

**An Active Hemovigilance Program to Characterize
the Safety Profile of 16,631 Platelet Components Prepared
with Photochemical Pathogen Inactivation Treatment
Transfused in Routine Clinical Practice**

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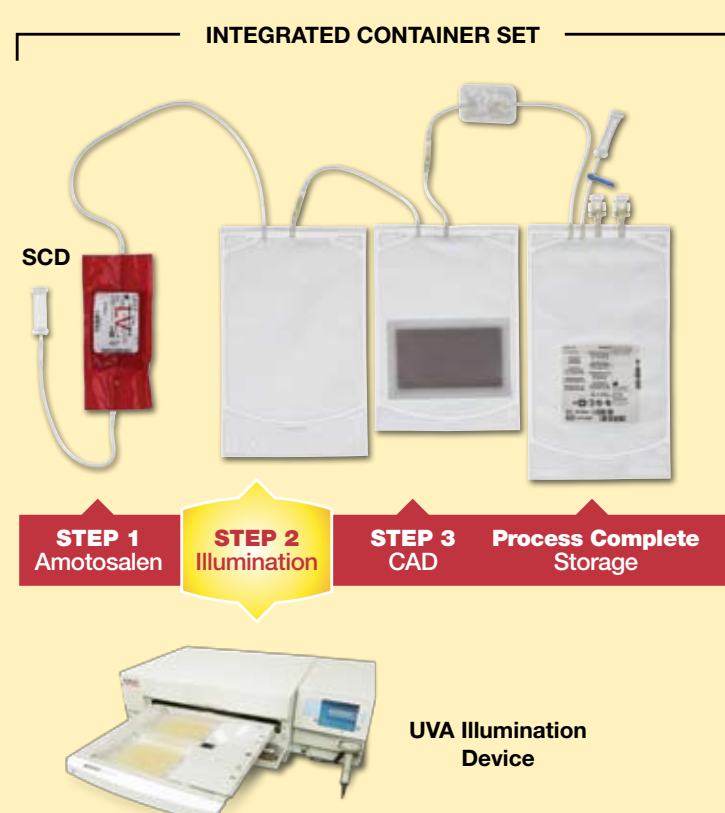
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Background

Inactivation of pathogens and leukocytes in platelets using INTERCEPT Blood System™ (Figure 1) is in routine use in many European blood centers. To characterize and extend the safety profile of INTERCEPT™ platelets (I-PLT) in routine use, an active hemovigilance (HV) program has been implemented and on-going for more than 5 years. The program allows collection and reporting of safety information on a real time basis and accommodates data collection at multiple sites over extended periods of time.

Figure 1: The INTERCEPT Blood System for Platelets

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



Aims

This report summarizes 16,631 I-PLT txn administered to 3,274 patients at 16 different sites in 7 European countries (Table 1) and provides a safety profile of I-PLT transfused in routine practice to a broad patient population.

Table 1: HV Participating Sites and INTERCEPT Platelet Transfusions

Site	Country	Number of Transfusions (%)
Transfusion Center, UCL, Yvoir	Belgium	7,551 (45.4%)
Erasmus University Hospital, Brussels	Belgium	899 (5.4%)
BTC, AZ St Jan Brugge AV, Brugge	Belgium	440 (2.6%)
EFS Alsace, Strasbourg	France	2,048 (12.3%)
EFS Auvergne Loire, St. Etienne	France	855 (5.1%)
EFS Bretagne, Rennes	France	501 (3.0%)
EFS Ile de La Reunion, Saint Denis	France	1,950 (11.7%)
CHEMICYL, Valladolid	Spain	381 (2.3%)
Hospital Clinic Provincial, Barcelona	Spain	117 (0.7%)
Madrid BTC, Madrid	Spain	156 (0.9%)
Transfusion Center, Spanish RC, Madrid	Spain	189 (1.1%)
Haukeland University Hospital, Bergen	Norway	322 (1.9%)
St.Olav Hospital, Trondheim	Norway	139 (0.8%)
University Hospital, Uppsala	Sweden	1,004 (6.0%)
University Blood bank, Luebeck	Germany	77 (0.5%)
Transfusion Center, Pescara Hospital, Pescara	Italy	2 (0.01%)

Total: 16,631 (100%)

Methods

Apheresis or pooled buffy-coat platelet components were leukoreduced, suspended in ~35% plasma and 65% InterSol™, treated with the INTERCEPT Blood System and stored for up to 7 days. INTERCEPT treatment replaced bacterial screening at all sites and gamma irradiation for 97.5% (16,325/16,631) of I-PLT transfusion. Blood centers using INTERCEPT platelets completed a data form after each transfusion regardless of whether

a reaction occurred. The focus was the response to transfusion within the first 24 hours. A common INTERCEPT Hemovigilance Transfusion Report Form was utilized. Investigators recorded: patient demographics, primary diagnosis and indication for transfusion, and type of I-PLT product. For each occurrence of an adverse event (AE), the following data were collected: time of adverse event following transfusion, clinical description of event, vital signs,

clinical and laboratory data (radiographs, bacterial cultures), event severity (grade 0-4), serious or non-serious classification, and causal relationship to transfusion (unrelated, probably unrelated, possibly related, probably related, or related). An acute transfusion reaction (ATR) was defined as an AE possibly related, probably related, or related to platelet transfusion. Serious adverse events (SAE) are followed for 7 days after each transfusion.

