

Cumulative Clinical Data of INTERCEPT Blood System for Platelets Demonstrate Ability to Replace Gamma Irradiation in Routine Clinical Use for TA-GVHD Prevention

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Background

The INTERCEPT Blood System™ (IBS) for platelets received CE Mark registration as a Class III Medical Device in 2002 for pathogen inactivation treatment of platelet components (Figure 1). IBS has been in routine clinical use for 8 years in Europe, Russia, and the Middle East. Prior to CE registration of INTERCEPT™, gamma irradiation was the standard method used to prevent transfusion-associated graft versus host disease (TA-GVHD). A specific indication for INTERCEPT treatment to replace gamma irradiation for prevention of TA-GVHD received CE Mark approval in 2008. Subsequently, country-specific regulatory agencies including the Paul Ehrlich Institute (PEI) of Germany, the Agence Française de Sécurité Sanitaire des Produits de Santé (Afsaps) of France, and the SwissMedic of Switzerland separately approved the use of INTERCEPT in place of gamma irradiation

for prevention of TA-GVHD for all patient populations at risk.

Approval of IBS to replace gamma irradiation was supported by *in vitro* and *in vivo* studies including a clonal T cell proliferation assay by limiting dilution analysis demonstrating robust inactivation of T cells by INTERCEPT treatment to the same level as gamma irradiation, but with a 3000-fold efficacy margin (Figure 2). Additional complimentary assays demonstrated high levels of genomic DNA modification (1 adduct/83 base pairs) (Figure 3), complete inhibition of cytokine synthesis (Figure 4), and elimination of early activation antigen presentation. *In vivo* animal studies confirmed that INTERCEPT inactivated T-cells could not initiate TA-GVHD in immuno-compromised recipients.

Aim

To evaluate the efficacy of INTERCEPT for prevention of TA-GVHD in clinical use.

Methods

We analyzed 8 years of cumulative experience obtained from clinical trial and routine use of INTERCEPT treated platelet components, without gamma irradiation, transfused in a broad patient population. Data were obtained from clinical trial databases and hemovigilance (HV) studies. The populations studied were enriched for immune-compromised hematology-oncology patients at risk for TA-GVHD, and hematopoietic stem cell transplantation (HSCT) recipients.

