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PROGRAM OF ABSTRACTS

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POSTER PRESENTATIONS

Meet the Poster Authors: Sunday, October 26, 2025, 12:00 pm – 1:00 pm

Comparison of Automated-Whole-Blood-Processing Derived Pathogen-Reduced Platelets With Apheresis Pathogen-Reduced Platelets

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BACKGROUND/CASE STUDIES: Automated whole-blood processing was introduced in 2018 in our center to facilitate the production workflow and increase product uniformity. To mitigate infectious risk, the automated production process was adjusted for compatibility with amotosalen/UVA pathogen reduction (PR). In all our platelet units 53-68% of the plasma is replaced by PAS to reduce the risk of transfusion reactions (TRALI, allergic reactions, other). Aim of the study is the comparison of quality markers of PR-apheresis platelet concentrates (APCs) and automated whole-blood processing derived, PR-pooled platelet concentrates (PPCs) in 53-68% PAS.

STUDY DESIGN/METHODS: CPD whole blood (average 470 mL) was collected from voluntary donors. Units were processed immediately or after O/N storage using the automated Reveos device (Terumo BCT). Five ABO-identical intermediate platelet units (IPUs) with a target volume of 35 mL each were pooled with 200 mL PAS (T-PAS+, Terumo BCT). Apheresis platelets were collected with a Trima Accel (Terumo) or MCS+ (Haemonetics) device in 53-68% Intersol (Fresenius Kabi). All PCs were pathogen-reduced with amotosalen/UVA (INTERCEPT Blood System, Cerus). The WBC count was assessed with an ADAM-rWBC Analyzer (NanoEnTek Inc.), the platelet count with a DxH 900 or 690T (Beckman Coulter) and the pH with a HI 2212 pH-meter (Hanna Insturments). Blood culture was assessed with a BacT/Alert 3D system (Biomerieux), sampling 8-10 mL per culture bottle. Results are reported as mean ± standard deviation, the p-value was determined with the two-sample t-test.

RESULTS/FINDINGS: In 2023, 13928 PCs were produced (67.5% PR-APCs and 32.5% PR-PPCs), in 2024 14807 PCs were produced (72.2% PR-APCs and 27.8% PR-PPCs). The reduced share of PPCs in 2024 compared to 2023 correlates with a 17.5% reduction of whole blood collections. The average discard rate of IPUs pre-pooling and pre-PR was 20.0% ± 2.2 (reasons: quality, ABO group, positive infectious diseases tests, other). Four units per month per platelet type were sampled 2023 and 2024 for quality control (n=48 per year per PC type) at day 2-3 of storage. The mean PR-APCs platelet dose (3.7×10^{11} ± 0.4) and concentration (1116.5×10^{9}/mL ± 111) in 2023/2024 was significantly higher compared to PR-PPCs (3.4×10^{11} ± 0.4) and (982.11×10^{9}/mL ± 127.66) ($p < 0.001$ for both). The mean pH of PR-APCs (6.7 ± 0.2) and PR-PPCs (6.7 ± 0.2) as well as the mean WBC count (0.3×10^{6} ± 0.2 and 0.3×10^{6} ± 0.4) were not significantly different ($p > 0.05$). All PR-treated units were blood culture negative.

CONCLUSIONS: Automated, whole-blood processing derived PR-PPCs were not significantly different in quality from APCs, the platelet dose per unit was in average 8.1% lower in PPCs. All units met local and AABB guideline requirements.

T cell Inactivation Efficacy: Comparison of Amotosalen-UVA Pathogen Inactivation and Gamma Irradiation Using a Validated EdU Incorporation Assay to Detect T-Cell Proliferation

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BACKGROUND: Transfusion-associated graft-versus-host disease (TA-GVHD) is a rare but fatal complication caused by donor T cell proliferation in immunocompromised blood transfusion recipients. This study compares the efficacy of Amotosalen-UVA pathogen reduction treatment (AMO-UVA PRT) and gamma irradiation in inactivating donor T cells in platelet concentrates. A validated, non-radioactive EdU incorporation assay was used to assess T cell proliferation. Unlike traditional methods that rely on radioactive isotopes (H^3 thymidine assay), the EdU assay utilizes 5-Ethynyl-2'-deoxyuridine (EdU) -a thymidine analog containing an alkyne group - which is incorporated into newly synthesized DNA enabling single-cell detection of proliferating T cells. A fluorescent dye with an azide group is then added and, in the presence of a copper catalyst, an azide-alkyne cycloaddition forms a stable covalent bond between the EdU and fluorophore, labelling proliferating cells and enabling flow cytometry detection.

METHODS: Three-arm pool and split studies were conducted using apheresis-derived platelet concentrates (100% plasma) spiked with 1×10^6 CD3+ T cells/mL. The arms were treated with AMO-UVA PRT using either INT100 Illuminator (UVA 320-400 nm), the recent CE marked INT200 Illuminator (340-350nm), or irradiated with a dose of 2500 cGy gamma rays. Treated units were stimulated with CD3/CD28 Dynabeads, PHA-L, and rhIL-2. Parallel cultures were prepared with no stimulation to serve as unstimulated controls. Donor T cell dilutions were seeded in 96- or 12-well plates, depending on the cell number, with each dilution replicated in 10 wells containing allogeneic stimulator cells. Plates were cultured for 10 days before EdU was added. Cells were harvested the next day for CD3 surface staining and EdU incorporation assay. T cell proliferation was quantified using an Attune™ NxT Acoustic Focusing Cytometer by selecting for CD3+ T cell leukocytes that were labeled with EdU. Twelve replicates using independent T cell donors were performed.

RESULTS: AMO-UVA PRT treatment using both INT100 and INT200 Illuminators resulted in a log reduction of >5.7 ± 0.4 log T cells/mL. Similarly, following treatment with 2,500 cGy dose of gamma irradiation, >5.7 ± 0.4 log T cells/mL were inactivated. No proliferation of T cells was detected following either AMO-UVA PRT treatment or gamma irradiation.

CONCLUSION: Using the validated EdU incorporation assay to detect T cell proliferation, this study demonstrated that both INT100 and INT200 AMO-UVA PRT can effectively inactivate contaminating T cells, with a log reduction of at least 5.7±0.4 log T cells/mL. This inactivation is robust and consistent with that achieved with gamma irradiation.

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Table 1: Inactivation of CD3+ T Cells in Platelets Prepared in 100% Plasma with AMO-UVA PRT Using the INT100 and INT200 Illuminator or Gamma Irradiation

Pre-Treatment Control[a] (Calculated T cells)		AMO-UVA PRT		Gamma Irradiation
		INT100 Illuminator	INT200 Illuminator	
T cell/mL Range	**Log T cell/mL**	**Log Inactivation (T cell/mL)**	**Log Inactivation (T cell/mL)**	**Log Inactivation (T cell/mL)[b]**
Proliferation Detected in any Replicate?		NO	NO	NO
9.6×10^4 to 9.4×10^5	5.0 to 6.2	>5.0 to >6.2	>5.0 to >6.2	>5.0 to >6.2
Mean±SD	**5.7±0.4**	**>5.7±0.4**	**>5.7±0.4**	**>5.7±0.4**

a. Pre-treatment control (calculated T cells) determined using the following equation: (cells/mL added to unit) × (%CD3+ of cell population) × (progenitor frequency)

b. When no proliferation was detected, log inactivation was determined by using the input T cells/mL of the pre-treatment control as the limit of inactivation.

In Vitro Function of Platelets in PAS-3 Treated with INT200 Illuminator Following 7 Days of Storage

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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). A next-generation LED-based illumination device, the INT200, has recently received CE mark approval. The INT200 is not approved in the US. A series of studies was performed to compare the *in vitro* performance of platelets in 35% Plasma/ 65% PAS-3 treated with the INT200, or its predecessor, the INT100, and stored up to 7 days. The INTERCEPT® Blood System for Platelets is currently approved for 5 days in the US.

METHODS: Apheresis PCs in 35% plasma/65% PAS-3 were pooled (N=21) and split into two identical units for treatment with the INTERCEPT Blood System for Platelets. The Control units were illuminated with the INT100 Illuminator and the Test units were illuminated with the INT200 Illuminator. *In vitro* platelet function was evaluated before and after treatment and after 5 and 7 days of storage post-collection.

RESULTS: PCs treated with the INT200 Illuminator (Test) and the INT100 Illuminator (Control) had platelet counts and mean platelet volumes (MPV) that trended similarly over the 7-day storage duration. pH-values (22°C) at end of storage were similar between each Test and Control unit and remained above 6.7. There were no statistically significant differences in platelet metabolism parameters (pH, lactate, glucose, and adenosine triphosphate (ATP)). Flow cytometry analysis was performed to assess retention of granular and cytoplasmic contents. There were no statistically significant differences observed in phosphatidylserine (PS) exposure, a marker for platelet activation and apoptosis. There was a small, but statistically significant difference in P-selectin expression, a marker of α-granule secretion. The mean difference between Test and Control was small, suggesting similar levels of activation. There were no differences in Supernatant LDH as % Total LDH. Extent of shape change (ESC), hypotonic shock response (HSR), and platelet morphology analyses were performed as measures that may predict *in vivo* recovery, survival and function. Test and Control PCs performed comparably for these parameters.

