

**An Active Hemovigilance Program Provides Real-Time Data
to Monitor the Safety of INTERCEPT
Platelet and Plasma Components**

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in collaboration with the INTERCEPT Hemovigilance Study Centers**

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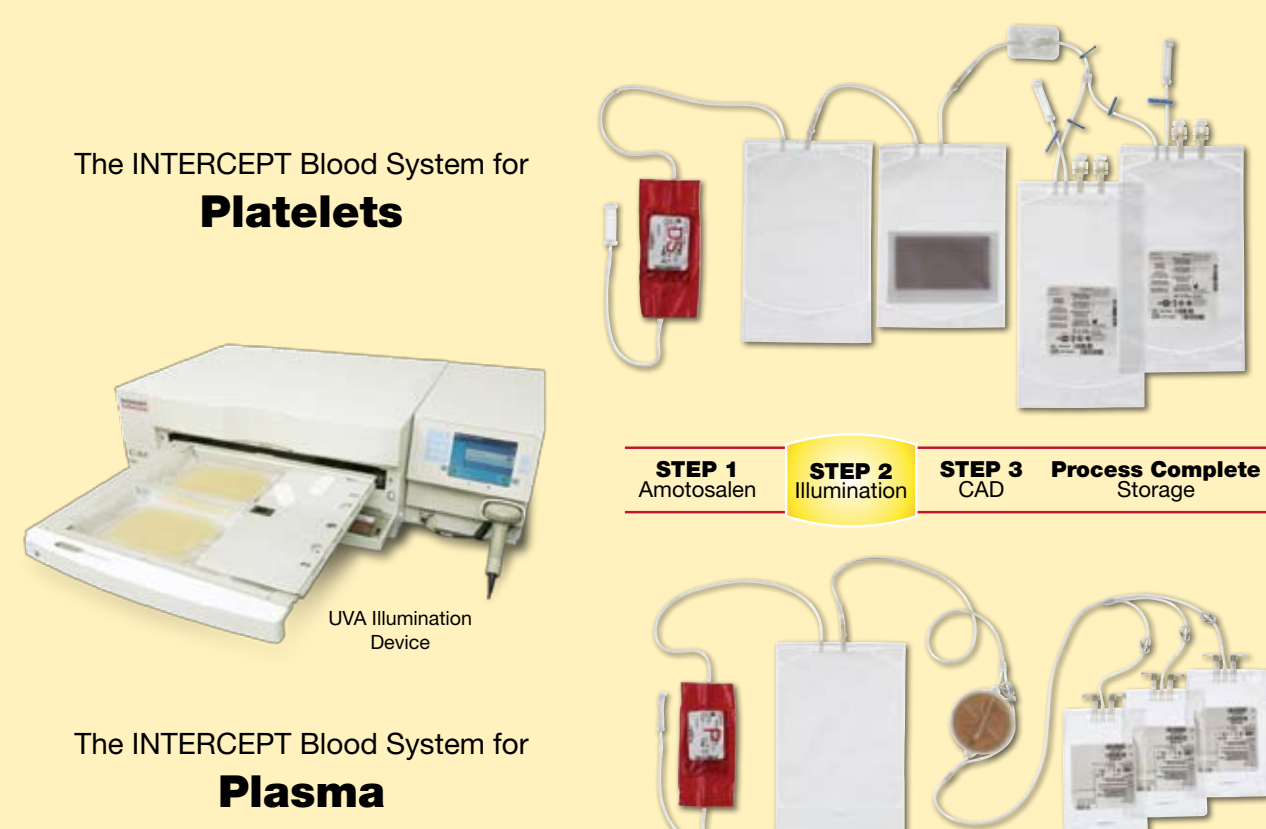
An Active Hemovigilance Program Provides Real-Time Data to Monitor the Safety of INTERCEPT Platelet and Plasma Components

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Background

The INTERCEPT Blood System™ is a CE Mark approved Class III medical device that inactivates pathogens and leukocytes using amotosalen and UVA light in platelet and plasma components (Figure 1). The INTERCEPT Blood System has been in routine clinical use since 2003 for platelets and 2007 for plasma. An active hemovigilance (HV) program has been on-going for more than 7 years to characterize and extend the safety profile of INTERCEPT™ platelets (I-PLT) and INTERCEPT plasma (I-PLA) in routine use. The HV program allows web based electronic data collection and reporting of safety information from multiple sites in real time.

Figure 1: INTERCEPT Processing Set



Aims

This report summarizes data for 41,638 transfusions of INTERCEPT platelet and plasma components. Hemovigilance data have been collected for 13,781 patients in routine practice at 23 different centers in 12 countries to provide a safety profile in a broad patient population (Table 1).

