Table 3 Assessment of risk of bias in the randomized controlled trial

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Patients were randomized before chemotherapy and the development of thombocytopenia but the method of randomization was not stated.
Allocation concealment (selection bias)	Low risk	Randomization results were concealed from ward physicians and nurses
Blinding (performance bias and detection bias)	Unclear risk	The assessment of bleeding was not well described (i.e. who assessed the bleeding outcomes). Physicians and nurses were blinded, however it is unclear whether the study personnel was blinded.
Incomplete outcome data (attrition bias)	Low risk	Of the total 78 patients, two patients from the group receiving unmatched platelets and one patient from the HLA matched group were withdrawn from the study because of bleeding that required more than two platelet transfusions within 24 hours.
Selective reporting (reporting bias)	Unclear risk	Details of all outcomes to be assessed were not specified.
Protocol deviation	Low risk	Although only 3.5% patients were reported to have received transfusions that differed from those assigned, the allocation group of these patients was

		not stated. Data was analyzed according to platelets received.
Other threats to validity	High risk	The sample size was not predetermined to assess a difference in bleeding.

Table 4 Characteristics of Non-Randomized Studies

Author, Year	Country	Centre Status	Population	Definition of Refractoriness
Prospective				
Marktel S, 2010 [24]	Italy	Single centre	Pediatric thalassemia undergoing HSCT	NA
Levin M D, 2003[25]	Netherlands	Single centre	HT	NA
Petz LD, 2000[16]	United States	Single centre	Refractory patients with no non immune factors, (1 to 80 yrs)	Three platelet transfusions yielded 1 hr PPR < 30% or 20 hr PPR < 20%
Hogge DE, 1995[26]	Canada	Single centre	Pediatrics with HT N=20 had other diseases	NA
Friedberg RC, 1994[27]	United States	Single centre	Refractory patients	1 hr CCI ≤ 7500 on successive days
Moroff G, 1992[45]	United States	Multicentre	Refractory patients with no non immune factors	1 hr CCI <10000/uL after at least two RDP tx
Bishop JF, 1988[46]	Australia	Two centres	Adult HT	NA

Murphy MF, 1986[28]	United Kingdom	Single centre	Acute leukemia excluding patients with HLA, anti platelet antibodies or GRAN, (17 to78 yrs)	No measurable recovery 20 hr after transfusion in the absence of non-immune factors
Ware R, 1985[29]	United States	Single centre	Refractory HT with no non immune factors (10-68 yrs)	CCI < 10000 on at least two occasions of RDP tx
Dahlke MB, 1984[30]	United States	Single centre	Refractory patients with no non immune factors	NR
Hester JP, 1978[31]	United States	Single centre	HT	NA
Macpherson BR, 1979[32]	United States	Single centre	Refractory patients	16 hr CCI <3000
Duquesnoy RJ, 1977[13,20]	United States	Single centre	Refractory patients with no non immune factors	24 hr PPR < 10% on at least 2 occasions
Wu KK, 1977[33]	United States	Single centre	Refractory acute leukemia	Lack of expected responses to RDP on two occasions in the absence of non-immune factors
Herzig RH, 1975[34]	United States	Single centre	Refractory patients with no non	NR

			immune factors	
Retrospective				
Fontaine M, 2011[35]	United States	Single centre	Alloimmunized, refractory patients with no non immune factors and CPRA of 94% by IgG SAB	Two or more consecutive 1 hr CCI < 5 x 10^9/L
Pai S-C, 2010[21]	Taiwan	Single centre	Alloimmunized, refractory patients	At least 2, 1 hr CCI < 7.5/L or 24 hr CCIs < 4.5 /L
Brooks EG, 2008[47]	United States	Multicentre	Refractory patients with no non immune factors	At least two RDP with a 1 hr CCI <10000/uL
Nambiar A, 2006[22]	United States	Single centre	Refractory aplastic anemia; (11 to 72 yrs)	Consistently poor increments following RDP and evidence of HLA alloimmunization
Levin MD, 2004[36]	Netherlands	Single centre	HT	NA
McFarland JG, 1989[37]	United States	Single centre	Refractory patients 72% alloimmunized	1 hr increment <5 x 10^9/L with a minimum of six RDP on at least two consecutive