SUMMARY/CONCLUSIONS: The results for the *in vitro* function studies show that platelet components treated under the specified conditions with the INTERCEPT Blood System for Platelets were comparable when illuminated with either the INT100 Illuminator or the INT200 Illuminator following 7 days of storage.

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Table 1: *In Vitro* Platelet Function Data Summary for Platelets in 35% Plasma/ 65% PAS Treated with INTERCEPT (Small Volume, Large Volume, and Dual Storage) using either the INT100 (Control) or INT200 (Test) Illuminator Mean ±SD (Min – Max), N=21 Paired Replicates

Parameter	Day 1 (Pre-Treatment)		Day 7	
	Control (INT100 Illuminator)	Test (INT200 Illuminator)	Control (INT100 Illuminator)	Test (INT200 Illuminator)
Platelet Count ($\times 10^3/\mu L$)	1240 ±416 (850 - 1975)		1194 ±380[a] (841 - 1829)	1184 ±376[b] (822 - 1822)
Platelet Dose per Unit ($\times 10^{11}$)	3.8 ±0.8 (3.0 – 5.0)	3.8 ±0.8 (3.0 – 5.1)	3.4 ±0.5[a] (2.5 – 4.2)	3.4 ±0.5[b] (2.6 – 4.3)
Volume (mL)	320.2 ±48.0 (255.0 – 390.1)	320.9 ±47.7 (255.7 – 389.8)	297.4 ±50.6 (228.9 – 372.0)	299.2 ±51.1 (223.7 – 371.7)
Platelet Dose Loss through INTERCEPT Processing Set (%)	-		12.3 ±5.5[a] (0.4 – 21.4)	12.1 ±5.4[b] (0.0 – 20.3)
Mean Platelet Volume (MPV, fL)	9.9 ±0.5 (9.2 – 10.6)		9.6 ±0.6[a] (8.6 – 10.6)	9.6 ±0.6[b] (8.6 – 10.6)
pH (22°C)	7.1 ±0.1 (6.8 – 7.2)		6.9 ±0.1[a] (6.8 – 7.1)	6.9 ±0.1[b] (6.7 – 7.1)
Supernatant Lactate (mmol/L)	6.24 ±1.86 (3.57 – 11.11)		13.61 ±1.71[a] (10.80 – 16.70)	13.54 ±1.61[a] (11.16 – 17.38)
Supernatant Glucose (mmol/L)	4.84 ±1.41 (0.04 – 7.02)		0.53 ±0.56[c] (0.02 – 1.59)	0.53 ±0.57[a] (0.00 – 1.56)
Normalized Total ATP (nmol/10^8 plts)	5.2 ±1.7 (3.2 – 8.8)		3.5 ±1.5[c] (1.7 – 7.4)	3.7 ±1.5[a] (1.8 – 7.8)
P-selectin (CD62P, % expression)	59.3 ±9.9 (42.2 – 78.6)		70.2 ±9.0[a] (55.8 – 85.5)	69.3 ±8.8[b]* (53.8 – 83.1)
PS Exposure (%)	5.5 ±5.1a (1.0 – 19.9)		12.2 ±7.8[a] (3.7 – 35.8)	11.7 ±6.9[b] (3.8 – 30.6)
Supernatant LDH as % Total LDH (%)	3.9 ±2.0 (2.0 – 9.8)		7.3 ±3.2[c] (4.3 – 16.3)	7.1 ±3.4[c] (4.1 – 17.3)
Extent of Shape Change (ESC, %)	28.0 ±6.9 (7.7 – 38.2)		17.1 ±6.0[a] (1.9 – 24.9)	17.4 ±5.8[b] (2.8 – 26.1)
Hypotonic Shock Response (HSR, %)	41.2 ±10.6 (19.3 – 66.2)		27.3 ±9.8[a] (1.9 – 45.9)	29.0 ±9.1[b] (6.4 – 44.9)
Morphology score (max 400)	285 ±14 (263 – 305)		256 ±17[a] (228 – 294)	255 ±17[b] (236 – 302)

a. Calculated from N=19. b. Calculated from N=20. c. Calculated from N=18.

*Denotes statistically significant difference between Test and Control ($p<0.05$).

Emergence of Various Platelet Subpopulations With Specific Hemostatic Properties in Cold-Stored Amotosalen-UVA Pathogen-Reduced Platelet Concentrates

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BACKGROUND/CASE STUDIES: Current increase in the need for therapeutic versus prophylactic platelet transfusions leads to growing interest in cold-stored platelets (CSP), owing to their potentially advantageous characteristics as compared to standard room temperature platelets (RTP). We assessed the emergence of various platelet subpopulations and related functional properties in platelet concentrates (PCs) treated with amotosalen-UVA pathogen reduction and stored at 22°C or 4°C for 21 days (D).

STUDY DESIGN/METHODS: A pool-and-split strategy was used to obtain double-dose buffy-coat (BC)-PCs collected into PAS-C/plasma(55/45%) treated with amotosalen-UVA and stored at 22°C with constant agitation or at 4°C without agitation. Eight platelet subpopulations were identified using a combination of markers (P-selectin and phosphatidylserine (PhtdSer) exposure, DYm, PAC-1 binding for activated GPIIbIIIa) analyzed by multicolor flow cytometry (FCM). Functional testing included thrombin generation by calibrated automated thrombography, aggregometry, thrombus formation on a collagen-coated surface under flow conditions (1500 s^{-1}) and clot viscoelasticity of reconstituted whole blood (Quantra QPlus, HemoSonicsLLC, Stago). Statistical comparisons were done by Pearson's correlation and two-way ANOVA followed byTukey's post-hoc test (n=4)

RESULTS/FINDINGS: Multicolor FCM analysis indicated that the subpopulation of resting platelets decreased from 78±3% to 45±2% at D7 at 22°C and to 8±1% at 4°C. In CSP, procoagulant (30 ±4% from D7 to D21) and apoptotic (53±3% by D21) platelets, both exposing PhtdSer, supplanted resting platelets. This activated pattern remained unaltered upon TRAP + convulxin stimulation as of D7, indicating maximally activated platelets in PCs. CSP displayed enhanced thrombin generation capacity as of D7 compared to RTP ($p< 0.01$), consistent with increased proportion of procoagulant platelets ($r=-0.7776$ $p< 0.01$).

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Aggregation to various agonists (collagen, TRAP, arachidonic acid) decreased progressively during storage and was lower in CSP *vs* . 7-day RTP (D21 $p < 0.01$), consistent with high procoagulant platelet content (r =-0.6829 $p< 0.05$) characterized by loss of aggregation capacity. Thrombus formation on collagen under flow with reconstituted hirudinated whole blood was best preserved at 4°C at least up to D14, compared to only D7 at 22°C. Platelet contribution to clot stiffness was lower with CSP as of D7 when compared with 7-day RTP ($p< 0.01$), consistent with a high proportion of procoagulant platelets (r =-0.7227 $p < 0.01$), lacking the ability to aggregate, contract and contribute to clot strengthening.

CONCLUSIONS: CSP is a promising strategy to prolong platelet storage, leading to phenotypic changes with resting platelets replaced by PhtdSer-bearing procoagulant and apoptotic platelet subpopulations with increased thrombin production, reduced aggregation and clot firmness.

Contribution of Platelets and their Subpopulations to the Mechanics of Clot Formation According to Platelet Concentrate Storage Conditions

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BACKGROUND/CASE STUDIES: Platelets form a homogenous population in buffy-coat platelet concentrates (BC-PCs) stored at 22°C for 7 days, unlike at 4°C. Using multicolor flow cytometry analysis of platelet activation markers, we recently highlighted the emergence of procoagulant and apoptotic platelet subpopulations that progressively supplanted native platelets during cold storage of PCs up to 21 days. We evaluated the effects of storage conditions on the contribution of platelets and their subpopulations to clot formation using the Quantra viscoelastic analyzer (HemoSonics LLC,Durham, NC, USA), providing quantification of the Platelet Contribution to Clot Stiffness (PCS), enabling acomprehensive understanding of how platelets contribute to the mechanics of clot formation.

STUDY DESIGN/METHODS: A pool-and-split strategy was used to obtain double-dose BC-PCs collected into PAS-III/plasma (55/45%) treated with amotosalen-UVA (INTERCEPT™ Blood System) and stored at 22°C with constant agitation or at 4°C without agitation up to 21 days. Platelet samples were reconstituted with washed red blood cells and thawed fresh frozen plasma (Ht 40%; platelet count 300 x 10^9 /L) as a model of whole blood to measure clot viscoelasticity (Clot Time CT, Clot Stiffness CS, Fibrinogen Contribution to clot Stiffness FCSand PCS) with the Quantra. Statistical comparisons were done by Pearson's correlation and two-way ANOVA followed by Tukey's post-hoc test.

