Hemostatic efficacy of pathogen-inactivated vs untreated platelets: a randomized controlled trial

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Supplementary Appendix

Supplement to:

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Contents **page**

Principal investigators and study centers by country

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Canada: Michael Trus, Juravinsky Hospital, Hamilton; Alan Tinmouth, Ottawa Hospital, Ottawa; Yulia Lin, Sunnybrook Health Sciences Centre, Toronto; Cyrus Hsia, London Health Sciences Center, London; David Lee, Kingston General Hospital, Kingston.

Numbers of included patients per study site

HagaZiekenhuis, The Hague (NL)	219
Leiden University Medical Center, Leiden (NL)	83
Maastricht University Medical Center, Maastricht (NL)	55
Erasmus Medical Center, Rotterdam (NL)	55
Haukeland University Hospital, Bergen (No)	23
Juravinsky Hospital, Hamilton (Can)	61
Ottawa Hospital, Ottawa (Can)	34
Sunnybrook Health Sciences Centre, Toronto (Can)	13
London Health Sciences Center, London (Can)	16
Kingston General Hospital, Kingston (Can)	8

Supplementary tables.

Table S1. Analyzed populations

Primary bleeding endpoint	
ITT	Every inclusion, no exclusions due to off-protocol transfusions, no grade ≥2 bleeding at randomization, bleeding observation ***from randomization*** until first grade ≥2 bleed (Table 2)
PP	Every inclusion, only if ≥75% on-protocol transfusions from randomization to first ≥2 bleed, no grade ≥2 bleeding at randomization neither at day of first transfusion, bleeding observation ***from first transfusion*** until first grade ≥2 bleed (Table 2)
PPO	Every inclusion, only if 100% on-protocol transfusions from randomization to first ≥2 bleed, no grade ≥2 bleeding at randomization neither at day of first transfusion, bleeding observation ***from first transfusion*** until first grade ≥2 bleed (Suppl.)
Efficacy endpoints	
ITT	Every inclusion, no exclusions due to off-protocol transfusions, no grade ≥ 2 bleeding at randomization (Table 4)
PP	Every inclusion, only on-protocol transfusions, no exclusions due to off-protocol transfusions, no grade ≥ 2 bleeding at randomization (Table 4)
Alloimmunization	
ITT	First inclusion, no exclusions due to off-protocol transfusions, at least two samples available for antibody testing, first sample negative for allo-antibodies (Suppl)
PP	First inclusion, only if ≥75% on-protocol transfusions, at least two samples available for antibody testing, first sample negative for allo-antibodies (Suppl)
PPO	First inclusion, only if 100% on-protocol transfusions, at least two samples available for antibody testing, first sample negative for allo-antibodies (Figure 3)

Table S2. Bleeding complications (per protocol only)

		Control	Intervention
No. of transfusion treatment periods		200 (163 patients)	164 (142 patients)
Primary endpoint			
WHO grade 2, 3 or 4 bleeding[#]		87 (44%)	85 (52%)
No. of days from *first transfusion* to first grade 2, 3, or 4 bleeding	median (IQR)	3 (1-4)	2 (1-4)
Percentage of days with grade 2, 3, or 4 bleeding[$]	median (IQR)	0 (0-15)	4 (0-17)
No. of days with grade 2, 3, or 4 bleeding	median (IQR)	0 (0-2)	1 (0-2)
Bleeding details			
Highest grade of bleeding			
None or grade 1		113 (57%)	79 (48%)
Grade 2		78 (39%)	82 (50%)
Grade 3		4 (2%)	2 (1%)
Grade 4		5 (3%)	1 (1%)

WHO = world health organization; IQR=interquartile range;

[#] *difference: 8 percentage points, 95% CI (-2 to 19), p-value for non-inferiority 0.216*

after correcting for stratification factors (center, diagnosis AML/non-AML and treatment phase conventional/stem cell):

difference: 10 percentage points, 95% CI (1 to 19), p-value for non-inferiority 0.28

[$] *p-value for superiority of mean percentages 0.483*

Table S3. Platelet transfusion characteristics and pre transfusion platelet count (intention to treat)

