC, ≤1.10^6), residual red blood cells (≤4.10^6/ml, visual assessment) plasma ratio (32-47%) and swirling.

RESULTS: Results were similar for the “2 EFS” and combined. All units exhibited RBC contamination in conformity with the limit (≤4.10^6/ml) and maximum swirling after preparation. All INTERCEPT process guard bands for the DS set were met (**Table 1**) except for one unit containing 8,3x10^{11} platelets which could be volume reduced before INTERCEPT treatment.

CONCLUSIONS Leukocyte-depleted "double dose" buffy coat platelets with a high platelet content and ready for pathogen reduction with the INTERCEPT DS processing set, can be produced with the IPP pooling and leukodepletion set.

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Table 1: Characteristics of Double Dose Platelet Concentrates from Pools of 8 Buffy-Coats Ready for Pathogen Reduction (n=200, n=63 for plasma ratio)

	Volume (mL)	Plt Conc. G/L	Plt content 10^{11}/U	Res. WBC 10^{6}/U	Plasma / PAS ratio %
Average	397	1753	7,0	0,06	41,2
Standard deviation	12	164	0,6	0,05	2,8
Min	365	1026	4,1	0,02	34,8
Max	420	2075	8,3	0,46	46,4
Requirement / Target	300-420 (375-420)	-	2,5-7,0 7,1-8,0	≤1,0	32 - 47
% conformity	100 %		99%	100%	100%

Amotosalen/UVA-Treated Platelets have Similar Thrombin Generating Capacity as Conventional Untreated Platelets

Shelby Kardel, Kaja Kaastrup, Nina Mufti, Subramanian Yegneswaran

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BACKGROUND/CASE STUDIES: Amotosalen/UVA treatment is an effective method to inactivate pathogens in platelet concentrates, thus reducing the risk of transfusion-transmitted infections and of transfusion-associated graft-versus-host disease. Here we have examine the effect of treatment on *in vitro* platelet function and the ability of these platelets to support thrombin generation.

STUDY DESIGN/METHODS: ABO matched platelet components (PC) suspended in 100% plasma were pooled-and-split into two; one was untreated (Control) and the other was treated with INTERCEPT Small Volume (SV) Platelet Processing Set (Test). Both Test and Control PCs were stored with constant agitation at 22-24°C. Samples were withdrawn from the pool, and at Day 5 and Day 7 of storage post donation for analyses. Blood gases, pH, ATP, morphology, extent of shape change (ESC), hypotonic shock response (HSR), p-selectin expression, swirl and platelet lysis were measured along with the capacity of the platelets to support thrombin generation in a calibrated automated thrombogram assay (CAT, Stago). A panel of coagulation proteins was also measured. Six independent replicates were performed. Test PCs were compared to paired Control PCs using t-test and ≤ 20% bioequivalence.

RESULTS/FINDINGS: Test PCs and untreated Control PCs had similar metabolic parameters, morphology scores, pH22°C, ESC, HSR, swirl scores over 7 days of storage. % Corrected lysis for Test PCs (Day 5; 1.1 ±0.2 %, Day 7; 1.8 ±0.4 %) were statistically higher than Control PCs (Day 5; 0.2 ±0.1%, Day 7; 0.4 ±0.1%). Test PCs (Day 5; 43.2 ±7.3%, Day 7; 60.0 ±11.0%) showed increased p-selectin surface expression compared to Control PCs (Day 5; 29.8 ±3.1 %, Day 7; 44.6 ±5.1%). In the CAT assays, Test PCs (Day 5; 2,244.74 ±551.18 nM.min, Day 7; 2,042.18 ±657.80 nM.min) had similar endogenous thrombin potential (ETP) compared to Control PCs (Day 5; 2,250.53 ±468.99 nM.min, Day 7; 1,957.50 ±396.33 nM.min). Peak height (Test: Day 5; 160.02 ±47.81 nM, Day 7; 144.92 ±43.70 nM, Control: Day 5; 158.95 ±43.58 nM, Day 7; 142.23 ±13.49 nM) and lag time (Test: Day 5; 8.67 ±1.26 sec, Day 7; 8.11 ±0.82 sec, Control: Day 5; 9.78 ±1.71 sec, Day 7; 8.91 ±0.99 sec) were also similar. Further, no significant differences were measured in key coagulation proteins FV, FVIII, FVII between Test and Control PCs.

CONCLUSIONS: Amotosalen/UVA treated PCs suspended in 100% plasma showed a similar ability to generate thrombin as Control PCs. A small but significant and equivalent loss of ETP occurred between Day 5 and Day 7 of storage in Test and Control platelets suggesting that both had the ability to support thrombin generation after 7 days of storage. Our *in vitro* results assays suggest amotosalen/UVA treated platelets maintain hemostatic function after 5- and 7-day storage.

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US. Clinical trials are in progress: ClinicalTrials.gov Identifier: NCT04022889.

