

**An Active Hemovigilance Program
to Assess the Safety Outcome for 32,480
INTERCEPT Plasma Component Transfusions**

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on behalf of the INTERCEPT Plasma Hemovigilance Study Group**

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**Presented at the
12th International Haemovigilance Seminar (I.H.S)
Dubrovnik, Croatia • February 17-19th, 2010**

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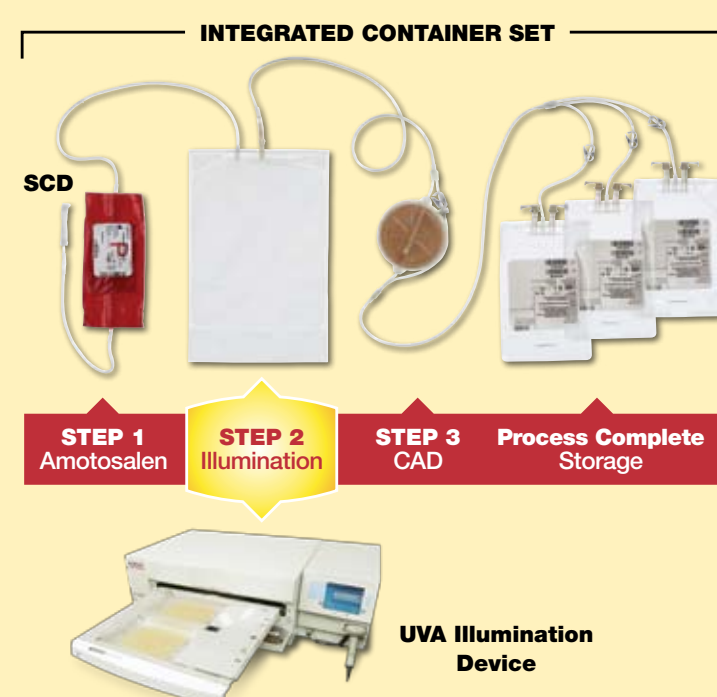
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Background

Inactivation of pathogens and leukocytes in plasma components using amotosalen and UVA light (INTERCEPT Blood System™) (Figure 1) received the CE mark in 2006 and has seen expanding clinical use in Europe. To measure post-approval safety, we established an active hemovigilance program utilizing electronic data capture to document acute transfusion reactions (ATRs) and serious adverse events (SAEs) after introduction of this novel product (Transfusion, doi: 10.1111/j.1537-2995.2009.02579.x).

Figure 1: The INTERCEPT Blood System for Plasma

Using a sterile connecting device (SCD), the plasma container is sterilely connected to the INTERCEPT kit. Amotosalen (1) is added by gravity flow and the plasma mixture is illuminated with UVA light (2). Residual amotosalen and its photoproducts in the plasma mixture are reduced to low levels using a compound adsorption device (CAD) (3) before the plasma is transferred to the storage containers.



Aims

To summarize safety outcome measures for 12,597 INTERCEPT™ plasma transfusion episodes involving 32,480 INTERCEPT components administered to 5,466 patients with clinical indications for plasma transfusion in routine clinical practice.

Methods

To capture safety data comprehensively, blood centers using INTERCEPT plasma components (IPL) completed a standardized web-based data form following each IPL transfusion episode regardless of the outcome. A transfusion episode constituted the transfusion of consecutive IPLs without a cessation of >2hr. The primary outcome measures were the occurrence of an acute transfusion

reaction (ATR) within 24 hr of each transfusion or a serious adverse event (SAE) within 7 days of each IPL transfusion. An ATR was defined as an AE possibly related, probably related, or related to the plasma transfusion. Investigators recorded: patient demographics, primary diagnosis and therapy, and type of plasma product (apheresis or whole blood). For AEs, the following data were collected: time

of event following transfusion, clinical description, objective clinical parameters (vital signs), results from clinical and laboratory tests (radiographs, bacterial cultures), severity (grade 0-4), serious or non-serious nature, and causal relationship to the transfusion (unrelated, probably unrelated, possibly related, probably related, or related).