RESULTS/FINDINGS: When stored at 22°C, CT and CS of BC-PCs remained stable from D1 to D7. In contrast, CT of cold-stored BC-PCs was faster at D7 (189±4 s) compared to D1 (277±10 s, p=0.005), while CS was reduced (8±1 vs. 19±4 hPa, p=0.0004). FCS remained stable, highlighting a reduced contribution of platelets to clot stiffness during cold storage, evidenced by reduced PCS at D7 compared to D1 (6±1 vs. 17±4 hPa, p=0.0003). Interestingly, the procoagulant platelet subpopulation inversely correlated with CT and only in cold-stored PCs (r=-0.778, p=0.0041). At 22°C, the platelet count (r=0.8848, p< 0.0001), the proportion of native platelets (r=0.8585, p=0.0004) and the ability of platelets to aggregate (r=0.6901, p=0.0003) highly correlated with PCS, while the proportion of apoptotic platelets showed strong inverse correlation (r=-0.8788, p=0.0002) with PCS. At 4°C, only the proportion of native platelets remained highly correlated with PCS (r=0.8922, p< 0.0001), while procoagulant platelets in addition to apoptotic were strongly inversely correlated with PCS (r =-0.7227 p=0.0079), in line with the loss of their aggregation properties.

CONCLUSIONS: At 4°C, platelets display faster clot formation but lower clot stiffness than at 22°C, as evaluated with the Quantra analyzer. These results are consistent with the decline in aggregation and the emergence of procoagulant and apoptotic platelet subpopulations during storage.

The Quality and Functional Properties of Amotosalen-UVA-Treated Buffy-Coat Platelet Concentrates are Better Preserved in PAS-E Additive Solution as Compared to PAS-C for 7-day Storage at +22°C

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BACKGROUND/CASE STUDIES: Deterioration in the quality of platelet concentrates (PCs) during storage may be influenced by the methods used for their preparation and pathogen inactivation, the duration of storage and the type of platelet additive solutions (PAS). We evaluated the *in vitro* quality of buffy-coat (BC)-PCs treated with amotosalen-UVA (INTERCEPT Blood System, Cerus) and stored up to 7 days in two additive solutions, PAS-C (InterSol/PAS-III, Fresenius) or PAS-E (SSP, Macopharma), a modification of PAS-C containing 5 mM KCl and 1.5 mM MgCl.

STUDY DESIGN/METHODS: A pool-and-split strategy was used to obtain double-dose BC-PCs collected into PAS-C/plasma or PAS-E/plasma (55/45%) treated with amotosalen-UVA and stored at +22°C with constant agitation. The *in vitro* quality and function of PCs were tested over 7 days, including thrombus formation under flow at 1500 s^{-1}. Platelet subpopulations were identified using a combination of markers (P-selectin and phosphatidylserine (PhtdSer) exposure, DYm, PAC-1 binding for activated GPIIbIIIa) analyzed by multicolor flow cytometry. Statistical comparisons were done by two-way ANOVA followed by Tukey's post-hoc test (n=4-7).

RESULTS/FINDINGS: Platelet counts were conserved in both types of PCs during storage, while mean platelet volume was significantly increased in PAS-C as compared to PAS-E, as of day (D) 3 (D7 $p< 0.001$). Storage in PAS-E resulted in a significant reduction in glucose consumption and lactate generation as compared to PAS-C with better maintenance of pH levels during late storage ($p< 0.001$). Notably, sufficient glucose was still available on D7 in PCs stored in PAS-E (2.3±0.4 mM). Spontaneous P-selectin exposure (α-granule secretion) was significantly increased in PCs stored in PAS-C as of D3 (D3 $p= 0.008$; D7 $p< 0.001$), as was spontaneous PhtdSer exposure (platelet activation and apoptosis) during late storage of PCs in PAS-C (D7 $p=0.002$) unlike in PCs stored in PAS-E, suggesting that PAS may influence platelet activation state. Resting platelets dominated up to D7 in PAS-E (D3 82±3% vs. 58±5% $p= 0.006$; D7 67±2% *vs*. 45±2% $p< 0.001$) replaced by activated platelets in PAS-C while procoagulant and apoptotic platelets emerged only in PAS-Cat D7 (1±0% *vs*. 5±1% $p= 0.017$ and 3±0% vs. 8±2% $p= 0.009$ respectively). Lactate dehydrogenase (LDH) release (platelet lysis) was significantly reduced in PCs stored in PAS-E at D7 ($p= 0.008$). Thrombus formation on collagen under flow with reconstituted hirudinated whole blood was better preserved at D7 in PAS-E ($p < 0.01$).

CONCLUSIONS: Use of PAS-E instead of PAS-C in INTERCEPT-treated BC-PCs improved platelet metabolism, reduced LDH release and reduced spontaneous activation. PAS-E preserved resting platelets without emergence of procoagulant and apoptotic platelet subpopulations, resulting in better maintained functional properties of thrombus formation under flow up to D7.

Amotosalen or Photo-Induced By-Products in Pathogen-Reduced Blood Products do not Induce Non-Specific *In-Vitro* Activation or Degranulation of Basophil from Healthy Volunteers

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BACKGROUND/CASE STUDIES: Platelet concentrates (PCs) and fresh frozen plasmas (FFPs) are the leading cause of hypersensitivity transfusion reactions (HTRs). PCs and FFPs can be treated with amotosalen and UV-A (INTERCEPT™ Blood System – IBS, Cerus) for pathogen reduction. The imputability of amotosalen or by-products in HTRs remains elusive but not supported by epidemiology. Our aim is to assess effects of free amotosalen or photo-induced by-products in IBS-treated PCs/FFPs on non-specific *in-vitro* activation of basophils from healthy volunteers using basophil activation test (BAT).

STUDY DESIGN/METHODS: Free amotosalen (0.0003 to 30 μM) or supernatants derived from IBS-FFPs and IBS-PCs (1:10 and 1:20) were added to citrated whole blood for 30 min at 37°C. Samples were analysed by flow cytometry to identify basophils (IgE/CD203c). Activation status was assessed by the percentage of CD63 cells (correlated to histamine release) and the stimulation index (SI) based on CD203c upregulation (MFI of stimulated divided by resting basophils) with a threshold at 1.6. Positive controls were a mouse anti-human IgE monoclonal antibody (clone G7-18) and fMLP (anIgE-independent activating peptide). Statistical comparisons were done by mixed model or two-way ANOVA followed by Tukey's post-hoc test (n=5).

RESULTS/FINDINGS: Free amotosalen had no effect on CD203c-SI or CD63 exposure at any concentrations (3 μM = 10 FFPs or 2-3 PCs) as FFPs (1:10 = 10 FFPs) tested before and after treatment, then after CAD and 48 hours after storage liquid at +4°C. When PCs were stored at +22°C, CD63 exposure remained at basal levels, while CD203c-SI tended to increase up today 3 only at 1:10 (equivalent to 2-3 PCs) without reaching statistical significance and remained stable thereafter up to day 7. Interestingly, untreated (non-IBS) PC supernatants also displayed a non-significant increase in CD203c-SIover time at 1:10, suggesting that amotosalen or photo-induced by-products were not responsible for this effect.

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When IBS-PCs were stored at +4°C ("cold-stored platelets") up to day 21, the same tendency was observed at 1:10 for CD203c-SI as early as day 3 and then remained stable until day 21, while CD63 was not exposed. Of note, PCs stored up to day 21 at +22°C exhibited a similar tendency but reaching statistical significance only at day 21 at 1:10 ($p < 0.05$). These data suggest storage lesions as the main mechanism for non-specific basophil activation (without CD63 exposure).

CONCLUSIONS: These results indicate that a wide range of concentrations of free amotosalen is unable to activate blood basophils from healthy volunteers *in-vitro*. Moreover, PC supernatants and FFPs, including residual free amotosalen and photo-induced by-products, are unable to induce non-specific basophil activation or granule release.

Amotosalen/UVA Treatment of Buffy Coat Platelet Concentrates in SSP+ to Inactivate Bacterial Strains of Clinical Importance

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BACKGROUND/CASE STUDIES: Amotosalen and UVA light were used to inactivate pathogens and leukocytes in platelet concentrates. Platelets are typically stored up to 5 days prior to transfusion, but in combination with PR, platelets can be stored up to 7 days in Canada and other geographies where BCPC are manufactured.

STUDY DESIGN/METHODS: To evaluate whether the inactivation of bacterial strains of clinical importance is complete at Day 7 post-treatment, BCPC units were prepared and suspended in 47% plasma/53% SSP+ and pooled to a volume of 420 mL with a platelet dose of 7.1 to 8.0 × 10^{11}. A minimum of four replicates were performed for each bacterial strain. The BCPC units were inoculated with bacteria and treated with amotosalen/UVA. Samples were taken pre- and post-UVA illumination, post-CAD, Day 3, Day 5 and Day 7 post-treatment and were analyzed for bacterial titer by plating on appropriate media (100 µL – 5 mL/plate) and incubated for at least 24 hours.

RESULTS/FINDINGS: Treatment of inoculated BCPC units with amotosalen/UVA resulted in bacterial inactivation out to Day 7 of post-treatment storage (**Table 1**).

CONCLUSIONS: Amotosalen and UVA light were used to inactivate clinical bacterial strains in BCPC. While the limit of inactivation may differ depending on the bacterial strain, for each strain tested, no viable bacteria were detected at the end of Day 7 post-treatment.