Amotosalen/UVA Treatment of Apheresis PC Using the INTERCEPT Platelet Processing Set with Triple Storage Containers Inactivated Bacteria to Sterility after 7 Days of Storage

Thea Lu, Pallavi Nahata, Melissa McCormack, Bianca Muñoz, Marina Besprozvannaya, Josh Ison, Peter Bringmann

Cerus Corporation, Concord, California, USA

BACKGROUND/CASE STUDIES: The INTERCEPT™ Blood System for platelets has been developed for the inactivation of pathogens and leukocytes in platelet concentrates (PC). The system utilizes amotosalen and UVA light and is available for the treatment of apheresis and Whole Blood (WB) derived platelets in Europe, and the treatment of apheresis platelets in the US (TRIMA™ in 100% plasma or AMICUS™ for 65% PAS). The INTERCEPT Platelet Processing Set with Triple Storage (TS) containers (CE Marked and in development in the US) would allow INTERCEPT treatment of double or triple dose single-donor apheresis or pooled WB platelet components. The objective of the study was to evaluate the inactivation of 11 bacteria using the INTERCEPT Blood System for platelet TS set at high PC volume and dose through 7 days of storage post- donation to assess sterility.

STUDY DESIGN/METHODS: Apheresis PC were pooled and resuspended in 65% PAS, yielding ~720 mL of platelets with dose of 6 to 14 × 10^{11} platelets per component. Every PC was spiked with each strain at a different titer. to define the threshold that can be inactivated to sterility. The contaminated units were amotosalen/UVA treated in an INTERCEPT TS kit and PC were split and stored in three INTERCEPT storage containers. Samples were taken: pre- and post-inactivation treatment, post-CAD , and at 3, 5 and 7 days of storage. Samples were analyzed by plating with media appropriate for each strainbacteria (100µL-10 mL). The remainder from each storage bag was added to flasks in a sample to media ratio of 50:50.

RESULTS/FINDINGS: Treatment of contaminated platelets with amotosalen resulted in bacterial inactivation to the limit of detection. No viable bacteria were detected up to day 7 when the input titer displayed in Table 1 were used. (**Table 1**). Pathogen reduction to sterility was supported by sampling the entire platelet unit.

CONCLUSIONS: This study evaluated the inactivation of 11 bacteria using the INTERCEPT Platelet Processing Set with Triple Storage (TS) containers. Bacteria at specified input titers were treated with amotosalen/UVA and inactivation was confirmed throughout 7-day storage using whole unit sampling. These results define the bacterial input titer that the INTERCEPT Blood System for Platelets is capable of inactivating to sterility.

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US. Clinical trials are in progress: ClinicalTrials.gov Identifier: NCT04022889. The INTERCEPT Blood System triple storage container set is not approved in the U.S.

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Table 1: Bacterial Inactivation in INTERCEPT Treated platelets with Sampling to 7 Days Storage

Bacteria	Input Titer (log cfu/mL)	Titer (cfu/mL)		Inactivation Titer (log cfu/PC)
		Post-illumination	Day 7	
K. pneumoniae	3.4±0.2	0.0±0.0	0.0±0.0	>6.2±0.2
E. cloacae	6.8±0.8	0.0±0.0	0.0±0.0	>9.7±0.8
E. coli	6.0±0.7	0.0±0.0	0.0±0.0	>8.9±0.7
S. aureus	7.1±0.8	0.0±0.0	0.0±0.0	≥10.0±0.8
S. epidermidis	6.8±0.7	0.0±0.0	0.0±0.0	>9.6±0.7
S. pyogenes	6.2±0.4	0.0±0.0	0.0±0.0	>9.1±0.4
C. perfringens	6.1±0.6	0.0±0.0	0.0±0.0	>8.9±0.6
P. aeruginosa	6.8±0.1	0.0±0.0	0.0±0.0	≥9.6±0.1
S. choleraesuis	7.2±0.1	0.0±0.0	0.0±0.0	≥10.0±0.1
L. delbrueckii	5.7±0.3	0.0±0.0	0.0±0.0	>8.5±0.3
C. koseri	7.1±0.1	0.0±0.0	0.0±0.0	>10.0±0.1

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US. Clinical trials are in progress: ClinicalTrials.gov Identifier: NCT04022889. The INTERCEPT Blood System triple storage container set is not approved in the U.S.

Hemovigilance Data Track the Safety of Amotosalen/UVA Platelets in France Over 9 Years and Contribute to Post-Market Surveillance Requirements

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BACKGROUND/CASE STUDIES: Medical device regulators require manufacturers to document significant changes in the frequency or severity of adverse events related to approved devices. France's health authority, ANSM, collects data on transfusion reactions (TRs) via a national hemovigilance (HV) system. Cerus Corporation, manufacturer of the INTERCEPT (amotosalen/UVA) pathogen reduction system for platelets (PLTs), tracks TRs in France via annual ANSM reports. An analysis of TRs possibly, probably or certainly related to PLTs (all severity grades) in France is presented for 2 time periods – 2010-14 (P1) and 2015-18 (P2) – during which France transitioned from a partial to a 100% amotosalen/UVA PLT supply.

STUDY DESIGN/METHODS: PLT and TR data were manually extracted from ANSM HV reports. TRs were stratified by frequency. TR counts were extrapolated from published rates and annual PLT totals. TR rates per 100,000 PLTs were transformed into proportions. Regression analysis was performed on all years. Mean annual percent changes for the top 5 TRs and number of PLTs issued per year were compared for both periods. Chi-square testing assessed annual changes.