		Control	Intervention
No. of platelet transfusions		*1568*	*1659*
Characteristics			
Product type according to protocol		*1400 (89%)*	*1373 (83%)*
Indication of PLT transfusion			
Prophylactic		*1349 (86%)*	*1436 (87%)*
Therapeutic		*139 (8.6%)*	*178 (11%)*
Other/Unknown		*80 (5.1%)*	*45 (2.7%)*
Major ABO incompatibility		*107 (6.8%)*	*98 (5.9%)*
PLT content	10^{11} ± *SD*	*3.46 ± 0.78*	*3.34 ± 0.56*
Storage time	*days ± SD*	*4.1 ± 1.6*	*3.9 ± 1.6*
No. of PLT transfusions stored 6 or 7 days		*294 (19%)*	*265 (16%)*
Pre transfusion PLT count	10^9/*L*	*16 ± 14*	*14 ± 9*

ITT = intention-to-treat; PLT = Platelet; SD = Standard deviation

Table S4. Platelet transfusion characteristics and pre transfusion platelet count (per protocol)

		Control	**Intervention**
No. of platelet transfusions		*1166*	*1269*
Characteristics			
Product type according to protocol		*1103 (95%)*	*1137 (90%)*
Indication of PLT transfusion			
Prophylactic		*1005 (86%)*	*1137 (90%)*
Therapeutic		*95 (8.1%)*	*104 (8.2%)*
Other/Unknown		*66 (5.7%)*	*28 (2.2%)*
Major ABO incompatibility		*83 (7.1%)*	*77 (6.1%)*
PLT content	10^{11} ± *SD*	*3.38 ± 0.67*	*3.33 ± 0.54*
Storage time	*days ± SD*	*4.2 ± 1.6*	*3.9 ± 1.6*
No. of PLT transfusions stored 6 or 7 days		*219 (19%)*	*205 (16%)*
Pre transfusion PLT count	10^9/*L*	*15 ± 15*	*14 ± 9*

PP = Per-protocol; PLT = Platelet; SD = Standard deviation

Table S5. Transfusion reactions, adverse and serious adverse events.

		Control	**Intervention**
No. of transfusion treatment periods		*279*	*277*
No of transfusion reactions		*44*	*63*
No of transfusion treatment periods with 1 or more transfusion reaction	N (%)	*39 (14)*	*45 (16)*
No of AEs		*168*	*127*
No of transfusion treatment periods with 1 or more AEs	N (%)	*83 (30)*	*89 (32)*
No of SAEs		*52*	*37*
No of transfusion treatment periods with 1 or more SAEs	N (%)	*42 (15)*	*34 (12)*
No of SAEs related to PLT transfusion		*1*	*1*

AEs = Adverse events; SAEs = Serious adverse events; PLT = Platelet; ITT = Intention-to-treat

Supplementary Figures

Figure S1 shows the study scheme.

