

An Active Hemovigilance Program Provides Safety Data for Transfusing INTERCEPT™ Platelet and Plasma Components in Routine Clinical Practice



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Background

The INTERCEPT Blood System™ is a Class III CE Marked medical device that inactivates infectious pathogens (viruses, bacteria, protozoa) and leukocytes using amotosalen and UVA light in platelet and plasma components (Figure 1). The INTERCEPT Blood System

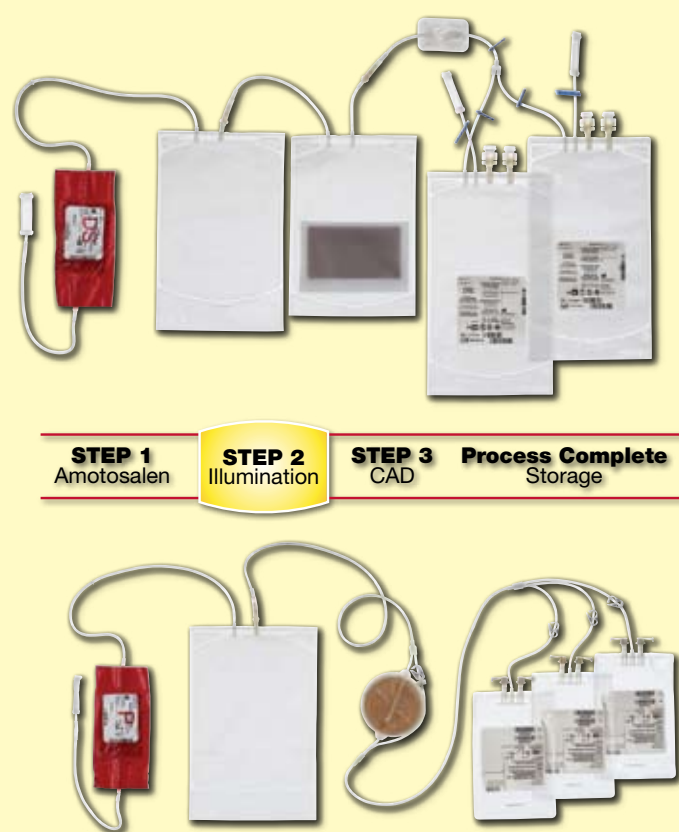
has been in routine clinical use since 2003 for platelets and 2007 for plasma. An active hemovigilance (HV) program has collected data to characterize and extend the safety profile of INTERCEPT™ platelets (I-PLT) and INTERCEPT plasma (I-PLA) in routine use since 2003.

Figure 1: The INTERCEPT Blood System for Platelets and Plasma

The INTERCEPT Blood System for Platelets



The INTERCEPT Blood System for Plasma



Aims

To summarize data for 41,276 transfusions of INTERCEPT platelet and plasma components to 13,734 patients during routine clinical practice in 22 study centers in 11 countries. The objective was to provide a comprehensive safety profile in a broad patient population over 8 years.

Table 1: INTERCEPT Hemovigilance Study Centers

| Country | Number of Study Centers |
|----------------|--------------------------------|
| Belgium | Platelet HV (3); Plasma HV (1) |
| Czech Republic | Platelet HV (1) |
| Germany | Platelet HV (1) |
| France | Platelet HV (4); Plasma HV (2) |
| Iceland | Platelet HV (1) |
| Italy | Platelet HV (2) |
| Norway | Platelet HV (2) |
| Portugal | Platelet HV (1) |
| Slovenia | Platelet HV (1) |
| Spain | Platelet HV (5); Plasma HV (2) |
| Sweden | Platelet HV (1) |

Methods

Study center participation in the active hemovigilance program was voluntary. There were no inclusion or exclusion criteria. The participating centers (Table 1) used a standardized data capture form to record basic patient demographics, primary diagnosis, indication for transfusion, and type of INTERCEPT product transfused. Trained hemovigilance personnel recorded patient safety data following each transfusion including: clinical observations, intensity Grade (0-4), and relationship to transfusion (Figure 2). Adverse events were classified as non-serious or serious according to standardized regulatory reporting criteria. 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 I-PLA or I-PLT components. An ATR was defined as any 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 definition of any SAE (Grade 2-4 events) was consistent with international regulatory guidance: outcomes that were fatal, life-threatening, required or prolonged hospitalization, resulted in congenital anomaly or birth defect, resulted in persistent or significant disability, or other important medical conditions. The INTERCEPT treatment system is approved to replace use of gamma irradiation, CMV testing, and bacterial detection.