RESULTS/FINDINGS: Average annual increases in issued PLTs declined from 2.3% (P1) to 1.5% (P2) per year (p=0.66). Above average annual increases occurred in both periods (P1: 2011 (+5.2%), 2012 (+2.7%); P2: 2018 (+3.8%)). The proportion of amotosalen/UVA PLTs ranged from 7.9%-8.5% in P1 and 11% -99.9% in P2. Overall TR rates declined from 526 to 396.4 per 100,000 PLTs issued. Allergic reactions declined significantly from 2010-18; there were no significant trends in the other top 5 TRs. Severe or life-threatening TR rates were stable (2012-18). Statistically significant annual increases occurred in FNHTR (2013) and immunologic incompatibility (2015). Significant annual declines occurred in allergic reactions (2011, 2012), alloimmunization (2018) and ineffective transfusions (2011, 2017). Mean annual percent changes for the top 5 TRs were not statistically different in P1 and P2. Transfusion-transmitted bacterial infection (TTBI) rates declined from 2.9 (2010) to 0 (2018) per 100,000 PLTs issued. No TTBI were reported in amotosalen/UVA PLTs.

CONCLUSIONS: HV data from France document a period of stability for the top 5 TRs with no significant differences in TR rates between 2 time periods during which France transitioned to 100% amotosalen/UVA PLTs. The number of PLTs issued annually grew 15% between 2010-18; however, rates of annual growth in P1 and P2 were statistically stable. The single year increase in PLTs issued in 2018 bears monitoring. This analysis shows how national HV data can contribute to post-market surveillance requirements. Limitations include variable TR reporting rates by facility.

Costs and Reimbursements for Bacterial Risk Control Strategies for Platelets: Results from a Hospital Budget Impact Model

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BACKGROUND/CASE STUDIES: Evolving FDA guidance pertaining to bacterial risk control strategies (BRCS) for platelets presents challenges in understanding the costs of these options. The objective of this analysis was to compare costs and shelf life impact of these BRCS from the perspective of a mid-sized US hospital transfusion service.

STUDY DESIGN/METHODS: A previously published Excel-based hospital platelet budget impact model was updated to include all new BRCS per the Dec. 2018 and Sept. 2019 FDA draft guidances. Four scenarios were generated to compare annual costs of acquisition, wastage, dispensing/transfusion, and septic adverse events for a hospital that purchases 100% of its platelet components (PCs): 1) 100% conventional (C-PC), 2) 100% large volume delayed sample (LVDS) ≥36 hour hold, 3) 100% pathogen-reduced (PR), 4) mix of 75% PR/25% LVDS. Model assumptions were informed by published literature and a prior national survey of hospital transfusion services. Costs are presented in $US 2019.

Model Assumptions

- 3,016 5-day apheresis PC purchased annually
- 60.7% of non-PR PC are irradiated by supplier
- Supplier's add-on NAT testing cost for emerging diseases is $7.50/unit
- PR replaces irradiation, CMV testing, secondary bacterial detection strategies, and emerging disease testing
- Secondary bacterial testing is not considered
- 26.3% of PC are outpatient transfusions (reimbursable) with half of transfusions billed to private insurance and half to CMS, 200% markup above unit cost for private insurance, and 75% payment for private insurance charges
- Unit costs
    - *C-PC* $557.70 non-irradiated; $607.70 irradiated
    - *LVDS* $585.59 non-irradiated; $638.05 irradiated
    - *PR* $665.20
- Mean age at time of receipt from supplier is 3 days for C-PC and LVDS and 2.37 days for PR
- Sepsis costs $80,000/case with probabilities of 1:10,288 for non-PR, 0 for PR

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RESULTS/FINDINGS:

Table 1: Annual Costs, Outpatient Reimbursements, and Shelf Life Impact

	100% C-PC	100% LVDS	100% PR	75% PR/ 25% LVDS
ANNUAL COSTS				
Acquisition	$1,795,643	$1,884,237	$2,006,243	$1,975,742
Wastage (expiration)	$126,200	$132,460	$90,043	$100,647
Wastage (mishandling)	$58,573	$61,478	$55,221	$56, 786
Dispensing and transfusion	$106,808	$106,808	$106,808	$106,808
Sepsis	$20,869	$20,869	$0	$5,217
Total hospital cost	**$2,108,093**	**$2,205,852**	**$2,258,315**	**$2,245,200**
ANNUAL OUTPATIENT REIMBURSEMENTS	**$671,858**	**$695,183**	**$744,158**	**$731,915**
SHELF LIFE IMPACT				
Mean age at acquisition (days)	3.00	3.00	2.37	2.53
Maximum usable platelet life (days)	2.00	2.00	2.63	2.48

CONCLUSIONS: After offsetting annual costs by reimbursements, the model predicts cost increases of 5.4% for PR versus C-PC, 0.2% for PR versus LVDS, and 0.2% for the mixed scenario with 75% PR/25% LVDS versus 100% LVDS. The 100% PR scenario represents an increase in usable shelf life of 31.7% versus 100% C-PC and 100% LVDS, and 6.4% versus the mixed scenario. Economic models are important tools for hospitals considering novel technologies.

Replacement of Vector-Borne Disease Deferrals by Robust Pathogen Reduction Technology (PRT): A Study Based on Pathogen Loads in Blood Donors and Inactivation Efficacy

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BACKGROUND/CASE STUDIES: Amotosalen (A)/ultraviolet A light (UVA) PRT reduces infectious pathogen levels in plasma and platelets. Food and Drug Administration (FDA) allows A/UVA PRT as an alternative to donor screening for Zika virus, Babesia, and most recently malaria. Similar considerations could be given to other vector-borne pathogens. We compared the highest pathogen loads observed in blood donors to A/UVA PRT inactivation capacity for West Nile virus (WNV), *B. microti, P. falciparum* and *T. cruzi*, and donor retention if A/UVA PRT was used as an alternative to deferrals.