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Table 1: Bacterial Inactivation Using Amotosalen/UVA Treatment of Buffy Coat Platelet Concentrates in SSP+

	Log cfu/mL	
Bacteria	**Input Titer [a,b]**	**LRF (Log Reduction Factor)**
Cutibacterium acnes CDHS 00A-6608	6.9 ± 0.1	6.9 ± 0.1
Klebsiella pneumoniae CDHS 92A-2214	2.9 ± 0.1	2.9 ± 0.1
Pseudomonas aeruginosa CDHS 91A-5818	5.4 ± 0.2	5.4 ± 0.2
Serratia marcescens CDHS 2574-3-79	4.6 ± 0.2	4.6 ± 0.2
Staphylococcus aureus CDHS 89A-3667	7.7 ± 0.2	7.7 ± 0.2
Staphylococcus epidermidis CDHS 85A-2560	6.8 ± 0.0	6.8 ± 0.0

a. Input titers assessed were determined previously to be the limit of inactivation with no detectable bacteria post-treatment.

b. Pre-UVA samples were taken prior to illumination.

A Time/Motion Study to Assess Irradiated and Pathogen Reduced Platelet Component Inventory Management and Workflow at Transfusion Service Sites

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BACKGROUND/CASE STUDIES: Transfusion-associated graft versus host disease (TA-GVHD) is a rare, yet often fatal, adverse event caused by residual donor T-cells in donated blood. Nuclear source irradiation and amotosalen-UVA are FDA approved methods to mitigate TA-GVHD risk in platelet components (PC). PR also is approved to replace bacterial screening and CMV serology. In the US, the practice of irradiation is heterogenous. Most facilities use irradiated PC as needed, by patient indication, while others use it universally to avoid errors. Some hospital institutions perform irradiation in-house, while others purchase irradiated PC from their suppliers. Here we evaluate a blood bank workflow comparison between irradiation and the use of PR PC. We hypothesize that PR provides simplification of inventory management as well as increased platelet availability in different hospital blood bank settings.

STUDY DESIGN/METHODS: A time/motion analysis is designed to compare the workflow and inventory management of irradiated and PR PCs at hospitals with different characteristics. Direct observation and mapping of process steps are planned for 2-3 institutions that include the following variables:

- Hold an inventory of both conventional and PR platelet
- Perform irradiation on-site or purchase irradiated product from suppliers
- Perform irradiation on-demand or hold irradiated product in inventory
- Varied distances between hospital and supplier

RESULTS/FINDINGS: The following workflow has been characterized through literature review [1-5] and hospital interviews. Further information will be shown upon completion of a detailed workflow study.

CONCLUSIONS: PR PCs provide an alternative to irradiated PCs which may simplify inventory management in different hospital settings. An additional benefit may include the reduced risk of error due to the transfusion of non-irradiated components to patients for which TA-GVHD mitigation is indicated.

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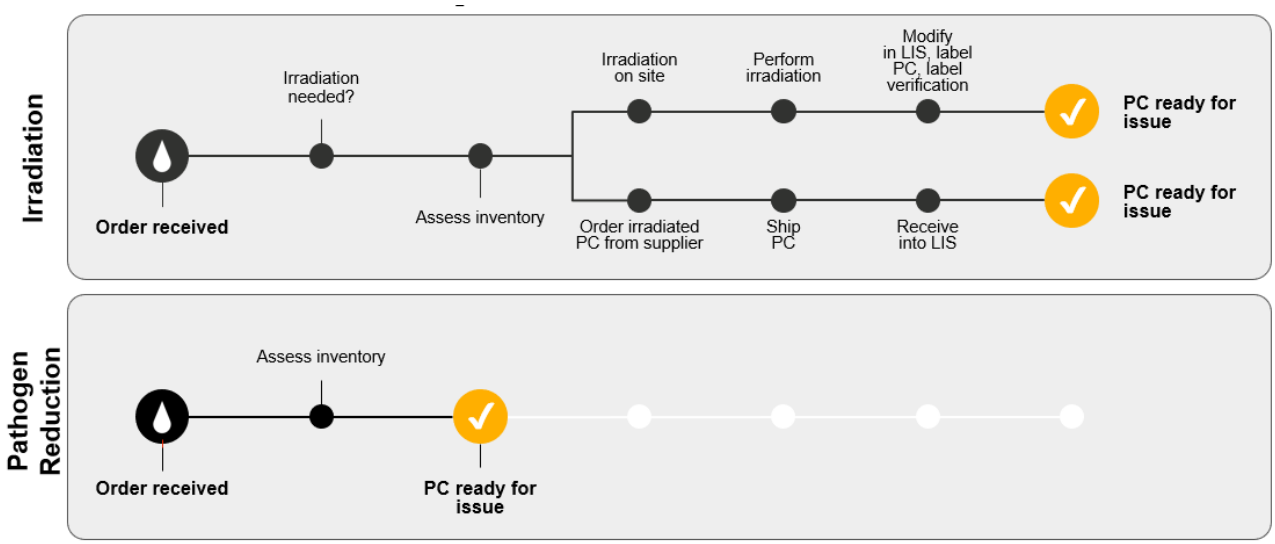

Amotosalen and UVA Inactivation of California Encephalitis Virus in Human Apheresis Platelets

Natalie Stoker, Kelsey Goldbeck, Maria Silva Gomez, Laarni Batin, Dennis Hicks, Adeel Khan, Gurvani Singh, Felicia Santa Maria

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BACKGROUND/CASE STUDIES: Since late 2023, outbreaks of Oropouche virus (OROV) have been documented in South America and the Caribbean, prompting the CDC to issue a level 2 travel health notice in some regions. This outbreak has again highlighted the risk of arthropod-borne viruses to blood supply sustainability and safety, even in areas not directly impacted by the outbreak, as travel-associated cases have already been confirmed in regions of North America and Europe. California encephalitis virus (CEV), along with OROV, is part of the *Orthobunyavirus* genus, in the family *Peribunyaviridae*. CEV, like OROV, is a negative sense, single-stranded RNA virus that is transmitted to humans through the bite of an infected mosquito. Although CEV and OROV belong to separate serogroups, they have similarities in their genome and virion structure as members of the same genus. Though CEV infection in humans is relatively rare, it was used as a representative for *orthobunyaviruses* to determine the efficacy of the amotosalen and UVA (AMO-UVA) pathogen reduction technology (PRT) to mitigate the increased risks associated with the growing OROV outbreak.

STUDY DESIGN/METHODS: Spiking and inactivation experiments with CEV were performed using the INTERCEPT® Blood System for Platelets PRT. Eight replicates were performed, four in platelet concentrates (PC) suspended in 100% plasma and four in PC suspended in 35% plasma/65% platelet additive solution (PAS). For each replicate, PC from individual donors were adjusted to approximately 285mL. Each replicate was contaminated with CEV to achieve a titer of approximately 4 log pfu/mL in each platelet unit. After contamination, each replicate was dosed with approximately 150 µM amotosalen and a pre-treatment control sample (pre-UVA) was taken. Each unit was then treated with a single target dose of 3.6 J/cm^2 UVA and a post-treatment sample (post-UVA) was taken. The Vero76 cell-based plaque assay system was used to determine the pre- and post-UVA viral titers. The log reduction factor was calculated based on the difference between the log pfu/mL values in the pre- and post-UVA samples.

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RESULTS/FINDINGS: The table shows the average log reduction factor for CEV achieved in both PC suspended in 100% plasma and in 35% plasma/65% PAS using AMO-UVA PRT.

CONCLUSIONS: Treatment with AMO-UVA PRT inactivated 3.9 log pfu/mL of CEV in PC suspended in 100% plasma and 4.5 logpfu/mL of CEV in PC suspended in 35% plasma/65% PAS. These results indicate that AMO-UVA treatment effectively inactivates CEV in platelet components. Considering the similar genome and virion structure between CEV and OROV, these results suggest that AMO-UVA PRT may also be effective in reducing the risk of OROV transfusion transmitted infections.

Table 1: The Average Log Reduction Factor for CEV Achieved

Blood Component	Log pfu/mL		
	Pre-UVA Control	Post-UVA Test	Log Reduction Factor
Platelets in 100% Plasma	4.3	~0.4	3.9
Platelets in 35% Plasma/65% PAS	4.5	NC[a]	4.5

a. NC: log titer not calculatable – 0.1 pfu/mL residual in 1 replicate

Expanding the Donor Pool Through Pathogen Reduction: Feasibility and Potential Impact of Accepting Malaria-Risk Donors

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BACKGROUND/CASE STUDIES: Malaria exposure donor deferrals significantly reduce the donor pool in many U.S. regions, especially during seasonal travel peaks. The U.S. Food and Drug Administration (FDA) now permits collection of apheresis platelets or plasma from donors at risk of malaria due to travel, if components undergo pathogen reduction (PR) with an FDA-approved device. FDA has proposed extending this to donors deferred for malaria-risk due to prior residency. As of 2023, more than half of all apheresis platelets distributed in the U.S. are pathogen reduced. This study describes the implementation of a PR-based pathway to accept malaria-risk donors, focusing on feasibility, process controls, and indicators of operational success.