Figure 1: The INTERCEPT Blood System for Platelets

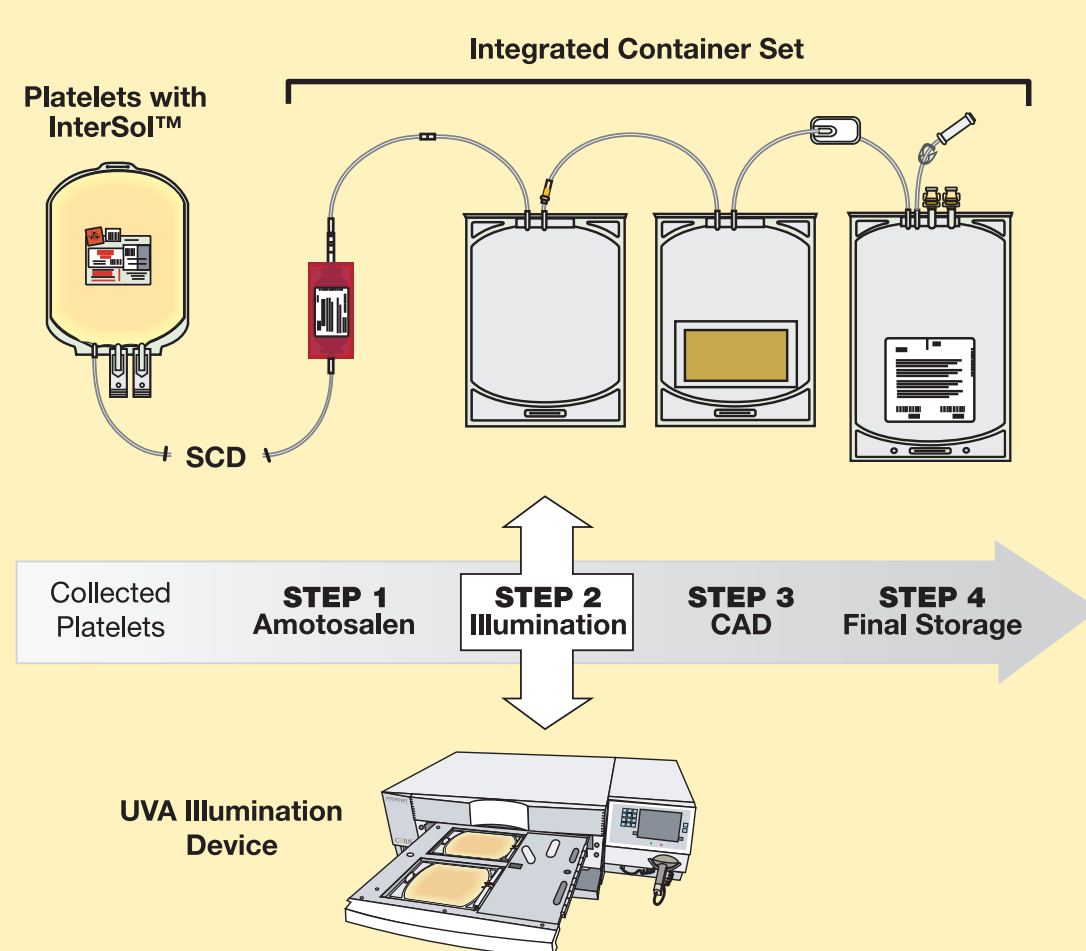


Figure 2: INTERCEPT PI treatment inactivates T leukocytes with an increased efficacy margin vs. gamma irradiation