STUDY DESIGN/METHODS: Antibody status and pathogen loads were collected from US blood donors identified as NAT-positive for WNV (n=1,683) and *B. microti* (n=89). Maximum infectivity titers were derived from maximum pathogen loads and aligned with PRT $\log_{10}$ reduction factors (LRF)/mL. Donor retention after removal of deferrals for vector-borne agents were estimated at the American Red Cross for 2019 based on: *B. microti* NAT reactives in 14 states plus DC (assuming rates of 1:1000-1:100,000 and 1,613,301 tested donations in those states), malaria deferrals (1 yr+3 yr) for all donor presentations, WNV NAT reactive results for 4,618,585 donations (deferrals based on a 3-year average due to annual variation), and *T. cruzi* antibody reactive results for 920,939 total donations.

RESULTS/FINDINGS: Maximum pre-seroconversion pathogen loads in blood donors and associated maximum infectivity titers for WNV and *B. microti* were compared to infectivity LRFs for A/UVA (**Table**). A/UVA PRT reduced the infectivity level of WNV and *B. microti* to comparable levels as those recognized by FDA as suitable to replace other donor screening strategies (babesiosis and malaria). If donors identified in 2019 with a risk of WNV (n=164), babesia (n=231), malaria (n=30,504), or Chagas disease (n=943) were converted into apheresis platelet donors treated with A/UVA PRT, up to 31,842 donors could be retained, each able to donate multiple donations (average 5/year) for up to 318,420 additional doses/year.

CONCLUSIONS: Robust A/UVA PRT as the sole intervention provides an opportunity to replace donor health questions (malaria), selective antibody detection (*T. cruzi*), and NAT for vector-borne pathogens (WNV and *B. microti*) and enables significant donor retention increasing platelet availability.

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	Pathogen load in blood donors			A/UVA PRT LRF (Log/mL)			U.S. mitigation strategies	# of deferred donors
	Max Copies Log/mL	Ratio infectivity/ copies	Max infectivity Log/mL	PLT PAS	PLT 100%	Plasma		
WNV	5.8	1/100	3.8	>6.3	>6.3	>5.5	MP-NAT/ ID-NAT	164
B. microti	4.0	1/10	3.0	≥4.9	>4.5	≥4.9	Deferral, ID-NAT, PRT	231
P. falciparum	NA	NA	NA	≥6.6	>6.7	>6.5	Deferral, PRT	30,504
T. cruzi	NA	NA	NA	≥7.8	>8.4	>6.7	Deferral, first time serology	943

Is the BEST Protocol the Best for Preparing Stored Apheresis Platelets for Radiolabeled Recovery and Survival Studies?

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BACKGROUND/CASE STUDIES: *In vivo* recovery and survival studies are currently required by FDA for evaluating platelet function. Radiolabeled platelets from Test product (e.g., apheresis platelets after 7 days storage) are compared with fresh whole-blood-derived (WBD) platelet Controls, using either Cr51 or In111 to track platelet recovery and survival *in vivo*. The recommended protocol (the Biomedical Excellence for Safer Transfusion (BEST) protocol) for platelet preparation before radiolabeling includes addition of ACD-A (pH 4.9) followed by a soft spin to remove contaminating red blood cells (RBC). Cerus has shown this step to result in platelet loss and increased platelet activation that may impact *in vivo* platelet viability.

The hypothesis that omitting the ACD-1 addition/soft spin step for apheresis platelet (AP) preparations (Variant 1 protocol) results in improved platelet physical recovery without significantly increasing RBC and WBC contamination compared to the BEST method, was tested.

STUDY DESIGN/METHODS: RBC and WBC content of fresh control WBD platelets and stored INTERCEPT®- AP prepared by the BEST method was compared to INTERCEPT-AP using Variant 1. RBC content in platelet preparations were measured using three methods; a) automated hematology counters, b) manual hemocytometry, and c) flow cytometry-based measurement of CD235a antibody. WBC counts were assessed using flow cytometry-based BD Leucocount™ kit that stains nucleated cells.

RESULTS/FINDINGS: RBC and WBC content for WBP prepared by the BEST method (Day 1), INTERCEPT® treated AP prepared using the BEST method and INTERCEPT® AP prepared by Variant 1 method (Day 7) are summarized in **Table 1**. The mean % adjusted residual platelet recoveries of platelets prepared by BEST method (Day 1: 79±11%; Day 7: 78±5%) were significantly lower than AP prepared by Variant 1 method (Day 1: 98 ±6%; Day 7: 93±4%).

CONCLUSIONS: The BEST method results in a significant loss of platelets during preparation. AP prepared by both BEST and Variant 1 methods contained fewer RBC and WBC than WBP prepared using the BEST method. Lower platelet recovery may indicate that the BEST procedure biases the outcome of recovery and survival studies using apheresis platelets by selecting for a subpopulation of platelets that may not be reflective of the normally transfused platelet population.

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US. Clinical trials are in progress: ClinicalTrials.gov Identifier: NCT04022889.