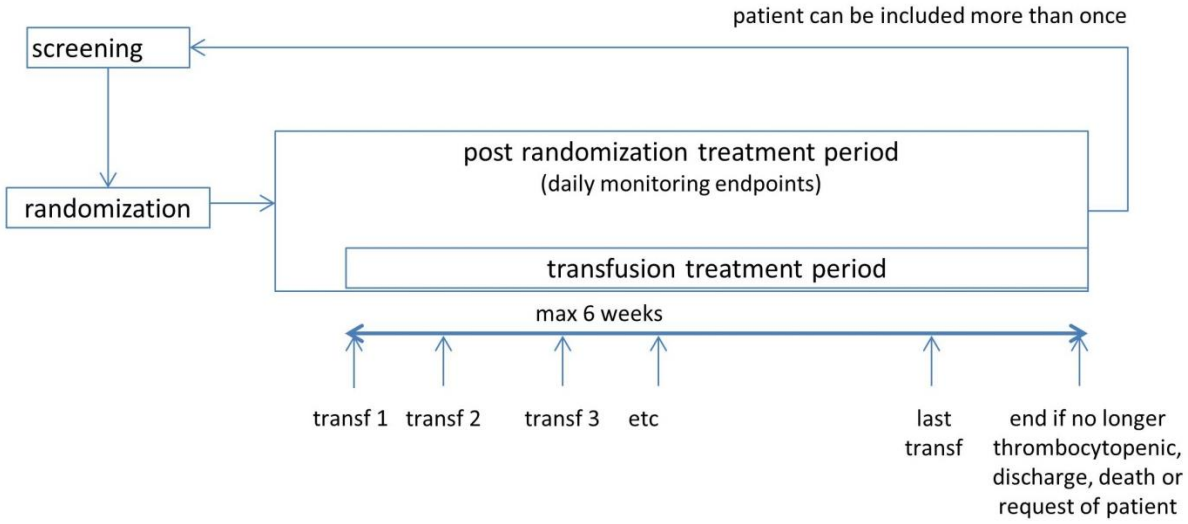

Figure S2 shows the time to the appearance of HLA-class I allo-antibodies in the intention to treat population. In the control arm 6 of the 197 patients developed antibodies as opposed to 15 of 209 in the intervention arm. The risk ratio for cumulative event probabilities at 60 days was 1.75 (95% CI 0.67 – 4.59, p = 0.25).

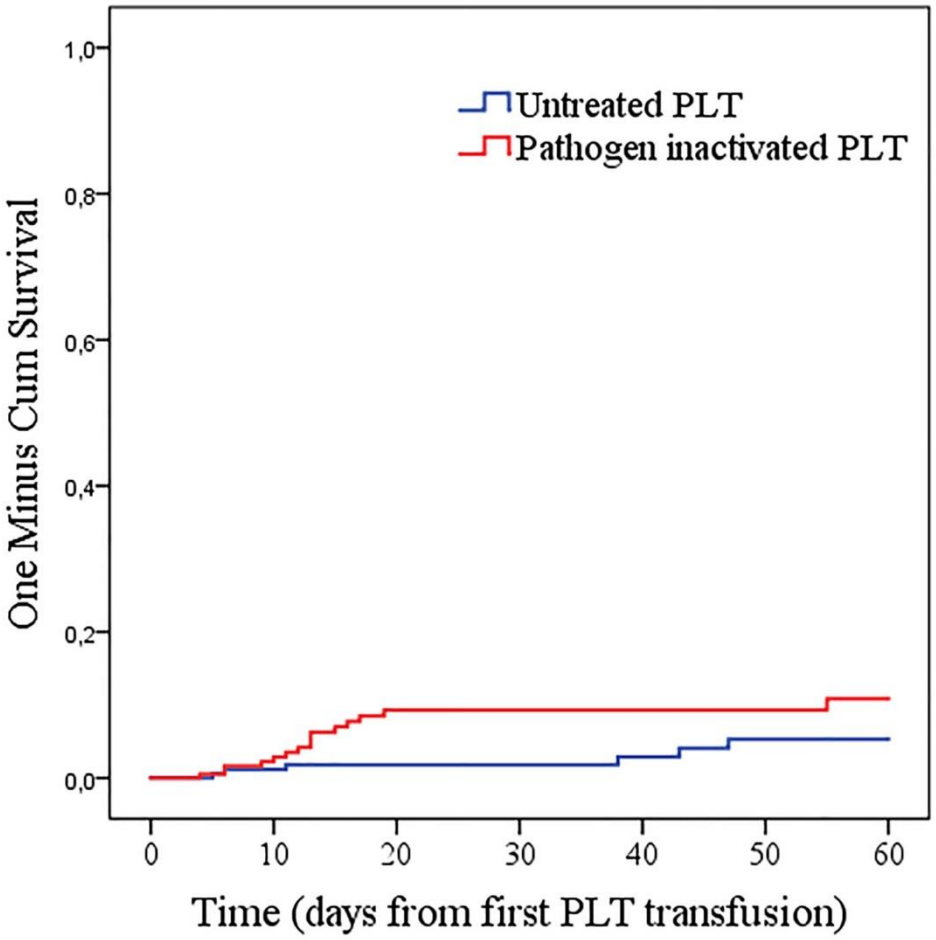

Figure S3 shows the time to the appearance of HLA-class I allo-antibodies in the per protocol population. In the control arm 6 of the 185 patients developed antibodies as opposed to 10 of 193 in the intervention arm. The risk ratio for cumulative event probabilities at 60 days was 1.53 (95% CI 0.55 – 4.30, p = 0.42).