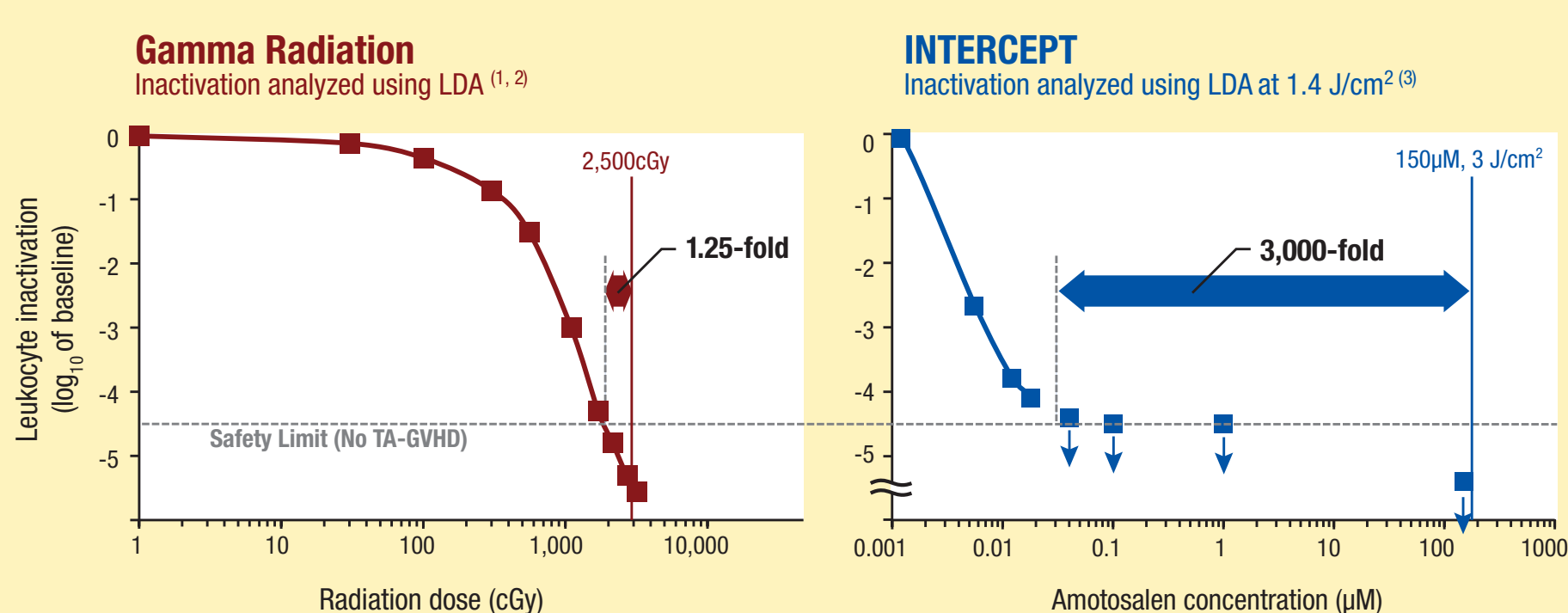


Figure 3: INTERCEPT Mechanism of Action

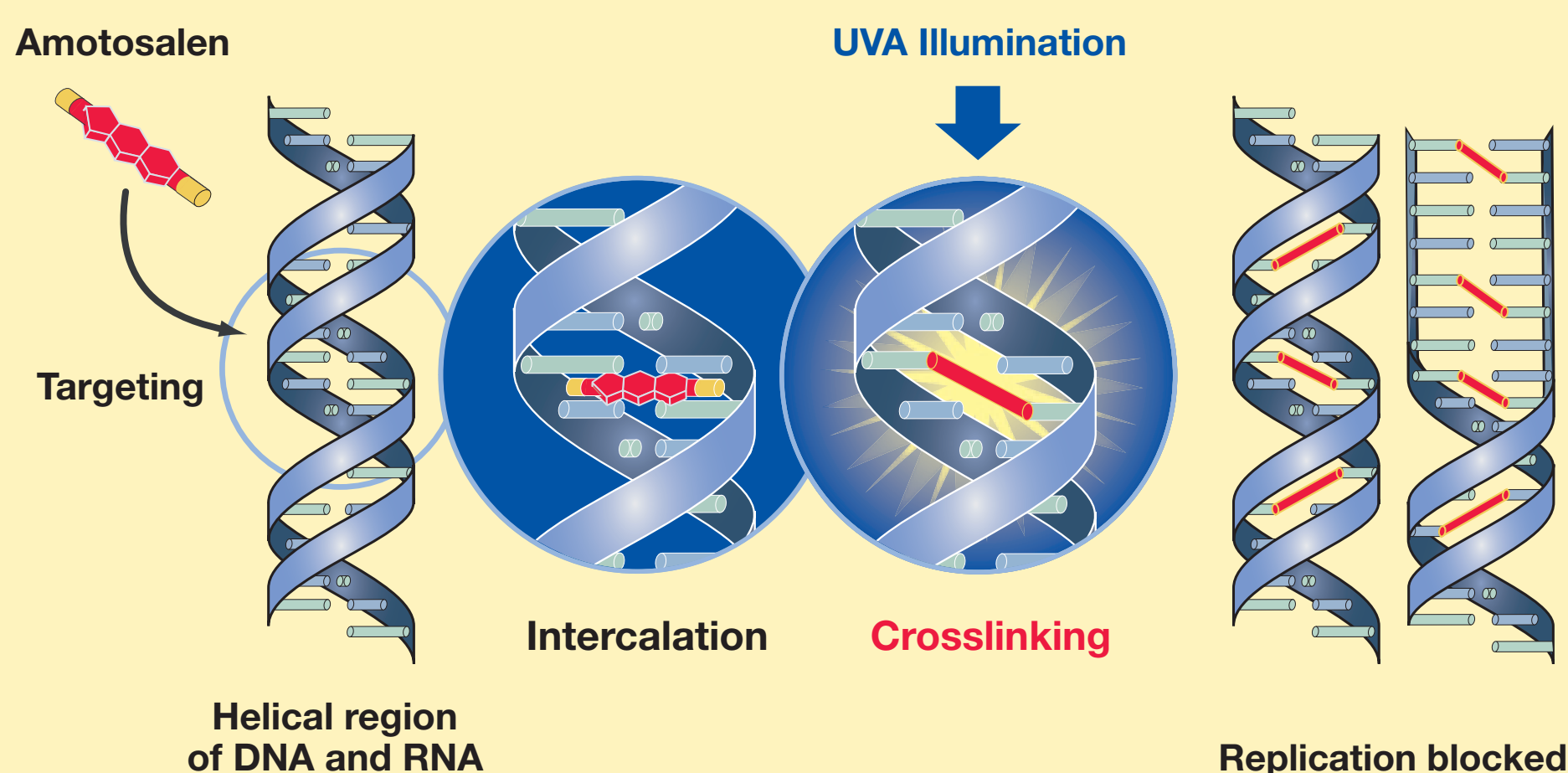
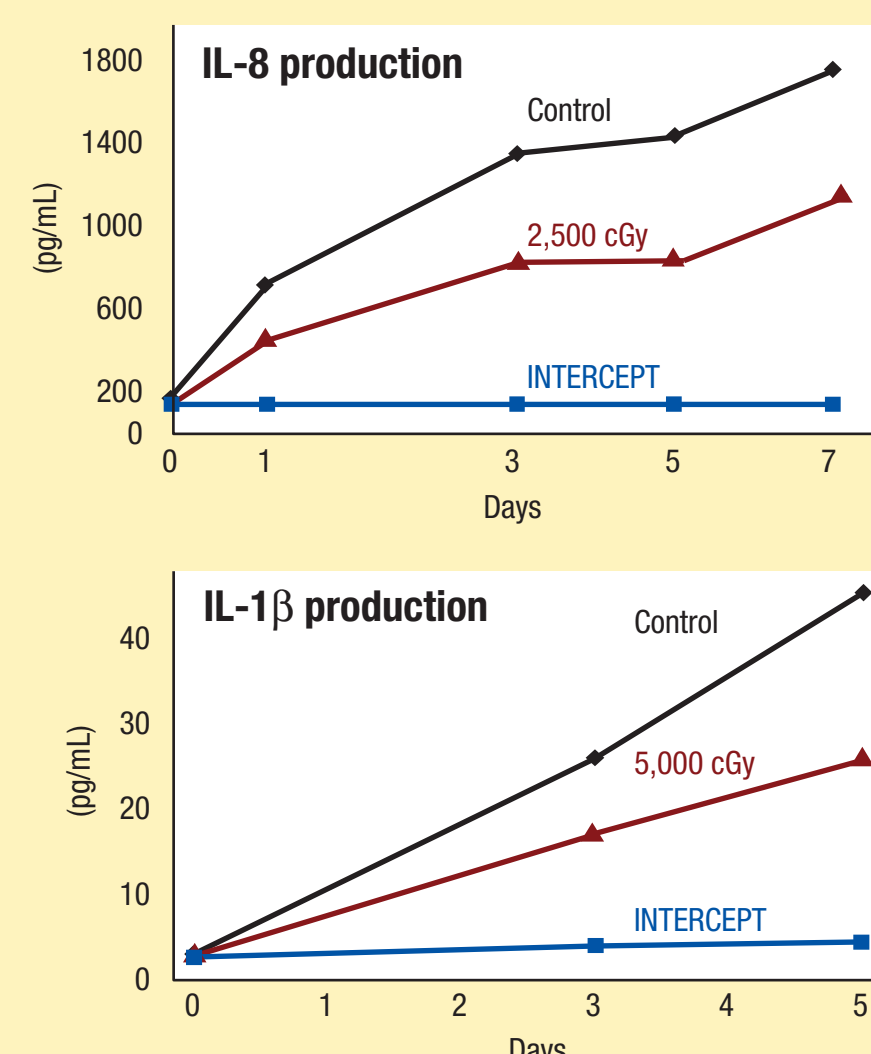