Methods

Study Center participation in the HV program was voluntary. There were no inclusion criteria for patients, other than the need for a transfusion. The participating centers used a standardized data capture form to record basic patient demographics, primary diagnosis, indication for transfusion, type of INTERCEPT product transfused, and patient safety data following each transfusion. Data were recorded for all patients and each transfusion regardless of the transfusion outcome. Adverse events (AE) within the first 24 hours and serious adverse events (SAE) within 7 days following each transfusion were recorded. The primary outcome measure was the incidence of acute transfusion reactions (ATR) following transfusion of INTERCEPT plasma or platelet components. An ATR was defined as an AE possibly related, probably related, or related to the INTERCEPT transfusion. A serious adverse reaction (SAR) was defined as an SAE possibly related, probably related, or related to the INTERCEPT transfusion. The INTERCEPT treatment replaced use of gamma irradiation, CMV testing, and bacterial detection.

Results

Data from the active HV program are summarized for 13,781 patients and 41,638 INTERCEPT transfusions, representing 19,534 I-PLT units and 55,258 I-PLA units (22,104 I-PLA transfusion episodes). The I-PLT were prepared from apheresis platelets (65%) or buffy-coat platelets (35%) and the I-PLA were prepared from apheresis plasma (99%) or whole blood plasma (1%) (Table 2).

The transfusion recipients represented a broad patient population from 12 countries and 23 centers. Overall, transfusion recipients were 0-93 years old, including 490 (3.6%) infants (< 1 year) and 439 (3.3%) pediatric patients (age 1-18 years). Transfusion recipients included patients with hematology-oncology diagnoses (51% of I-PLT and 18% of I-PLA recipients); surgical diagnoses (18% of I-PLT and 37% of I-PLA recipients); and for "other" diagnoses (30% of I-PLT and 45% of I-PLA recipients). Approximately 12% of the patients received I-PLT in support of stem cell transplant (SCT). Most patients received their first transfusion as hospital inpatients or in an intensive care unit (Table 3). Patients received up to 156 I-PLT and up to 186 I-PLA transfusion episodes.

The incidence of ATR was rare in all studies (Tables 4). The signs and symptoms of these ATRs were within the spectrum of known AEs following transfusion of conventional platelets and plasma. The intensity and the types of ATR have been consistent throughout the course of the HV program. Most ATR were non-serious (grade 1). In the platelet program: chills, urticaria, and pyrexia were the most frequently recorded events (Table 5-6). In the plasma study: chills, urticaria, rash, pruritus, and pyrexia were the most frequently recorded events (Table 5-6). SARs were very rare (Table 4). Only 8 patients (<0.1%) experienced a SAR. The "serious" criteria included Grade 2-4 events, classified as fatal, life-threatening, hospitalization, or other important medical events. The signs and symptoms of these SARs were also within the spectrum of known AEs following transfusion of conventional platelets and plasma; including allergic reactions, hypotension, and respiratory symptoms. The ATRs and SARs were considered related to the transfusion of the platelet or plasma components, but not specifically to the INTERCEPT process. No cases of TRALI, TA-GVHD, or transfusion transmitted infection were reported.

Table 2: INTERCEPT Component Characteristics

Transfusion Episodes	Platelet HV N=19,534	Plasma HV ^a N=22,104
Component		
Apheresis (%)	12,609 (65%)	21,846 (99%)
Buffy Coat (%)	6925 (35%)	NA
Whole blood (%)	NA	258 (1%)
Number of transfusions per patient (range)	1-156	1-186
Mean no. transfusions per patient	4.75	2.29

a. Interim data as of January 13, 2011; studies closed to enrollment, data analysis is in progress.

Table 3: Patient Demographics

Patients	Platelet HV N=4113	Plasma HV N=9668
Male (%)	2468 (60%)	5676 (59%)
Mean Age	NA	59
Hematology (%)	2100 (51%)	1743 (18%)
Surgery (%)	748 (18%)	3566 (37%)
Other (%)	1247 (30%)	4356 (45%)
SCT^a (%)	478 (12%)	Not collected
Location of 1st Transfusion		
Outpatient (%)	6%	0.1%
Inpatient (%)	66%	52%
ICU (%)	28%	48%

a. Stem Cell Transplant (data for autologous vs. allogeneic were not collected).

Table 4: Summary of AEs by Patient and Transfusion

AEs by Patient			
Patients	Platelet HV ^a N=4113	Plasma HV N=9668	Platelet and Plasma HV N=13,781
All AE	143 (3.5%)	44 (0.5%)	187 (1.4%)
Related AE (ATR)	99 (2.4%)	32 (0.3%)	131 (1.0%)
SAE	23 (0.6%)	16 (0.2%)	39 (0.3%)
Related SAE (SAR)	2 (<0.1%)	6 (<0.1%)	8 (<1.0%)
AEs per Transfusion Episode			
Transfusions	Platelet HV ^a N=19,534	Plasma HV N=22,104 (~55,260 units ^b)	Platelet and Plasma HV N=41,638
All AE	196 (1.0%)	55 (0.2%)	251 (0.6%)
Related AE (ATR)	128 (0.7%)	42 (0.2%)	170 (0.4%)
SAE	27 (0.1%)	17 (<0.1%)	44 (0.1%)
Related SAE (SAR)	2 (<0.1%)	6 (<0.1%)	8 (<0.1%)

a. Interim data as of January 13, 2011; studies closed to enrollment, data analysis is in progress.
b. One unit per platelet transfusion; approximately 2.5 units per plasma transfusion.