				occasions
Heal JM, 1987[38]	United States	Single centre	Refractory patients	At least two 1 to 4 hr CCI < 7500/uL
Klingemann HG, 1987[39]	United States	Single centre	Refractory aplastic anemia for PBSCT (4 to 67 yrs)	1 hr increment <5 x 10^9/L with 6-8 units of RDP on two separate occasions
Levy L, 1984[40]	New Zealand	Single centre	Refractory patients without non immune factors (n=11 alloimmunized) (13 to 77 yrs)	1 hr increment < 10 x 10^9/L to repeated transfusion
McElligott MC, 1982[41]	United States	Single centre	Refractory patients without non immune factors	Failure to respond to RDP on two successive occasions
Daly PA, 1980[42]	United States	Single centre	Refractory and non refractory patients	18 to 24 hr increment of $\leq$ 10 x 10^3/uL
Tosato G, 1978[12]	United States	Single centre	Refractory aplastic anemia with no non immune factors (5 to 52 yrs)	CCI < 2500 on at least three consecutive occasions
Mittal KK, 1976[43]	United States	Single centre	HT	NA

Lohrmann HP, 1974[44]	United States	Single centre	Alloimmunized, refractory patients (11to 66 yrs)	20 hr CCI <2500 in the absence of non immune factors

CCI = corrected count increment; CPRA= calculated percent reactive antibody ; GRAN = granulocyte transfusion; hr = hour; HSCT = hematopoietic stem cell transplantation;HT = hypoproliferative thombocytopenia; NA = not applicable; NR = not reported; PBSCT = peripheral blood stem cell transplant; PPR = percent platelet recovery; RDP = random donor platelet transfusion; tx = transfusion; yrs = years

Table 5 Quality of Non Randomized Studies

Author, Year	Source of sample appropriate	Sampling method appropriate	Sample size pre-determined	Eligibi-lity criteria clearly defined	Control group acceptable *	Comparable characteristics	Clear definitions of outcomes	Blind outcome assessment	Quality control†	Missing data reported	Confoun-ding factors analyzed
Prospective											
Marktel S, 2010[24]	NR	NR	No	No	NA	NA	Yes	No	NA	No	No
Levin MD, 2003[25]	NR	Random sample, randomiza-tion not defined	No	No	NA	NA	Yes	No	No	NR	Yes
Petz LD,	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes

2000[16]											
Hogg DE, 1995[26]	Yes	Yes	No	Yes	NA	NA	Yes	No	No	NR	No
Friedberg RC, 1994[27]	Yes	Yes	No	Yes	NA	NA	Yes	No	No	Yes	Yes
Moroff G, 1992[45]	Yes	NR	No	Yes	NA	NA	Yes	No	No	NR	No
Bishop JF, 1988[46]	Yes	Yes	No	Yes	NA	NA	Yes	No	NA	NR	Yes
Murphy MF, 1986[28]	Yes	NR	No	Yes	Yes	Yes	Yes	No	No	NR	No
Ware R 1985[29]	NR	NR	No	Yes	NA	NA	Yes	No	Yes	No	No
Dahlke	Yes	NR	No	No	NA	NA	No	No	No	NR	No

MB, 1984[30]											
Hester JP, 1978[31]	Yes	NR	No	No	NA	NA	Yes	No	No	NR	No
Macphers on BR, 1978[32]	Yes	NR	No	No	NA	NA	Yes	No	No	NR	No
Duques-noy RJ, 1977[13,20]	Yes	NR	No	Yes	NA	NA	Yes	No	No	NR	No
Wu KK, 1977[33]	Yes	NR	No	No	NA	NA	Yes	No	No	NR	No
Herzig RH, 1975[34]	Yes	NR	No	No	NA	NA	Yes	No	No	NR	No
Retrospective											