STUDY DESIGN/METHODS: A process map (**Figure A**) was developed to identify eligible donors, ensure appropriate component collection, and adhere to PR process requirements. The blood establishment computer system (BECS) was configured with process controls that permit only platelet collection from malaria-risk donors found otherwise eligible via the Uniform Donor History Questionnaire. Safeguards ensure that: (a) only products intended for PR were collected (i.e. apheresis platelets with no concurrent products), (b) all products underwent PR treatment, and (c) any untreated components were quarantined and prevented from being distributed. Production and discard rates were tracked over 12 months.

RESULTS/FINDINGS: Ten donors who would otherwise have been deferred for malaria travel risk were accepted during the study period. Each donation was successfully PR-treated, resulting in one or more transfusable platelet units. No products were discarded due to PR processing issues. No deviations or compliance issues were identified.

CONCLUSIONS: Routine acceptance of malaria-risk donors when treating platelets with PR is demonstrated as operationally feasible, with no product loss and good staff compliance. The initial number of reinstated donors was modest as it was limited to those with recent travel to malaria-endemic areas. The approach, however, has clear potential for broader adoption to address longer and recurring deferrals related to prior residency in endemic regions; currently 90 individuals are in the center's database, representing an immediately accessible donor pool. As FDA guidance evolves to permit the use of PR for residency-based deferrals, this approach may offer a scalable pathway to reinstate and retain donors who would otherwise be excluded long-term, while avoiding the cost of malaria testing. Given that apheresis donors at this center average 5.9 donations annually and yield approximately 2 platelet products per donation, even modest re-engagement of this population could materially strengthen platelet availability without compromising safety.

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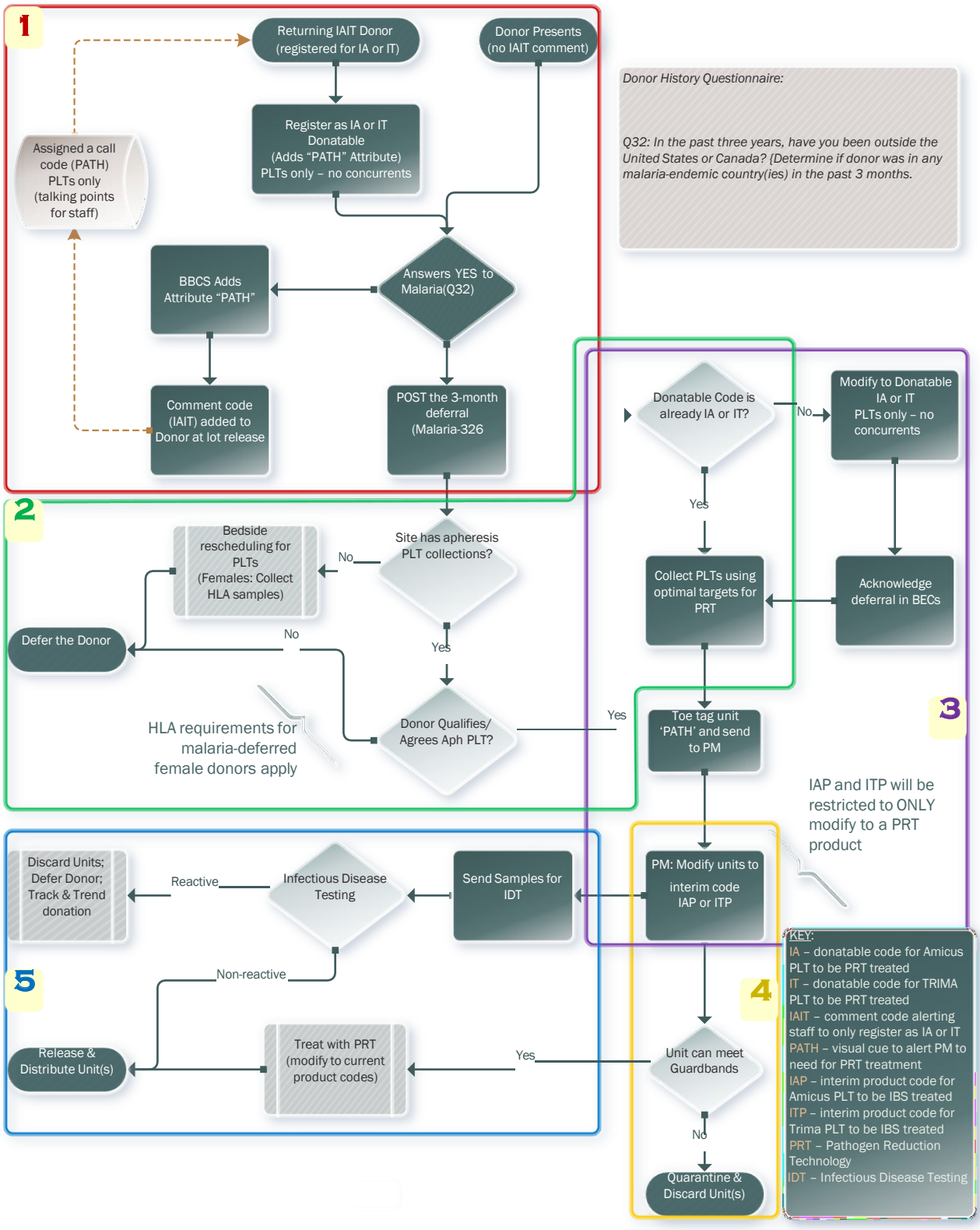
Accepting Malaria Donors when treating with PRT



Amotosalen/UVA Treatment of Plasma to Inactivate Bacteria, Including Common Environmental Strains using the INTERCEPT Blood System with INT200 Illuminator

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

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BACKGROUND/CASE STUDIES: The INTERCEPT® Blood System for Plasma utilizes amotosalen and UVA light to inactivate a wide range of pathogens in plasma and is available in Europe, the US and other geographies. The system consists of two key components: amotosalen containing processing sets and a UVA Illuminator. This illuminator used in these studies will be referred to as the INTERCEPT LED illuminator (INT200 illuminator). Cerus has developed the recently CE-marked UVA light emitting diode (LED)-based technology as a replacement for the current INT100 illuminator using representative bacteria that include potential environmental contaminants.

STUDY DESIGN/METHODS: The aim of this study was to evaluate the inactivation of selected environmental bacteria in human plasma using amotosalen and UVA treatment with the INT200 device as part of the INTERCEPT LED Illuminator system. Human plasma donations were collected and pooled to yield individual units of ~650 mL. A minimum of three replicates were performed for each strain of transfusion-relevant bacteria, including *A. baumannii, C.minutissimum, L. lactis, S. epidermidis, S. saprophyticus, K. pneumoniae, S. aureus, P. fluorescens*, and *C. perfringens*, with each replicate consisting of one unit spiked with a single bacterial 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 (100 μL–5 mL/plate).

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

CONCLUSIONS: Amotosalen-UVA treatment with the INT200 illuminator consistently inactivated high titers of *A. baumannii, C. minutissimum, L. lactis, S. epidermidis, S. saprophyticus, K. pneumoniae, S. aureus, P. fluorescens*, and *C. perfringens* at the challenging condition of high plasma volume (650 mL). This high volume of 650 mL represents a challenge for pathogen inactivation due to the longer light path through the illumination container and the decreased amotosalen concentration of approximately 135 μM, compared to 150 μM at nominal volume (585 mL).

The data demonstrates robust inactivation, including common environmental transfusion-relevant bacterial strains using treatment with amotosalen and the INT200 Illuminator.

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

Bacteria	Input Titer (Log cfu/mL)	Post-UVA Treatment Titer (cfu/mL)	Log Reduction (Log cfu/mL)
Acinetobacter baumannii	7.4 ± 0.0	0.0 ± 0.0	7.4 ± 0.0*
Corynebacterium minutissimum	7.7 ± 0.2	0.0 ± 0.0	7.7 ± 0.2
Lactococcus lactis	6.4 ± 0.1	0.0 ± 0.0	6.4 ± 0.1*
Staphylococcus epidermidis	7.7 ± 0.1	0.0 ± 0.0	7.7 ± 0.1*
Staphylococcus saprophyticus	7.4 ± 0.1	0.0 ± 0.0	7.4 ± 0.1*
Klebsiella pneumoniae	6.4 ± 0.1	1.4 ± 0.11[a]	5.0 ± 0.2
Staphylococcus aureus	7.8 ± 0.2	0.0 ± 0.0	7.8 ± 0.2*
Pseudomonas fluorescens	7.9 ± 0.1	0.0 ± 0.0	7.9 ± 0.1
Clostridium perfringens	6.7 ± 0.1	0.0 ± 0.0	6.7 ± 0.1*

* No residual bacteria were detected post-treatment. a. Titer is expressed in log cfu/mL

Comparison of INT100 and INT200 Illuminator for Preparation of Pathogen Reduced Plasma with Amotosalen and UVA Light

Cally Toupin, Molly Carleton, Marc Bernal, Brittany Dillon, Kaja Kaastrup, Nina Mufti

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BACKGROUND/CASE STUDIES: The INTERCEPT® Blood System for Plasma uses amotosalen and UVA light for the *ex vivo* preparation of pathogen reduced plasma. The current generation INT100 Illuminator uses fluorescent bulbs (320-400 nm) to deliver a controlled dose of UVA light. A next-generation LED-based illumination device, the INT200, has recently received CE mark approval. The INT200 is not approved in the US. A study was performed to compare the 12-month stability of amotosalen/UVA light treated plasma illuminated with the INT100 (current generation) or INT200 Illuminator.