Figure 2: Data Capture Form: CLINICAL OBSERVATION

| | | |
|---|---|---|
| <input type="checkbox"/> Fever | <input type="checkbox"/> Jaundice | <input type="checkbox"/> Lower back pain |
| <input type="checkbox"/> Chills | <input type="checkbox"/> Bronchospasm | <input type="checkbox"/> Chest/abdominal pain |
| <input type="checkbox"/> Cardiac arrhythmia | <input type="checkbox"/> Pulmonary oedema | <input type="checkbox"/> Shock |
| <input type="checkbox"/> Itching | <input type="checkbox"/> Dyspnea | <input type="checkbox"/> Other specify: |
| <input type="checkbox"/> Hypotension | <input type="checkbox"/> Respiratory distress | |
| <input type="checkbox"/> Urticaria | <input type="checkbox"/> Nausea | |
| <input type="checkbox"/> Skin rash | <input type="checkbox"/> Vomiting | |
| Relationship to platelet transfusion | <input type="checkbox"/> 0 - excluded/unlikely <input type="checkbox"/> 1 - possible <input type="checkbox"/> 2 - likely/probable <input type="checkbox"/> 3 - certain | |
| Grade | <input type="checkbox"/> 0 - isolated dysfunction without clinical or biological manifestation <input type="checkbox"/> 1 - absence of immediate or long-term life-threatening <input type="checkbox"/> 2 - long-term life-threatening <input type="checkbox"/> 3 - immediate life-threatening <input type="checkbox"/> 4 - death | |

Results

Data from the active HV program included 13,734 patients and 41,276 INTERCEPT transfusion episodes, representing 19,175 I-PLT components and 57,171 I-PLA components (multiple I-PLA units were transfused during 22,101 I-PLA transfusion episodes). The I-PLTs were prepared from apheresis collections (64%) or pooled whole blood buffy-coats (36%) and the I-PLA were prepared from plasma collected by apheresis (99%) or whole blood (1%).

Transfusion recipients were <1 to 93 years old, including infants (<1 year) and pediatric patients (age 1-18 years). Transfusion recipients included patients with hematology-oncology, surgical, or other medical indications for transfusion. Approximately 12% of the patients received I-PLT in support of hematopoietic stem cell transplant (HSCT). Most patients received their first transfusion as hospital inpatients (Table 2). During the 8 year observation period patients received up to

156 I-PLT and up to 186 I-PLA transfusion episodes. Overall, the incidence of ATR was low; 0.4% of transfusions and 0.9% of patients (Table 3). Most ATR were non-serious (Grade 1). The most frequent characteristics of ATR's were similar to those reported for conventional platelet and plasma components (Tables 4 & 5). Serious adverse reactions (SAR's) were very rare (<0.1%) on either a per transfusion or per patient basis. The signs and symptoms of the SAR's were also similar to expected serious adverse events following transfusion of conventional platelets and plasma; including allergic reactions, hypotension, respiratory symptoms, and TACO. The ATR's and SAR's were considered related to the transfusion of the platelet or plasma components, but not specifically to the INTERCEPT process. No cases of TRALI, TAGVHD, anaphylaxis, or transfusion-transmitted sepsis were reported.

Table 2: Patient Demographics and Indication for Transfusion

| Patients | Platelet Recipients N=4067 | Plasma Recipients N=9667 |
|--|----------------------------|--------------------------|
| Male/Female ^a | 2441/1622 | 5675/3992 |
| Infants (<1 y) | 59 (1.5%) | 440 (4.6%) |
| Children (1-18 y) | 185 (4.5%) | 355 (3.7%) |
| Adults (>18 y) | 3823 (94.0%) | 8872 (91.8%) |
| Primary Diagnostic Indication for Transfusion ^c | | |
| Hematology Disorder | 2055 (51%) | 1743 (18%) |
| HSCT ^b | 478 (12%) | Not collected |
| Surgery : Intra and Peri-operative Support | 748 (18%) | 3567 (37%) |
| General Medical Condition | 1246 (31%) | 4357 (45%) |
| Location of 1st Transfusion | | |
| Outpatient | 235 (6%) | 13 (0.1%) |
| Inpatient-non ICU | 2663 (65%) | 5018 (52%) |
| Intensive Care Unit | 1167 (29%) | 4636 (48%) |

a. Gender was not recorded for 4 patients. b. Hematopoietic Stem Cell Transplant (autologous or allogeneic). c. Includes >1 indication