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Table 1: Characterization of Platelet, RBC and WBC Counts

Assay	Fresh WBP (N = 12)		INTERCEPT AP (Day 7) (N = 12)		Variant 1
	Input	BEST	Input	BEST	
Automated Platelet Count, 10^3/µL	214±53	1376 ±597	1111 ±148	2422 ±372	3446 ±419[1]
Automated RBC Count, 10^3/µL	3904±286	169 ±85	100 ±23	165 ±40	248 ±44[1]
Flow Cytometry based RBC count, 10^3/µL	3926±463	0.19 ±0.22	0.01 ±0.02	0.02 ±0.03	0.11 ±0.10[1]
Flow Cytometry based WBC Count, /µL	6603±1220	37±36	0.1±0.1	0.1±0.1	0.2 ± 0.3

1 significant between Day 7 BEST vs Variant 1

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US. Clinical trials are in progress: ClinicalTrials.gov Identifier: NCT04022889.

Efficient Inactivation of SARS-CoV-2 in Human Plasma with Amotosalen and Ultraviolet A Light Treatment

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BACKGROUND/CASE STUDIES: Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was identified in January 2020 as the responsible agent for COVID-19. First recognized in late 2019, the COVID-19 epidemic developed into a pandemic with , as of July 23rd, 2020, more than 15 million cases and 600,000 deaths reported globally. SARS-CoV-2 RNA was detected in blood samples and blood components from asymptomatic blood donors including frozen plasma units and platelet concentrates. This suggests that SARS-CoV-2 may be a potential blood-borne pathogen and pathogen reduction offers potential to reduce the risk of transfusion transmission. We investigated the efficacy of amotosalen/UVA light to inactivate SARS-CoV-2 in human plasma.

STUDY DESIGN/METHODS: Five pools of whole-blood derived human plasma units (630-650 mL each) were inoculated with a local clinical isolate (SARS-CoV-2/human/SAU/85791C/2020) with a 1:100 dilution. Spiked pools were used to evaluate the efficacy of amotosalen/UVA treatment (INTERCEPT® Blood System, Cerus Corporation, Concord, U.S.A.) to inactivate SARS-CoV-2 in plasma. Infectious and genomic viral titers were assessed by plaque assay and quantitative PCR (Altona Diagnostics, Hamburg, Germany), respectively, in spiked and treated samples in parallel with positive and negative controls.

RESULTS/FINDINGS: Treatment of spiked plasma (titer of the viral stock: 5.6 ±0.2 $\log_{10}$ pfu/mL) with amotosalen/UVA light resulted in complete inactivation of infectious viral titer with mean log reduction of >3.3±0.2 $\log_{10}$ pfu/mL. No viral replication or cytopathic effect (CPE) was observed in cells inoculated with inactivated samples even after 9 days of incubation and three successive passages. Evaluation of genomic titer expressed in genome equivalent (GEq/mL) in inactivated samples showed equivalent reduction to the limit of detection of 7.10±0.2 $\log_{10}$ GEq/mL.

CONCLUSIONS: Complete and efficient inactivation of SARS-CoV-2 was observed with amotosalen/UVA light treatment of spiked human plasma units suggesting that treatment of plasma with this pathogen reduction technology could reduce the risk of transfusion-transmitted SARS-CoV-2 infection. These findings are consistent with prior inactivation data with amotosalen/UVA for other human-pathogenic coronaviruses (SARS-CoV-1 and MERS-CoV) in platelets and plasma.

Evaluation of Amotosalen-UVA Pathogen Reduced Plasma Prepared with a DEHP Free Processing Set

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BACKGROUND/CASE STUDIES: The INTERCEPT® Blood System for plasma was approved by the FDA in December 2014 for the *ex vivo* preparation of pathogen-reduced, whole blood derived (WBD) or apheresis (Aph) plasma in order to reduce the risk of transfusion-transmitted infection (TTI) and as an alternative to gamma irradiation for prevention of transfusion-associated graft versus host disease (TA-GVHD). This study was conducted at two US blood centers to characterize the *in vitro* coagulation function INTERCEPT plasma prepared using a new DEHP-free INTERCEPT processing set for plasma.

STUDY DESIGN/METHODS: Plasma inputs (N=64) were pools of ABO matched WBD or Aph plasma (single donation or pooled). Control (C) units consisted of 180 to 220 mL of plasma and the Test (T) article consisted of plasma (585 to 650 mL) processed using the INTERCEPT Blood System for plasma to produce 3 final T components. Paired WBD T and C plasma were frozen ≤24 hours of donation (PF24) while Aph pairs were frozen ≤ 8 hours (FFP) and stored at ≤ -18°C for a ≥30 days. Paired T and C components were thawed, and samples frozen at ≤-65°C until analysis for coagulation.

RESULTS/FINDINGS: All T units met the FDA criteria ≥0.4IU/mL for protein S and alpha-2-plasmin inhibitor. At least one of 64 T and C pairs exceeded the ±20% bioequivalence criterion for all indices except pH, osmolality, total protein, prothrombin time, thrombin generation, FII, FV, ADAMTS-13 (functional), ATIII, Protein C and FVIIa. T demonstrated therapeutic levels of fibrinogen and thrombin generation, while excessive activation of the coagulation cascade was not exhibited (**Table 1**).

CONCLUSIONS: INTERCEPT Plasma demonstrated properties consistent with the hemostatic efficacy of conventional PF24 or FFP with the benefit of pathogen reduction and leukocyte inactivation.