Table 5: Most Frequent Clinical Characteristics of ATR by Patient

Patient	Platelet HV ^a N=4113	Plasma HV N=9668	Platelet and Plasma HV N=13,781
Any ATR	99 (2.4%)	32 (0.3%)	131 (1.0%)
Chills	67 (1.6%)	11 (0.1%)	78 (0.6%)
Urticaria	37 (0.9%)	11 (0.1%)	48 (0.3%)
Fever	26 (0.6%)	5 (<0.1%)	31 (0.2%)
Rash	14 (0.3%)	10 (0.1%)	24 (0.2%)
Pruritus	17 (0.4%)	6 (<0.1%)	23 (0.2%)
Dyspnea	13 (0.3%)	3 (<0.1%)	16 (0.1%)
Nausea/Vomiting	6 (0.1%)	4 (<0.1%)	10 (<0.1%)
Tachycardia	5 (0.1%)	5 (<0.1%)	10 (<0.1%)
Hypotension	4 (<0.1%)	3 (<0.1%)	7 (<0.1%)

a. Interim data as of January 13, 2011; studies closed to enrollment, data analysis is in progress.

Table 6: Most Frequent Clinical Characteristics of ATR by Transfusion

Transfusion	Platelet HV ^a N=19,534	Plasma HV N=22,104	Platelet and Plasma HV N=41,638
Any ATR	128 (0.7%)	42 (0.2%)	170 (0.4%)
Chills	79 (0.4%)	12 (<0.1%)	91 (0.2%)
Urticaria	41 (0.2%)	13 (<0.1%)	54 (0.1%)
Fever	27 (0.1%)	5 (<0.1%)	32 (<0.1%)
Pruritus	20 (0.1%)	8 (<0.1%)	28 (<0.1%)
Rash	16 (0.1%)	11 (<0.1%)	27 (<0.1%)
Dyspnea	13 (<0.1%)	3 (<0.1%)	16 (<0.1%)
Nausea/Vomiting	8 (<0.1%)	4 (<0.1%)	12 (<0.1%)
Tachycardia	6 (<0.1%)	5 (<0.1%)	11 (<0.1%)
Hypotension	4 (<0.1%)	3 (<0.1%)	7 (<0.1%)

a. Interim data as of January 13, 2011; studies closed to enrollment, data analysis is in progress.

Table 1: INTERCEPT Hemovigilance Study Centers by Country

Country	Platelet HV Centers	Plasma HV Centers
Belgium	Centre de Transfusion, Mont Godinne Erasmus University Hospital, Brussels BTC AZ St. Jan Brugge AV, Brugge	Centre de Transfusion, Mont Godinne
Czech Republic	Institute of Hematology and Blood Transfusion, Prague	
Germany	University Blood Bank, Luebeck	
France	EFS Alsace, Strasbourg EFS Auvergne Loire, Saint-Etienne EFS Bretagne, Rennes EFS Ile de La Reunion, Saint Denis	EFS Alsace, Strasbourg EFS Auvergne Loire, Saint-Etienne
Iceland	University Hospital, Reykjavik	
Italy	Transfusion Center Pescara Hospital, Pescara San Camillo, Rome	
Norway	Haukeland University Hospital, Bergen St. Olav Hospital, Trondheim	
Portugal	Lisbon Hospital, Lisbon	
Slovenia	Zavod Transfuzijsko Medicino, Ljubljana	
Spain	Transfusion Center Spanish RC, Madrid Madrid BTC, Madrid Centro de Transfusion de Galicia, Santiago de Compostela Hospital Clinic Provincial, Barcelona CHEMICYL, Valladolid	Transfusion Center Spanish RC, Madrid Madrid BTC, Madrid
Sweden	University Hospital, Uppsala	
Switzerland	BSD SRK Basel Red Cross, Basel	

Conclusions

- INTERCEPT platelet and plasma components were well tolerated in routine use in a wide range of patients
- ATRs following transfusion of INTERCEPT platelet and plasma components were infrequent
- ATRs following transfusion of INTERCEPT platelet and plasma components were similar to those for conventional components
- No unexpected AEs were observed
- A web based electronic data capture system is a valuable tool for real-time safety surveillance across multiple centers and countries

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