Table 3: Summary of Adverse Events by Patient and Transfusion

| AE's by Per Patient Analysis | | | |
|--|-------------------|-----------------|------------------------------|
| Patients | Platelet N=4,067 | Plasma N=9,667 | Platelet and Plasma N=13,734 |
| Total AE | 126 (3.1%) | 44 (0.5%) | 170 (1.2%) |
| Related AE (ATR) | 94 (2.3%) | 32 (0.3%) | 126 (0.9%) |
| SAE | 13 (0.3%) | 16 (0.2%) | 29 (0.2%) |
| Related SAE (SAR) | 2 (<0.1%) | 6 (<0.1%) | 8 (<0.1%) |
| AE's by Per Transfusion Episode Analysis | | | |
| Transfusion Episodes | Platelet N=19,175 | Plasma N=22,101 | Platelet and Plasma N=41,276 |
| Total AE | 167 (0.9%) | 53 (0.2%) | 220 (0.5%) |
| Related AE (ATR) | 123 (0.6%) | 41 (0.2%) | 164 (0.4%) |
| SAE | 14 (<0.1%) | 16 (<0.1%) | 30 (<0.1%) |
| Related SAE (SAR) | 2 (<0.1%) | 6 (<0.1%) | 8 (<0.1%) |

Table 4: Most Frequent Clinical Characteristics of Acute Transfusion Reactions (ATR) by Patient

| Patient | Platelet N=4067 | Plasma N=9667 | Platelet and Plasma N=13,734 |
|-----------------|-----------------|---------------|------------------------------|
| Total ATR | 94 (2.3%) | 32 (0.3%) | 126 (0.9%) |
| Chills | 58 (1.4%) | 11 (0.1%) | 69 (0.5%) |
| Urticaria | 35 (0.9%) | 11 (0.1%) | 46 (0.3%) |
| Fever | 23 (0.6%) | 6* | 29 (0.2%) |
| Rash | 11 (0.3%) | 10* | 21 (0.2%) |
| Pruritus | 14 (0.3%) | 6* | 20 (0.1%) |
| Dyspnea | 12 (0.3%) | 2* | 14 (0.1%) |
| Nausea/Vomiting | 6 (0.1%) | 4* | 10* |
| Tachycardia | 5 (0.1%) | 5* | 10* |
| Hypotension | 4* | 3* | 7* |

*<0.1%

Table 5: Most Frequent Clinical Characteristics of Acute Transfusion Reactions (ATR) by Transfusion Episode

| Transfusion Episode | Platelet N=19,175 | Plasma N=22,101 | Platelet and Plasma N=41,276 |
|---------------------|-------------------|-----------------|------------------------------|
| Total ATR | 123 (0.6%) | 41 (0.2%) | 164 (0.4%) |
| Chills | 77 (0.4%) | 12* | 89 (0.2%) |
| Urticaria | 41 (0.2%) | 13* | 54 (0.1%) |
| Fever | 26 (0.1%) | 6* | 32* |
| Pruritus | 16* | 8* | 24* |
| Rash | 12* | 11* | 23* |
| Dyspnea | 12* | 3* | 15* |
| Nausea/Vomiting | 8* | 4* | 12* |
| Tachycardia | 6* | 5* | 11* |
| Hypotension | 4* | 3* | 7* |

Conclusions

- INTERCEPT platelet and plasma components were well tolerated in routine use in a broad population of patients representing the spectrum of diagnostic indications for transfusion.
- Acute transfusion reactions following transfusion of INTERCEPT platelet and plasma components were infrequent.
- The signs and symptoms of acute transfusion reactions following transfusion of INTERCEPT platelet or INTERCEPT plasma components were similar to those described for conventional components.
- No unexpected adverse events associated with INTERCEPT components were reported.