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Table 1: T and C Components Characteristics

	WBD PF24 (N=33)		Aph FFP (N=31)	
Parameter	**T**	**C**	**T**	**C**
PT(s)	12.7 ±0.6	11.9 ±0.5	11.8 ±0.6	11.1 ±0.6
APPT(s)	30.9 ±2.0	28.1 ±1.5	28.8 ±2.0	26.5 ±1.6
Thrombin Generation ETP[a] (nM·min)	2168 ±227	2405 ±275	2667 ±310	2870 ±311
Fibrinogen (g/L)	2.0 ±0.2	2.6 ±0.3	2.2 ±0.4	2.7 ±0.5
FII (IU/mL)	0.9 ±0.1	1.0 ±0.1	0.8 ±0.1	1.0 ±0.1
FV (IU/mL)	0.9 ±0.1	1.0 ±0.1	0.9 ±0.1	0.9 ±0.2
FVII (IU/mL)	0.7 ±0.1	0.8 ±0.1	0.8 ±0.2	0.9 ±0.2
FVIII (IU/mL)	0.7 ±0.2	0.9 ±0.2	0.8 ±0.2	1.1 ±0.3
FIX (IU/mL)	0.8 ±0.1	1.0 ±0.1	0.8 ±0.1	1.0 ±0.2
FX (IU/mL)	0.8 ±0.1	0.9 ±0.1	0.8 ±0.1	0.9 ±0.2
vWF activity (IU/mL)	1.1 ±0.3	1.1 ±0.3	1.2 ±0.4	1.2 ±0.3
Antithrombin III (IU/mL)	1.0 ±0.1	1.0 ±0.1	0.9 ±0.1	1.0 ±0.1
Protein C (IU/mL)	0.9 ±0.1	1.0 ±0.1	0.9 ±0.1	1.0 ±0.1
Protein S (IU/mL)	0.9 ±0.1	0.9 ±0.1	0.8 ±0.2	0.9 ±0.2
Alpha-2-plasmin inhibitor (IU/mL)	0.9 ±0.1	1.1 ±0.1	0.9 ±0.1	1.1 ±0.1
Thrombin-Antithrombin Complexes (µg/L)[b]	4.3 ±5.8	4.6 ±6.2	3.7 ±8.2	3.9±8.8
FVIIa (ng/mL)[b]	3.1 ±0.0	3.1 ±0.0	3.1 ±0.0	3.1 ±0.0
C3a (ng/mL)	197 ±173	299 ±158	152 ±145	243 ±157

a Endogenous Thrombin Potential (5 pM tissue factor)

b Units below the lower limit of quantification (LLQ) were assigned to a value of the LLQ for data summary.

The Effect of Freezing Amotosalen-UVA Treated Plasma 8, 16, and 24 Hours Post-Collection on Coagulation Factor Retention in Cryoprecipitate

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BACKGROUND: The INTERCEPT® Blood System for plasma uses amotosalen and UVA light for pathogen reduction (PR) of donated plasma to reduce the risk of transfusion-transmitted infections due to viruses, bacteria, and protozoa and to inactivate leukocytes. PR Cryoprecipitate (Cryo) can be produced by precipitation of cold-insoluble proteins from frozen PR plasma. Conventional cryo, once thawed, has a 4-6 hour shelf-life due in part to the risk of bacterial contamination and proliferation post-thaw. Preparation of PR Cryo from PR plasma may provide an opportunity to extend the post-thaw shelf-life to 5 days.

STUDY DESIGN: This study examined the effect of freezing PR plasma at 8, 16, and 24 hours post whole blood (WB) collection on the retention of coagulation factors in thawed PR Cryo held at 20-24°C for up to 120 hours. Six replicates, each consisting of 6 pooled plasma donations, were prepared. Each plasma pool was split into 3 input units for INTERCEPT® treatment followed by freezing at 8, 16, and 24 hours post WB-collection, respectively, and subsequent cryo preparation. Plasma samples were collected from input units prior to PR treatment and post-treatment for FBN and FVIII levels. Thawed cryo was sampled immediately post-thaw and out to 120 hours post-thaw for a wider panel of assays, including Factor XIII, vWF, thrombin generation, and ROTEM.

RESULTS: There was no measurable decline in plasma FBN levels when freezing was postponed from 8 hours thru 24 hours whereas a 15% loss of FVIII activity on average was observed with each 8 hours that freezing was postponed. All thawed PR Cryo components met the target ≥300 mg of FBN per unit, even at 120 hours post-thaw. The additional *in vitro* functional characteristics assessed were also stable with no significant differences between the PR cryo components prepared from PR plasma frozen at different intervals (**see table**).

Table 1. Summary of Results (Avg ± stdev)

Post-collection freezing time (hours)	PR Cryo (T=120 hours post-thaw)					
	FBN (mg/unit)	FVIII (IU/unit)	FXIII (mg/unit)	vWF ristocetin (IU/unit)	MCF ROTEM (mm)	ETP CAT (nM•min)
8	670 ±82	204 ±47	492 ±62	296 ±57	56 ±6	1881 ±124
16	611 ±146	190 ±27	420 ±119	235 ±39	53 ±7	1763 ±167
24	608 ±109	192 ±38	420 ±66	298 ±39	55 ±7	1907 ±226

CONCLUSIONS: This study demonstrates that the combination of pathogen reduction and delayed freezing of plasma from 8 hours to 24 hours produces PR cryo with acceptable fibrinogen concentrations, *in vitro* functional characteristics, conversion of fibrinogen to fibrin, and integrated hemostatic capacity for thrombin generation. This indicates that the preparation method for PR cryo could be extended to allow for the freezing of plasma 16 hours later than what is currently recommended for conventional cryo.

