

Hemovigilance Surveillance of Therapeutic Plasma Prepared with Pathogen Inactivation Treatment During a Two Year Period

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ÉTABLISSEMENT FRANÇAIS DU SANG - ALSACE

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Background

EFS Alsace provides all labile blood components for 2 million inhabitants of the Alsace region. In 2007 pathogen inactivation (PI) treatment (amotosalen + UVA) of all plasma components (FFP) was implemented (INTERCEPT Blood System™, Cerus BV, Amersfoort, Netherlands).

Pathogen inactivation treatment of plasma was implemented to replace quarantine processing of therapeutic plasma. In compliance with regulations of the national medicinal agency (Afssaps) quality control and hemovigilance programs were utilized to monitor the quality and safety of FFP components.

Aims

- To determine the incidence of adverse events following the transfusion of plasma prepared with pathogen inactivation
- To monitor the quality of plasma prepared with pathogen inactivation in routine use

Methods

Plasma (650 mL) was collected by apheresis (Haemonetics MCS+, France). All components were treated with INTERCEPT (IA) according to manufacturer's directions and frozen within 8 hours of donation (Figure 1). Treated plasma was divided into three units each containing ≥ 200 mL and stored frozen until issued. Residual amotosalen levels were determined for 1% of components by quantitative HPLC assay and Factor VIII activity was measured

in 1% of units. Clinical response to transfusion was assessed under the Afssaps hemovigilance program (Transfusion 2001; 42: 1356) in which the response to each transfusion is evaluated for severity (Table 1) and imputability (Table 2). Adverse reactions with imputability score of 2 or > were classified as acute transfusion reactions (ATR). The incidence of ATR was compared for comparable time periods before and after introduction of FFP-IA.

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.

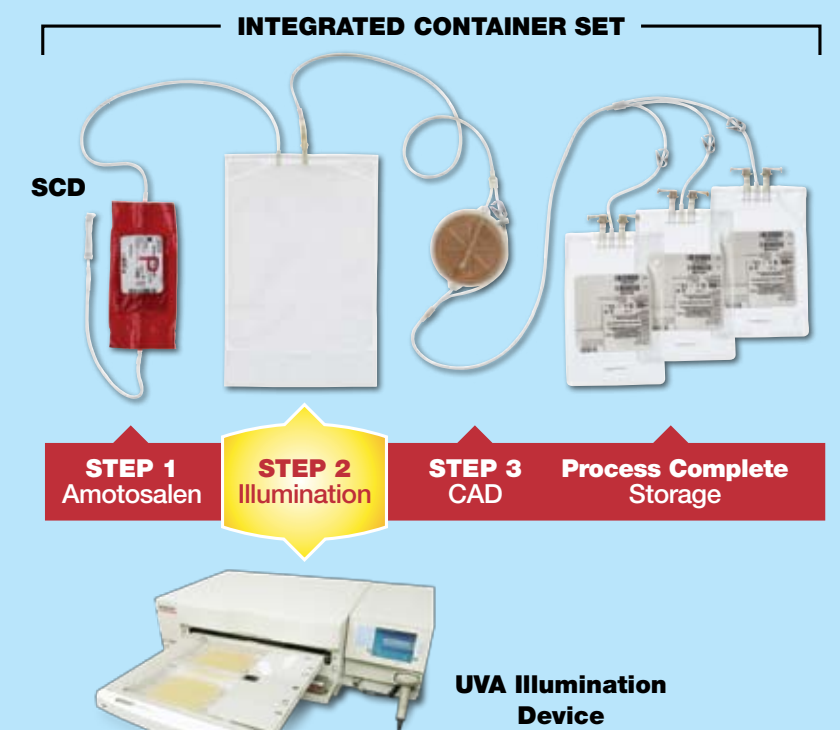


Table 1: Severity Grade System

Grade 1	Absence of immediate or long-term vital threat
Grade 2	Long term morbidity
Grade 3	Immediate vital threat
Grade 4	Death

Table 2: Imputability Score

Score = 0	No causal relationship
Score = 1	Doubtful
Score = 2	Possible
Score = 3	Likely
Score = 4	Unquestionable

Results

Plasma Characteristics: PI replaced quarantine plasma (FFP-Q) for routine production. A total of 30,957 FFP-IA units (41% A, 11% B, 31% O, and 14% AB) were prepared with an average volume of 205 ± 8 mL. 1% of production was tested for residual amotosalen with 100% conformance: Mean = 0.63 ± 0.10 μ M within the Afssaps requirements of < 2 μ M. 41 pools of 6 FFP-IA units were tested for Factor VIII activity (Mean = 0.8 ± 0.1 IU/mL) in conformity with requirements of ≥ 0.7 IU/mL.

Clinical Outcomes: Between 9.2007 and 5.2009 a total of 26,234 FFP-IA units were transfused and 21 acute transfusion reactions (ATR) were reported of which 14 occurred in association with transfusion of other blood components and 7 with FFP-IA alone. New RBC allo-antibodies to minor RBC antigens were detected in 10 patients, and are reported as adverse events in the Afssaps system. These patients also received RBC components. ATR ranged in severity from Grade 1 to 3 with no Grade 4 events and no deaths reported. The incidence rate per 1,000 FFP-IA units transfused was identical to the ATR incidence for quarantine plasma (FFP-Q) units transfused from 1.2004 to 1.2007 (Table 4). The comparative periods included 25 patients treated with therapeutic plasma exchange (TPE) using FFP-IA ranging from 1 to 71 TPE: median total volume exposure = 7.4 L (Range 1 – 154 L) compared to 17 patients with FFP-Q ranging from 2 – 32 TPE: median total volume exposure = 5.9L (Range 1.9 – 60.3L).

Table 3: Adverse Events Associated with Plasma Transfusions Classified as Acute Transfusion Reactions

ATR Severity Grade	Allergic Reaction	New RBC Allo-Antibody Detected	Febrile Non-Hemolytic	TRALI	Unknown	%
1	5		1		1	33
2		10				48
3	2			2		19

Table 4: The Incidence of Acute Transfusion Reactions Before and After Implementation of FFP-IA

Product	Plasma Units Transfused	ATR per 1,000 Plasma Units
FFP-Q	35,064	0.8
FFP-IA	26,234	0.8

Conclusions

- The incidence of ATR with FFP-IA was similar to that for FFP-Q during similar periods of observation
- Both periods included a population of patients treated with TPE requiring multiple exposures to large volumes of plasma
- FFP-IA exhibited an acceptable safety profile and suitable quality control characteristics for Factor VIII activity during 21 months of routine use