Fontaine M, 2011[35]	NR	NR	No	Yes	Yes	Yes	Yes	No	Yes	NR	No
Pai S-C, 2010[21]	NR	No	No	No	NA	NA	Yes	No	Yes	Yes	No
Brooks EG, 2008[47]	Yes	Yes	No	Yes	NA	Yes	Yes	No	Yes	NR	No
Nambiar A, 2006[22]	Yes	Yes	No	Yes	NA	NA	Yes	No	Yes	Yes	No
Levin MD, 2004[36]	NR	NR	No	No	NA	NA	Yes	No	No	NR	Only some factors analyzed
McFarland JG, 1989[37]	Yes	Yes	No	Yes	NA	NA	Yes	No	No	NR	Yes

Heal JM, 1987[38]	NR	Yes	No	Yes	NA	NA	NA	No	No	No	No
Klinge-mann HG, 1987[39]	Yes	NR	No	Yes	NA	NA	Yes	No	NR	NR	Yes
Levy L, 1984[40]	Yes	Yes	No	No	NA	NA	No	No	NR	Yes	No
McElligott MC, 1982[41]	Yes	Yes	No	Yes	NA	NA	Yes	No	No	NR	No
Daly PA, 1980[42]	NR	NR	No	No	NA	NA	Yes	No	No	NR	Addressed but not analyzed
Tosato G, 1978[12]	Yes	Yes	No	No	NA	No	Yes	No	NR	NR	No
Mittal KK,	NR	NR	No	No	NA	NA	Yes	No	NR	NR	No

1976[43]											
Lohrmann HP, 1974[44]	Yes	NR	No	No	NA	NA	Yes	No	No	NR	No

* Was the source of the controls acceptable?

† Quality control measures for the collection of data and laboratory tests e.g. accuracy and repeatability of observers, calibration and random calibration and accuracy of instruments, checks for errors in data recording

NA = not applicable; NR= not reported

APPENDIX: SEARCH STRATEGY

`Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1948 to Present>

Search Strategy:

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1 exp Platelet Transfusion/ (3906)

2 Blood Transfusion.mp. (63782)

3 limit 2 to yr="1966 - 1991" (27754)

4 Blood Platelets.mp. (61928)

5 limit 4 to yr="1966 - 1993" (37636)

6 Blood Component Transfusion.mp. (2402)

7 limit 6 to yr="1992 - 1993" (519)

8 Blood Platelets.mp. (61928)

9 transfusion.mp. (93570)

10 8 and 9 (3440)

11 limit 10 to yr="1972 - 1993" (1616)

12 "platelet transfusion*".mp. (5580)

13 1 or 3 or 5 or 7 or 11 or 12 (68462)

14 exp HLA Antigens/ (57905)

15 Histocompatibility.mp. (83517)

16 limit 15 to yr="1970 - 1972" (2546)

17 Histocompatibility Antigens.mp. (43353)

18 limit 17 to yr="1973 - 1974" (1699)

19 exp Antigens, Human Platelet/ (1141)

20 Antigens.mp. (526038)

21 limit 20 to yr="1966 - 1979" (69391)

22 Isoantigens.mp. (8999)

23 limit 22 to yr="1976 - 1991" (3981)

24 (HLA or HL-A or HPA antigen*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (85554)

25 14 or 16 or 18 or 19 or 21 or 23 or 24 (154531)

26 exp Thrombocytopenia/ (34130)

27 Blood Group Incompatibility/ (4984)

28 (alloimmunity or alloimmunization).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (1833)

29 (refractory or refractoriness).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (70396)

30 26 or 27 or 28 or 29 (109321)

31 13 and 25 and 30 (1118)

32 exp Thrombocytopenia, Neonatal Alloimmune/ (96)

33 "neonatal alloimmune thrombocytopenia".mp. (422)

34 (FNAIT or NAIT).mp. [mp=protocol supplementary concept, rare disease supplementary

concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (158)

35 32 or 33 or 34 (494)

36 31 not 35 (993)

37 limit 36 to "review articles" (146)

38 36 not 37 (847)

39 limit 38 to case reports (171)

40 38 not 39 (676)

41 limit 40 to english language (487)

42 limit 41 to humans (451)

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