STUDY DESIGN/METHODS: Freshly collected apheresis plasma was pooled and split into equal volume units for treatment using either the INT200 Illuminator or the INT100 Illuminator. After treatment, plasma units were frozen and placed into storage at -18ºC to -25ºC for 12 months. Six paired replicates were thawed at the end of 12 months of storage and stored at 1-6ºC for 5 days post-thaw. Plasma *in vitro* function parameters were assessed for pooled plasma units prior to treatment (data not shown), post-treatment prior to frozen storage, following 12 months frozen storage, and following thaw and refrigerated storage.

RESULTS/FINDINGS: Data for coagulation factors, inhibitors, VWF, ADAMTS13, and complement proteins as well as thrombin generation capacity were evaluated. There was a single parameter with a statistically significant difference between INT200 and INT100; following 12 months frozen storage, Factor VIII activity was marginally lower in the INT200 illuminated plasma. However, although FVIII activity decreased post thaw, the EDQM and ANSM activity requirements for 0.5 IU/mL FVIII were satisfied and thrombin generation capacity was retained. Overall stability of the parameters assessed was demonstrated for both illuminators following 12 months of frozen storage at -18ºC to -25ºC and subsequent refrigerated storage of thawed plasma for 5 days. Parameters were within previously established literature-based ranges and were comparable between INT200 and INT100 treated plasma.

CONCLUSIONS: This study demonstrates that the functionality and quality of amotosalen/UVA light treated plasma illuminated with the INT200 LED Illuminator was maintained following twelve months of frozen storage and 5-days post thaw at 1-6°C and is consistent with plasma illuminated with the INT100 Illuminator.

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Table 1: Summary of *In Vitro* Function Post Amotosalen/UVA Treatment after 12 Months Frozen Storage (Mean ± SD)

	INT100 Illuminator			INT200 LED Illuminator		
	Post-Treatment	Post 12-Month Frozen Storage	Post Thaw 5- day 1-6°C Storage	Post-Treatment	Post 12-Month Frozen Storage	Post Thaw 5- day 1-6°C Storage
Fibrinogen (g/L)	2.19 ±0.35	2.20 ±0.32	2.16 ±0.35	2.15 ±0.31	2.16 ±0.28	2.16 ±0.34
Factor II (IU/mL)	0.81 ±0.02	0.76 ±0.05	0.76 ±0.05	0.83 ±0.03	0.73 ±0.03	0.76 ±0.05
Factor V (IU/mL)	0.88 ±0.14	0.83 ±0.16	0.77 ±0.15	0.89 ±0.18	0.85 ±0.17	0.78 ±0.15
Factor VII (IU/mL)	0.82 ±0.09	0.72 ±0.08	0.95 ±0.45	0.79 ±0.11	0.71 ±0.07	0.92 ±0.49
Factor VIII (IU/mL)	1.03 ±0.35	0.91 ±0.30	0.57 ±0.18	0.99 ±0.33	0.84 ±0.27	0.56 ±0.17
Factor IX (IU/mL)	0.99 ±0.07	0.91 ±0.07	0.88 ±0.09	0.99 ±0.12	0.88 ±0.09	0.85 ±0.08
Factor X (IU/mL)	0.84 ±0.04	0.73 ±0.07	0.78 ±0.09	0.82 ±0.04	0.73 ±0.04	0.78 ±0.08
Factor XI (IU/mL)	0.90 ±0.09	0.87 ±0.08	0.87 ±0.08	0.91 ±0.10	0.88 ±0.15	0.90 ±0.11
Protein S (IU/mL)	0.76 ±0.09	0.70 ±0.07	0.48 ±0.12	0.74 ±0.09	0.68 ±0.10	0.50 ±0.12
Alpha-2-plasmin (IU/mL)	0.70 ±0.11	0.70 ±0.08	0.69 ±0.09	0.68 ±0.08	0.68 ±0.08	0.70 ±0.05
Thrombin-Antithrombin Complexes (ng/mL)	2.7 ±0.4	<2.5 ±0.3	3.2 ±0.9	2.9 ±0.5	<2.4 ±0.3	3.2 ±0.8
C3a (ng/mL)	23.52 ±7.83	64.91 ±24.42	663.99 ±848.20	25.99 ±9.59	56.73 ±16.74	633.05 ±845.93
C5a (ng/mL)	10,571±3,110	10,203±2,462	11,116 ±3,301	10,834 ±2,881	10,335±2,563	11,784±4,569
vWF activity (ristocetin cofactor, IU/mL)	0.90 ±0.42	0.82 ±0.39	0.85 ±0.42	0.84 ±0.38	0.86 ±0.39	0.77 ±0.35
ADAMTS-13 Activity (IU/mL)	0.94 ±0.14	0.96 ±0.13	0.96 ±0.15	0.93 ±0.13	0.94 ±0.14	0.99 ±0.18
Thrombin generation ETP-5 pM Tissue factor (nM×min)	1,704±268	1,454 ±230	1,365 ±286	1,644±274	1,451 ±230	1,388 ±357

A Call for Modernization of Biologics Licensing Process for Blood Centers

Richard Gammon[1], Jessica Drouillard[2], James Wade Atkins[3], Robert Harper[4], Sharon Garcia[5], Betzy Gonzalez[6], Bethany Brown[7], Steven Baker[7], Ludwig Frontier[8]

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BACKGROUND/CASE STUDIES: Blood centers operate under a regulatory framework designed to ensure the safety, potency, and efficacy of its blood products. However, some of the current regulatory requirements may not fully reflect advances in technology or current best practices. Having been implemented more than 80 years ago, the United States (US) Food and Drug Administration's (FDA's) biologics license application (BLA) process can present avoidable complexity and delay in providing patients with safe blood and blood products. To better understand these challenges, a cross-functional working group of industry experts convened to identify root causes and explore opportunities to simplify and modernize licensing pathways for blood centers.

STUDY DESIGN/METHODS: Using a fishbone (Ishikawa) diagram, a working group analyzed licensing challenges experienced by blood centers across the country (**Figure A**). Contributing factors were categorized into four major areas: unclear requirements, lack of transparency, inconsistent regulatory interpretations, and lengthy timelines. Findings were compiled from institutional case studies, correspondence with the FDA, and comparative reviews of licensing timelines and regulatory responses.

RESULTS/FINDINGS: FDA Form 356h, a required component of all BLAs, includes numerous fields irrelevant to blood products—leading to non-value-added activities that do not align with the Paperwork Reduction Act of 2024. FDA checklists are not consistently updated and provide lack of guidance on key advancements such as ISBT128 Standard. Inconsistent interpretation of regulations—for example, confusion over fixed vs. mobile sites or varying treatment of interstate vs. intrastate distribution—created disparities in access and potentially undermines the uniform safety and availability of the blood supply. Additionally, the process of implementing already approved collection and processing systems and devices remains overly complex, limiting flexibility, innovation, and responsiveness to operational needs.

CONCLUSIONS: Licensing challenges have downstream impacts on timely access to safe blood products. When licensing processes delay the adoption of new technologies or restricts interstate resource sharing, patient care may be compromised. This analysis highlights practical, collaborative opportunities to enhance the BLA process, reduce unnecessary burdens, improve efficiency, and help ensure equitable, timely access to life-saving blood products across the US. The working group invites further discussion with the FDA and other stakeholders to explore shared mutually beneficial solutions.