Results

From October 2003 to the present, data from 16,631 I-PLT transfusion (70% apheresis, 30% pooled buffy coats) administered to 3,274 pts (60% males/40% females) have been collected. Approximately 50% of the recipients were hematology/oncology patients (1,643 /3,274) many of whom received hematopoietic stem cell transplants (n=307). The majority of patients received I-PLT in non-intensive care hospital units (2,144, 66%), and the others were transfused in intensive care units (953, 29%) and outpatient clinics (177, 5 %) (Table 2). The average number of transfusions per patient was 5.1 transfusions (range 1-156) (Table 3).

A total of 152 adverse events occurred in 112 patients were reported, among the 152 events reported, 110 events in 82 patients were judged as “related” (possibly related, probably related, or

related) to I-PLT transfusion, thus classified as ATRs. Eleven AEs occurred in 10 patients were considered serious (SAE). Only one SAE (hypotension) was judged by the transfusion physician to be possibly related to I-PLT transfusion.

Transfusions associated with ATR following I-PLT transfusion were infrequent (110/16,631=0.66%). 2.5% patients (82/3,274) experienced at least one ATR following one or more INTERCEPT transfusion (Table 4). Most reactions were mild and of grade 1 severity and were representative of the events expected with conventional PLT transfusion. The most frequently reported signs/symptoms were chills, fever, and urticaria (Table 5). No cases of Transfusion Related Acute Lung Injury (TRALI), TA-GVHD, transfusion related sepsis or death due to INTERCEPT transfusions were reported.

Table 5: Clinical Characteristics of ATR

Signs/Symptoms*	Occurrence	% Per Patient	% Per Txn
Chills	70	2.1%	0.4%
Urticaria	35	1.1%	0.2%
Fever	23	0.7%	0.1%
Itching	10	0.3%	<0.1%
Skin rash	10	0.3%	<0.1%
Dyspnea	10	0.3%	<0.1%
Nausea/vomiting	8	0.2%	<0.1%
Tachycardia	4	0.1%	<0.1%
Hypotension	3	<0.1%	<0.1%
Lower back pain	1	<0.1%	<0.1%
Chest/abdominal pain	1	<0.1%	<0.1%
Facial redness	1	<0.1%	<0.1%

* Number of signs/symptoms can exceed the number of ATRs due to multiple observed symptoms per reaction.

Table 2: Demographics of Patients Transfused with INTERCEPT Platelets

	Total 3,274 Patients
Mean Age - Years (range)	58 (<1 - 96)
Male/Female (%) *	1,973 : 1,297 (60% : 40%)
Transfusion Location	
Hospital (Non-Intensive Care)	2,144 (66%)
Intensive Care	953 (29%)
Outpatient	177 (5%)
Indication for Transfusion	
Hematological disease	1,643 (50%)
Surgery	608 (18%)
General Medical	1,001 (31%)
Unknown diagnosis	22 (1%)

* Four patients had missing data on gender.

Table 3: INTERCEPT Platelet Characteristics and Patient Exposure to INTERCEPT Platelet

Type of Platelet Component	Number of Transfusions (%)
Apheresis	11,642 (70%)
Buffy Coat	4,989 (30%)
Transfusion Exposure	
Mean ± SD	5.1 ± 11.2
Range	1 - 156

Table 4: Clinical Adverse Events (AE)

	16,631 Transfusions Events (%)	3,274 Patients Events (%)
Any AE	152 (0.91%)	112 (3.4%)
Related AE (ATR)	110 (0.66%)	82 (2.5%)
Any SAE	11 (0.07%)	10 (0.31%)
Related SAE	1 (0.006%)	1 (0.03%)

Conclusions

- 99.34% of I-PLT administrations were without an I-PLT related acute transfusion reaction.
- Adverse events following I-PLT transfusion classified as possibly, probably, or related to transfusion were infrequent, mild in severity, and representative of the events expected with PLT transfusion.
- The use of an HV program to capture ongoing safety information is a valuable tool to characterize the safety of I-PLT.