Pathogen Reduced Cryoprecipiate Prepared from Whole Blood Derived Plasma Frozen within 24 Hours

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BACKGROUND/CASE STUDIES: Cerus Corporation has developed a process for preparation of INTERCEPT® pathogen reduced Cryoprecipitate (PR-Cryo) from INTERCEPT plasma, without requiring any changes to the INTERCEPT plasma treatment process. An interim processing container has been developed to freeze INTERCEPT plasma and aid in preparation of PR-Cryo. Prior to freezing, pools of up to 325mL of PR-Cryo can be made to reduce product variability and to facilitate clinical use.

STUDY DESIGN/METHODS: Pools of two ABO matched whole blood derived (WBD) plasma, 585 to 650 mL, were processed using the INTERCEPT Blood System for plasma and frozen in the INTERCEPT Cryo Processing Container (ICPC) within 24 hours (h) of WB collection. After 1 to 26 days storage at ≤ -18°C, the plasma was thawed at 4°C. Following centrifugation, supernatant was drained into two storage containers, 60 to 100mL of supernatant was used to suspend the PR-Cryo pellet. PR-Cryo pellets from a single, 2 or 4 ICPCs (2, 4 or 8 WBD plasma units, respectively) were transferred to an INTERCEPT plasma storage container, frozen at ≤-55°C and then stored at ≤-18°C for ≥30 days post-WB collection. PR-Cryo components were thawed and stored at 20-24°C for up to 120h. Samples were collected at 0 and 120h post-thaw for characterization of *in vitro* function and quality.

RESULTS/FINDINGS: Based on regulatory requirements that conventional cryo from a single WBD unit contain ≥150mg fibrinogen, all PR-Cryo components met the acceptance criteria of ≥300, 600 or 1200mg/unit for fibrinogen at 0h and over 120h of storage at 20-24°C. The mean retention of activity or concentration after 120 h post-thaw storage at 20-24°C compared to the t=0h was >80% for Fibrinogen, Factor VIII, Factor XIII antigen, vWF antigen, vWF activity, thrombin generation ETP and ROTEM MCF.

CONCLUSIONS: These results show acceptable *in vitro* functional characteristics, conversion of fibrinogen to fibrin and integrated hemostatic capacity for thrombin generation of INTERCEPT PR-Cryo from WBD INTERCEPT ≥30 days of frozen storage at ≤-18°C and over 5 days of storage at room temperature post-thaw for INTERCEPT PR-Cryo components.

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Table 1: *In Vitro* Characterization of PR Cryo

Parameter	PR-Cryo Type (number WBD Plasma Units in Pool)	Duration of Storage at 20°C to 24°C (h)	
		0 (Thaw)	120
Volume (mL)	2	81 ±8	-
	4	148 ±11	-
	8	279 ±24	-
Fibrinogen (mg/unit)	2	777 ±177	716 ±162
	4	1481 ±278	1378 ±248
	8	3174 ±516	2996 ±559
Factor VIII (IU/mL)	2	3.28 ±0.95	2.97 ±0.83
	4	3.24 ±0.88	2.96 ±0.82
	8	3.09 ±0.63	3.03 ±0.63
vWF Antigen (IU/mL)	2	7.14 ±2.49	7.33 ±2.54
	4	7.10 ±1.60	7.28 ±1.75
	8	7.36 ±0.21	7.57 ±1.29
vWF Activity (IU/mL)	2	5.25 ±1.75	4.19 ±2.03
	4	4.11 ±2.09	3.54 ±1.27
	8	3.51 ±1.19	3.26 ±1.41
FXIII Antigen (mg/dL)	2	6.3 ±1.3	6.2 ±1.4
	4	5.3 ±1.6	5.3 ±1.6
	8	6.4 ±1.7	6.4 ±1.7
ETP (nM·min)	2	1877 ±213	1827 ±198
	4	1835 ±173	1838 ±175
	8	1982 ±226	1975 ±201
MCF (mm)	2	55 ±9	58 ±9
	4	58 ±5	59 ±6
	8	61 ±6	62 ±7

**2 Pool n=36; 4 Pool n=16; 8 Pool n=16*

Screening for SARS-CoV-2 Convalescent Plasma (CPP) in Brazilian Blood Donors: Preliminary Lessons and Proposals to Increase Efficiency

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BACKGROUND/CASE STUDIES: As of May 15th, 2020 there are > 200,000 COVID-19 cases in Brazil, with >13,500 deaths. We started in early April a strategy of collecting convalescent COVID-19 Plasma (CPP) in two leader hospitals in Brazil (volunteer non-remunerated convalescent donors), as support of a case-controlled study for treatment of severe COVID-19.

STUDY DESIGN/METHODS: Convalescent donors with mild or moderate symptoms were summoned by several methods (journals, broadcast, social network, leaflets), containing appropriate information for CPP selection (age 18 - 60 yrs, body weight >55kgs, previous positive RT-PCR - nasopharyngeal swab, and full clinical recovery ≥14 days). Donors were then selected by a series of tests, namely: ABO type +irregular antibodies; infectious markers (HBV, HCV, HIV, HTLV 1-2, Chagas and syphilis); female donors were tested for anti-HLA antibodies. In addition, donors had to undergo a second molecular test for SARS CoV-2 RT-PCT (nasopharyngeal swab and/or peripheral blood-PB); if any of the PCR tests was positive, they were invited to test again after 14 days. If the test remained positive, they were rejected from the program. Donors were also selected by the cytopathic effect-based virus neutralization test (CPE-based VNT) and specific IgM, IgG and IgG nucleoprotein-based SARS-CoV-2 ELISAs.