Results

To date, of the 5,468 patients enrolled, a total of 5,466 patients with 12,597 transfusion episodes involving 32,480 IPL components have been reported in this program. More than 99% of IPL components were derived from apheresis. The patients were 60% male. The average age of patients was 57.6 years (4,945 patients >18 years; 217 patients were ≤18 age ≥1; and 306 patients < 1 year). Of the 5,466 patients, 1,166 (21%) received IPL transfusion for a haematologic disorder (including 27 patients with thrombotic thrombocytopenic purpura (TTP)), 1,753 (32%) for surgery or other invasive procedure, 2,546 (47%) for other indications including traumatic injury and massive hemorrhage. The mean number of IPL transfusion episodes per patient was 2.3 (range 1-68) the majority of patients received multiple IPL components (5.94 plasma components administered per patient) (Table 1). The occurrence of an ATR was infrequent (23/12,597, 0.18% per transfusion episode and 23/5466, 0.42% per patient basis). Of

the 23 ATRs in 17 patients, 19 ATRs were non-serious (all grade 1, the most frequent events were: urticaria, skin rash, itching and chills) and 4 ATRs in 4 patients were considered SAEs (Grade 3 and 4) (Table 2). One of the SAEs met the case definition for transfusion-

associated acute lung injury and one was considered transfusion-associated circulatory overload. Despite intensive IPL transfusions, only one TTP patient experienced a grade 1 ATR.

Table 1: Patient and INTERCEPT-Plasma Characteristics

	Number of Patients Total = 5,468*
Gender N (%)	
Male	3,262 (60%)
Female	2,206 (40%)
Age (years)	
Mean (min-max)	57.6 (<1 to 96)
< 1	306 (5.6%)
1-18	217 (4.0%)
>18	4,945 (90.4%)
Hematology	1,166 (21.3%)
Congenital Coagulation Deficiency	12 (1.0%)
Acquired Coagulopathy	1,109 (95%)
Immunodeficiency	26 (2.2%)
TTP	27 (2.3%)
Surgery	1,753 (32%)
Other diagnosis	2,546 (46.7%)
Patient location at time of administration	
Intensive care	2,778 (50.8%)
Non-intensive care	2,683 (49.0%)
Outpatient	7 (0.2%)
Number of transfusion episodes per patient	
Mean (range)	2.3 (1-68)
Number of PCT-plasma components administered per patient	
Mean (range)	5.94 (1-130)

* Two patients enrolled in this program didn't receive the IPL transfusions.

Table 2: Clinical Characteristics of Transfusion Adverse Events

	Per-Transfusion Basis N (% = N × 100/12,597)		Per-Patient Basis N (% = N × 100/5,466)	
	AEs Attributed To PCT-Plasma (ATR)*	SAEs† Attributed To PCT-Plasma (ATR)	AEs Attributed To PCT-Plasma (ATR)*	SAEs† Attributed To PCT-Plasma (ATR)
Number (%) with at least one AE	23 (0.18%)	4 (0.03%)	23 (0.42%)	4 (0.07%)
Signs/Symptoms‡				
Urticaria	8 (0.06%)	1 (0.01%)	8 (0.15%)	1 (0.02%)
Skin rash	6 (0.05%)	1 (0.01%)	6 (0.11%)	1 (0.02%)
Chills	5 (0.04%)	1 (0.01%)	5 (0.09%)	1 (0.02%)
Itching	5 (0.04%)	1 (0.01%)	5 (0.09%)	1 (0.02%)
Hypotension	3 (0.02%)	2 (0.02%)	3 (0.05%)	2 (0.04%)
Nausea	3 (0.02%)	1 (0.01%)	3 (0.05%)	1 (0.02%)
Tachycardia	3 (0.02%)	2 (0.02%)	3 (0.05%)	2 (0.04%)
Fever	2 (0.02%)	0 (0%)	2 (0.04%)	0 (0%)
Facial edema	2 (0.02%)	1 (0.01%)	2 (0.04%)	1 (0.02%)
Dyspnea	1 (0.01%)	1 (0.01%)	1 (0.02%)	1 (0.02%)
Bronchospasm	1 (0.01%)	1 (0.01%)	1 (0.02%)	1 (0.02%)
Pulmonary edema	1 (0.01%)	0 (0%)	1 (0.02%)	0 (0%)
Respiratory distress	1 (0.01%)	1 (0.01%)	1 (0.02%)	1 (0.02%)
Laryngeal edema	1 (0.01%)	1 (0.01%)	1 (0.02%)	1 (0.02%)
Cardiac failure	1 (0.01%)	1 (0.01%)	1 (0.02%)	1 (0.02%)

* All AEs reported in this study were classified as possibly related, probably related, or related to IPL-plasma transfusion, therefore, indicated as ATRs.

† SAE (Serious Adverse Event): Long-term life-threatening, immediate life-threatening, or death.

‡ Number of symptoms can exceed the number of transfusion reactions due to multiple observed symptoms per reaction.

Conclusions

- In this study to date, 99.8% of IPL transfusion episodes were not associated with an ATR.
- Adverse events following IPL transfusions classified as related were infrequent and representative of the events expected with transfusion of plasma components.
- These results suggest that IPL transfusions are well tolerated in a wide range of patients
- Use of an active HV program to capture the safety outcome from each transfusion is a valuable tool for post-marketing hemovigilance.