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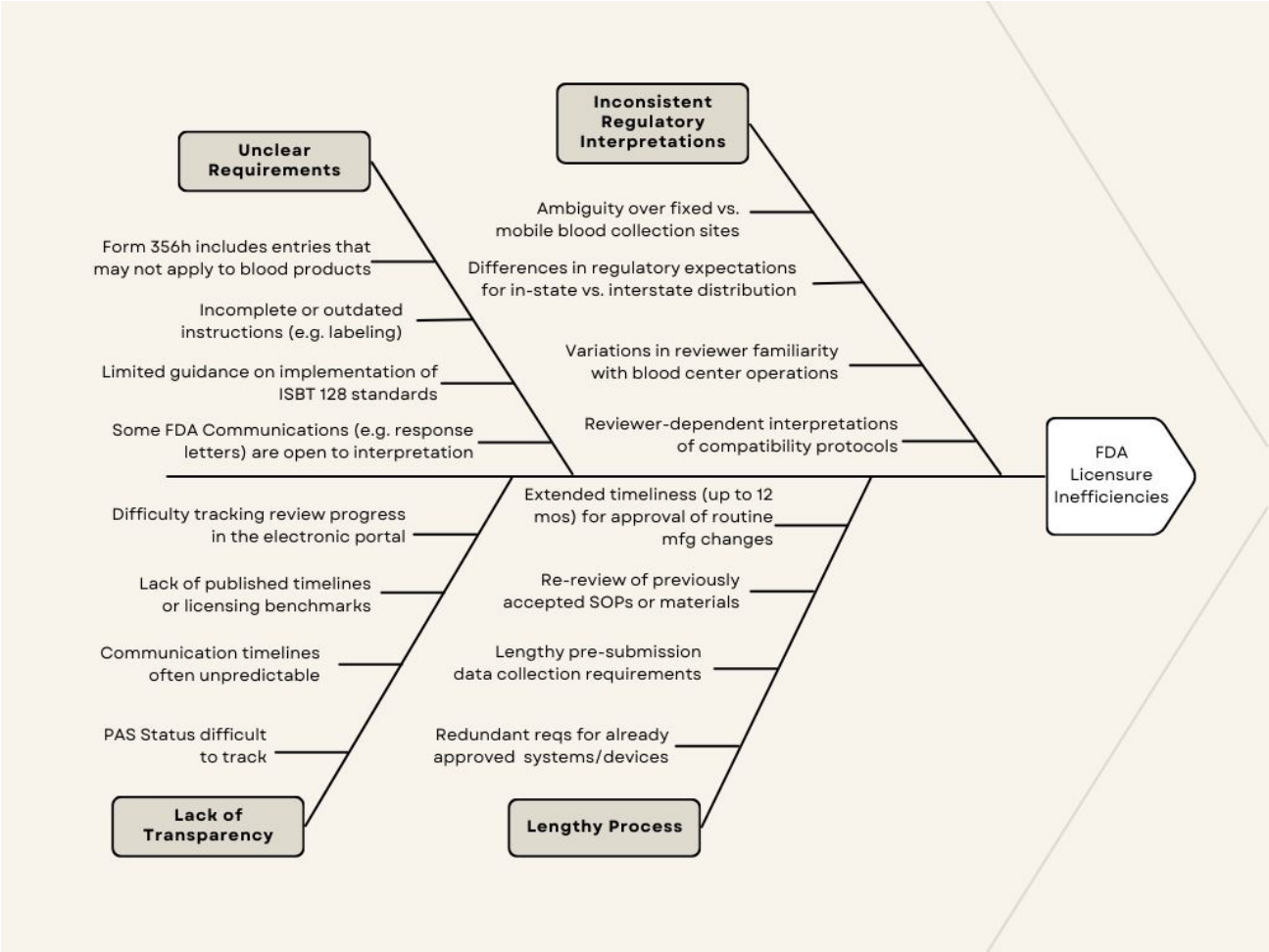
Figure A: Fishbone Diagram - Biologics License Application Process



Safety of Amotosalen/UVA Platelets and Plasma Transfused in Routine Clinical Use: Real World Evidence from 3 European Centers, 2019-25

John P. Pitman[1], Magdalena Letowska[2], Anna Krukowska[2], Dariusz Piotrowski[3], Zofia Przybylska[3], Konrad Rosskopf[4], Angelo Ostuni[5], Margherita Giannoccaro[5], Rossella Procacci[5], Christine Ernst[1], Johannes Irsch[6], Richard J Benjamin[1]

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BACKGROUND/CASE STUDIES: Amotosalen/UVA pathogen reduced (APR) platelets (PLTs) and plasma (PLS) were approved in Europe in 2002 and 2006 to reduce the risk of transfusion-transmitted infections and replace irradiation to prevent TA-GVHD. Between 2003-16, Cerus Corporation collected real world evidence (RWE) on the safety of 21,548 APR PLTs in 4,765 patients, and 57,428 APR PLS components in 9,813 patients in 11 countries. Cerus initiated a new cross-sectional study in Europe in 2019 to collect RWE on the nature, frequency and severity of transfusion reactions (TRs) in patients transfused with APR PLTs and/or PLS in centers that had adopted APR since 2016.

STUDY DESIGN/METHODS: Observational data were captured prospectively from routine blood bank records at transfusion centers in Graz, Austria, Warsaw, Poland, and Bari, Italy. Patient consent was not required for this single-arm, non-interventional study. Demographic information (sex, age), unit descriptions (e.g.,collection method) and TRs were captured for all patients transfused in selected wards during defined surveillance periods. De-identified patient data were stratified by sex, age and diagnosis. TRs were identified by physicians using ISBT definitions and routine hospital reporting systems. Descriptive statistics were calculated.

RESULTS/FINDINGS: A total of 3,425 APR PLT and 1,907 APR PLS components were transfused to 475 and 87 patients, respectively, between December 2019 and March 2025. 50.4% of patients were female; 36.8% were ≥65 years. All units were leukocyte reduced; none were irradiated or CMV tested. Surveillance periods ranged from 1-6 months; Graz and Warsaw completed multiple periods. Apheresis accounted for 44% of PLTs in Graz, 93% in Warsaw, and 11% in Bari; the remainder were pooled. All PLS in Graz and 52% in Warsaw were apheresis. All PLTs in Graz and Bari, and 76% in Warsaw were suspended in platelet additive solution. PLT shelf-life was 7 days in all sites: 71% were transfused on days 2-5 post-collection; ~20% on day 7. 1% of PCs in Warsaw were cryo preserved and transfused after day 7. PLT doses averaged 3.0 x 10^{11} (mean range: 2.6-3.4). Patients received a mean of 7.2 PLTs (range: 1-91) and 21.9 PLS (range: 1-294). Six PLT TRs (0.18% of PLTs) were reported in Graz and Warsaw: 3 FNHTR, 2 allergic and 1 transfusion-associated dyspnea. Two PLSTRs (allergic, unclassified) were reported in Warsaw (0.10% of PLS units) (**Table**). TRs were non-serious and moderate in severity; all patients recovered. TR rates were comparable to historical rates for non-PR components at all sites and lower than rates (~1%) in prior studies.

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CONCLUSIONS: Cross-sectional studies allow hospitals and manufacturers to monitor and reaffirm APR PLT and PLS benefit-risk profiles with RWE.

Table: Summary Hemovigilance Results

	APR Platelets			APR Plasma			Total APR components		
Sites	**Subjects (PLT)**	**Transfusions (PLT)**	**TRs (PLT)**	**Subjects (PLS)**	**Transfusions (PLS)**	**TRs (PLS)**	**Subjects (TOTAL)***	**Transfusions (TOTAL)**	**TRs (TOTAL)**
Graz	134	1,054	2	7	462	0	141	1,516	2
Warsaw	328	2,253	4	80	1,445	2	365	3,698	6
Bari	13	118	0	-	-	-	13	118	0
Totals	**475**	**3,425**	**6**	**87**	**1,907**	**2**	**519**	**5332**	**8**

Assessing Production Costs for Pathogen Reduced Cryoprecipitated Fibrinogen Complex and Cryoprecipitated Antihemophilic Factor – A Blood Center Budget Impact Model

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BACKGROUND/CASE STUDIES: Cryoprecipitated Antihemophilic Factor (Cryo AHF) and Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex, IFC) are used to supplement fibrinogen in patients with hypofibrinogenemia. Both are produced from pooled whole blood derived (WBD) plasma but differ in the manufacturing process which ultimately impacts product availability as well as production costs. Manufactured from Amotosalen/UVA treated plasma, IFC provides a fibrinogen source with a 5-day post-thaw shelf-life as well as reduced transfusion-transmission infection risk. Here we present a model that compares the financial impact of producing Cryo AHF and IFC from a blood center's perspective.

STUDY DESIGN/METHODS: An Excel model was built and populated with base case costs and workflow assumptions identified through a time/motion study and literature search. The model allows base-case assumptions to be overwritten with values specific to the institution. Annual costs for Cryo AHF and IFC production, including labor, QC testing, and kits/pooling sets, were compared for 4 scenarios, each representing a different production mix: 100% pooled Cryo AHF, 100% IFC, 50/50% Cryo AHF/IFC, and 70%/30% Cryo AHF/IFC.

Model Assumptions

- Blood center collects 20,000 units of WBD plasma
- IFC and Cryo AHF derived from 4 and 5 WBD plasma units, respectively
- An IFC 4-pool product provides approximately 1.5g of fibrinogen, comparable to the lower range of average fibrinogen content in a Cryo AHF 5-pool

Pricing to hospital:

- Pooled Cryo AHF: $375/unit
- Cryo-poor plasma from Cryo AHF: $50/unit
- IFC: $925/unit

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RESULTS/FINDINGS: The financial impact based on each of the four production-mix scenarios are shown below.

CONCLUSIONS: Though the model predicts increased production costs for IFC compared to Cryo AHF, blood centers may achieve greater revenue with IFC. This is largely because less WBD plasma is required for IFC (4-pool) vs. Cryo AHF (5-pool) leading to greater product availability. In addition, IFC provides benefits to hospitals and patients such as longer post-thaw shelf-life, faster time to issue when stored thawed, and reduced waste when compared to Cryo AHF.