Figure 4: INTERCEPT treatment of Platelets results in complete inhibition of cytokine synthesis during platelet concentrate storage, while gamma irradiation causes partial inhibition



Results

The cumulative frequency of TA-GVHD for patients transfused with INTERCEPT platelet components in place of gamma irradiation including hematology-oncology, HSCT recipients, and pediatric patients from 24 centers in 12 European countries were assembled (Table 1). A significant number of HSCT patients were evaluated and no cases of TA-GVHD were reported. In addition to the Phase III and HV studies, blood centers have purchased INTERCEPT kits representing production of more than 500,000 platelet components to date. Most blood centers using INTERCEPT have discontinued gamma irradiation and rely on the inactivation process to provide protection against TA-GVHD. No cases of TA-GVHD have been reported by these centers in association with transfusion of INTERCEPT platelet components.

Table 1: Summary of TA-GVHD Incidence in Patients Receiving Non-Gamma Irradiated INTERCEPT Platelet Components in Clinical Trials and Hemovigilance (HV) Studies

Study	Number of Transfusions	% Non-gamma irradiated	Total Number of Patients	Hem-Onc Patients	HSCT Patients	Incidence of TA-GVHD
Phase III Trials ^d	529	100%	87	82	28	0
HV1 ^e	5,106	97.3% ^a	651	378	47	0
HV2 ^f	7,437	98.9% ^b	1,400	748	121	0
HV3	6,632	95% ^c	2,016	929	310	0
Mt. Godinne ^g	3,645	100%	186	186	186	0
Pediatric ^h	500	100%	83	48	10	0
Basel ⁱ	551	100%	46	38	15	0
Lübeck ^j	560	100%	52	52	17	0
Strasbourg ^k	55,104	100%	~8,000	~4,400	not available	0

a. Prior to CE Mark gamma replacement approval 139 of the 5,106 products (2.7%) performed in Trondheim, Norway were gamma irradiated. b. Prior to Afsaps's approval, a small number of products (82 of 7,437, or 1.1%) performed in France were also gamma irradiated. c. Based on data up to Jan 2011. d. van Rhenen et al. Blood. 2003;101: 2426-33. Janetzko et al. Transfusion. 2005;45: 1443-52. e. Osselaer et al. Transfusion. 2008;48: 1061-71. f. Osselaer et al. Vox Sang. 2008;94: 315-23. g. Osselaer et al. Vox Sang. 2010;99:428. h. Van Haute I, et al. Vox Sang. 2006;91: 177. i. Stebler C, et al. Vox Sang. 2007;93: 172. j. Schlenke P, et al. Vox Sang. 2007;93: 171. k. JP Cazenave. 2010. Bull Acad Natle Med.

Conclusions

Cumulatively, the clinical experience supports use of INTERCEPT treatment in place of gamma irradiation to prevent TA-GVHD in at risk patients.

References

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