RESULTS/FINDINGS: 253 donors volunteered for the program (41 females, 212 males), with neutralizing antibodies (neutr abs) available in 229 cases. The final percentage of negative donors by PCR (swab or PB) was 67.8% and 88.4%, respectively (p=0.92). However, 42/155 (27.13%) PCR-ve and 18/74 (24.3%) PCR+ve donors had their final definition >28-days after full recovery, raising concern about this policy safety. In addition, 6/18 of reactive donors cleared only between 35-42 days. As for neutr abs, titers ≥80 or ≥160 were found in 76.9% and 65.1% of donors, respectively. There was a strong correlation (signal/cut-off - S/CO) between neutr abs and Ig levels, mainly for IgG. The probability of S/CO ≥5.0 with neutr abs ≥80 or ≥160 was respectively 86.4% and 79.7%. Finally, if we combine the final PCR negative with neutr ab ≥80 or ≥160, the final number of accepted donors was 117 (44.5%) or 98 (37.2%), respectively. So far, we have collected a total of 411 CPP units, where 66% were pathogen inactivated, and already transfused 59 patients.

CONCLUSIONS: We are still uncertain about the therapeutic role of CPP for severe COVID-19, but our strategy proved its viability in our region. However, there is a concern whether the 28-day period after full recovery could be considered safe, since 24.3% of PCR positive cases were cleared from 28 to 42 days.

Preservation of SARS-CoV-2 Neutralizing Antibodies (nAb) or Anti-Nucleocapsid Proteins (NP) in Convalescent Donor Plasma (CCP) Treated With Amotosalen/UVA Illumination (A/UVA)

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BACKGROUND/CASE STUDIES: Convalescent plasma (CCP) has been used for therapy in severely symptomatic COVID-19 patients. Pathogen reduction (PR) has been proposed to mitigate the risk of transfusion-transmitted infectious agents. We investigate the impact of A/UVA on nAbs and anti-NP (IgM, IgG and IgA) PR treatment of CCP units.

STUDY DESIGN/METHODS: Plasmapheresis CCP units (600 mL) were collected from a cohort of previously confirmed male RT-PCR positive [+ve] COVID-19 mild/moderate convalescent patients, all first-time and non-remunerated volunteers, with >14 days after full recovery of symptoms. CCP units were treated with INTERCEPT Blood System (Cerus Corporation, Concord, USA) according t manufacturer's instructions, either individually or pooled two by two. After treatment, units were separated into 200 mL doses. Pre- and post-PR treatment samples were harvested and kept at 4°C for 3-5 days prior to testing for nAb titers using a CPE-based virus neutralization assay (GenBank: MT MT350282), and specific IgM, IgG and IgA anti-NP antibodies by ELISA.

RESULTS/FINDINGS: A total of 16 individual and 94 pooled units were treated (n=110 CCP donations), rendering 330 x 200 mL treated CCP therapeutic doses. There were no statistical differences in samples harvested before versus after A/UVA treatment (all p>0.05, Wilcoxon test) for nAb titers or IgM, IgG and IgA anti-NP absorbance levels, as shown in the table.

CONCLUSIONS: Anti-NP IgM, IgG, IgA, and nAbs are not adversely impacted by A/UVA treatment, suggesting this PR technology can be employed to mitigate the risk of transfusion-transmitted infections after collection of CCP donors, who are often first time blood donors. With most CCP units destined to treat older, immunosuppressed patients with several comorbidities, the use of A/UVA PR treatment is not only safe and recommended, while preserving anti-SARS-CoV-2 antibodies in CCP units.

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Table

	nAb (titer)				IgM (absorbance)			IgG (absorbance)			IgA (absorbance)		
	pre (1)	pre (2)	post (1)	post (2)	pre (1)	pre (2)	post	pre (1)	pre (2)	post	pre (1)	pre (2)	post
Single (n=16), all p=NS (Wilcoxon test)													
mean (± sd)	440 (597)	NA	440 (597)	NA	0.3 (0.4)	NA	0.3 (0.4)	2.9 (1.1)	NA	2.9 (1.1)	0.4 (0.2)	NA	0.4 (0.2)
median	320	NA	320	NA	0.2	NA	0.2	3.2	NA	3.2	0.4	NA	0.4
range	80-2560	NA	80-2560	NA	0.1-1.5	NA	0.1-1.5	0.3-4.0	NA	0.3-4.0	0.1-0.8	NA	0.1-0.8
Pool (n=45, all p=NS (Wilcoxon test)													
mean (± sd)	557 (650)	771 (1580)	541 (653)	530 (642)	0.2 (0.1)	0.2 (0.2)	0.2 (0.1)	2.3 (1.2)	2.1 (1.1)	2.3 (1.2)	0.5-0.8	0.5-0.8	0.5
median	320	320	320	320	0.2	0.2	0.2	2.3	2.2	2.3	0.2	0.2	0.2
range	20-2560	40-10240	20-2560	20-2560	0.1-0.7	0.1-0.9	0.1-0.7	0.1-4.0	0.2-4.0	0.1-4.0	0.1 - 4.0	0.1 - 3.1	0.1 - 4.0

nAb (titer) and anti-NP IgM, IgG and IgA (absorbance) from CCP apheresis units (600 mL) before (pre) and after (post) INTERCEPT treatment, either as single units (1) or in pool (1 and 2). NA = non-applicable.

NOTES

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