Financial Impact Based on Each of the Four Production-mix Scenarios

	100% Cryo AHF	100% IFC	50% IFC	30% IFC
Total Costs	$ 114,880	$ 1,382,880	$ 756,560	$ 502,000
Consumables	$ 60,000	$ 1,360,000	$ 710,000	$ 450,000
Labor	$ 44,800	$ 17,600	$ 31,200	$ 36,640
QC Testing	$ 10,080	$ 5,280	$ 15,360	$ 15,360
Total Revenue	**$ 2,500,000**	**$ 4,625,000**	**$ 3,562,500**	**$ 3,137,500**
Cryo AHF	$ 1,500,000	$ -	$ 750,000	$ 1,050,000
Plasma Cryoprecipitate Reduced for fractionation	$ 1,000,000	$ -	$ 500,000	$ 700,000
IFC	-	$ 4,625,000	$ 2,312,500	$ 1,387,500
Net	**$ 2,385,120**	**$ 3,242,120**	**$ 2,805,940**	**$ 2,635,500**

Dithiolthreitol Treatment Eliminates Daratumumab Interference For Detection of Antibodies to Amustaline/Glutathione Pathogen-Reduced RBCs

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BACKGROUND/CASE STUDIES: The amustaline/glutathione pathogen reduction (PR) of red blood cells (RBCs) is designed to reduce the risk of transfusion-transmitted infections and to replace irradiation for the prevention of transfusion associated-graft-versus-host disease. The PR process leaves residual amustaline-derived acridine adducts on the RBC surface. In clinical trials of PR-RBCs, an indirect antiglobulin test (IAT) with reagent PR-RBCs is used to screen for baseline and treatment-emergent PR-RBC specific antibodies. Each screening panel includes cells with no (control), low and high amounts of surface acridine adducts. Daratumumab (DARA) used in the treatment of multiple myeloma interferes with blood compatibility screening, including the PR-RBC antibody screen. Dithiothreitol (DTT) treatment of RBCs has been shown to resolve DARA interference in standard blood compatibility testing. The objective of this study was to determine whether DTT treatment of reagent PR-RBCs resolved DARA interference while still allowing the detection of PR-RBC antibodies.

STUDY DESIGN/METHODS: Nine PR-RBC reagent panels were treated to remove DARA interference (0 or 0.2 M DTT, 35 min, 37°C). The panels were screened with control anti-acridine antibody in an IAT assay (Ortho ID-Micro Typing System IgG plus C3d gel card) using plasma from DARA-treated patients, with or without added anti-acridine monoclonal antibody (2S-197M1). Surface acridine adducts on panel RBCs were quantitated by flow cytometry using QuantiBrite calibrated beads (BD Biosciences).

RESULTS/FINDINGS: Mock treated cells (no DTT) behaved as expected in 9 panels of reagent PR-RBCs. DARA interference was noted in all cells tested with DARA plasma including the control, while the DARA plasma and control anti acridine antibody combination displayed DARA interference with the negative control showing a positive result (**Figure 1**). DTT treatment eliminated DARA interference in all panels, including the PR-RBC reagent controls (**Figure 1a**) and in the DARA plasma and control anti acridine antibody combination, with some modulation of the acridine signal observed (**Figure 1b**). Surface acridine levels were quantitated by flow of PR-RBC panel cells and showed an average reduction in PE molecules/cell of 52.2% (37.7 - 58.4%).

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CONCLUSIONS: The standard use of DTT to resolve DARA interference was applied to the PR-RBC antibody screening assay and resulted in the elimination of DARA interference. Although acridine levels were reduced following DTT treatment, the PR-RBC IAT assay was able to detect the presence of positive control anti acridine antibody following DTT treatment, both in the absence and presence of DARA patient plasma.

Figure 1a

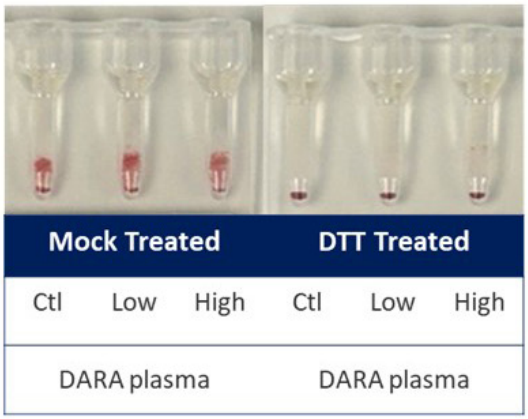
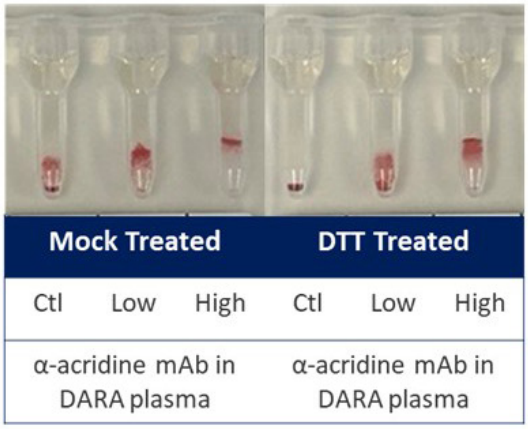


Figure 1b



Reduced Hemoglobin Use with Amustaline/Glutathione Pathogen-Reduced Red Cells in a Randomized, Controlled Trial in Complex Cardiac Surgery

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BACKGROUND/CASE STUDIES: The Red Cell Pathogen Inactivation (ReCePI) trial was a Phase III, randomized non-inferiority study comparing amustaline/glutathione pathogen-reduced (PR) and conventional red blood cells (RBCs) for the support of acute anemia during and for 7 days after complex cardiac or thoracic-aorta surgery.

STUDY DESIGN/METHODS: The primary endpoint was the incidence of acute kidney injury (AKI) defined as a change in serum creatinine (≥0.3 mg/dL) from baseline within 48 hours of surgery. Blood utilization (components and total Hb transfused) was assessed. Patient hemoglobin (Hb) levels were recorded at baseline, daily for 7 days and at 28 days after surgery. Surgical and post-operative blood loss were estimated from medical records.

RESULTS/FINDINGS: Subjects (581) were randomized in 18 US hospitals and 321 (159 Test and 162 Control) RBC-transfused recipients comprised the modified intent-to-treat (mITT) population. Test and Control subjects had similar histories, baseline characteristics, surgeries and 7-day total blood loss (median[IQR] Test 1500 [940-2475] mL, Control 1733 [1060-2880] mL, p=0.31) and had comparable Hb levels at baseline, post-surgery (median (IQR] 9.8 [8.9-10.9] g/dL Test, 9.6 [8.6-10.6] g/dL Control, p=0.16) and for 28 days. PR RBC units contained ~5% less total Hb (median [IQR] Test 58.0 (53.0-62.0) g Hb vs. Control 61.0 (57.0-66.0) g Hb, p< 0.001) and were stored longer prior to transfusion (median [IQR] Test 23.8 (16.9-29.4) days vs. Control 21.8 (15.0-28.3) days, p< 0.001). The Test arm received ~10% less total study plus non-study RBC Hb over 7-days (median Test 169.0g Hb vs. Control 188.0g Hb, p=0.01). Both groups received a median of 3 RBC components, However, Test subjects 32/159 (20.1%) required 5 or more RBC units within 7 days compared to Control 48/162 (29.6%, p=0.05), and more Control subjects required non-study RBC transfusions due to exceeding the available RBC supply [Test 35/159 (22.0%) subjects vs. Control 45/162 (27.8%) subjects]. Plasma utilization was significantly less in the Test group (median Test 2 units vs. Control 2 units, P=0.02) while platelet and cryoprecipitate use were not different. The incidence of AKI was 29.3%(46/157) for Test and 28.0% (45/161) for Control subjects in the mITT group. Non-inferiority for the incidence of AKI was achieved in both the mITT (p< 0.001) and the per protocol analyses (P=0.03). Adverse events, serious adverse events and deaths on study were not different.

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CONCLUSIONS: PR RBCs and conventional RBCs demonstrated equivalent support for patients undergoing cardiacor thoracic-aorta surgery while using ~10% less transfused total RBC Hb and fewer plasma units. The incidence of AKI was non-inferior to that with conventional RBCs.

Table 1: Transfusions within 7 Days of Surgery

	PR RBCs	Control RBCs	P-value
Total Study and Non-Study RBC units: Median (IQR)	3 (2-4)	3 (2-5)	0.09
Total Red Cell Hemoglobin: (g) Median (IQR)	169.0 (102.0-240.0)	188.0 (126.0-295.0)	0.01
Plasma Transfusions (subjects) (%)	39.6	41.3	
Median Plasma (units) (IQR)	2 (1-3)	2 (2-4)	0.02
Platelet Transfusions (subjects) (%)	52.8	58.0	
Median Platelets (units) (IQR)	2 (1-2)	2 (1-2)	0.65
Cryoprecipitate Transfusions (subjects) (%)	42.8	49.4	
Median Cryoprecipitate (units) (IQR)	2 (2-2)	2 (1-2)	0.38

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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, December 19, 2023. 2. The INTERCEPT Blood System for Cryoprecipitation for the manufacturing of Pathogen Reduced Cryoprecipitated Fibrinogen Complex Package Insert, Cerus Corporation, August 28, 2024. 3. The INTERCEPT Blood System for Plasma Package Insert, Cerus Corporation, September 6, 2022.