ELSEVIER

Blood 142 (2023) 4992–4993

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Effectiveness and Safety of Rabbit Anti-Thymocyte Globulin Versus Non-Anti-Thymocyte Globulin Regimens for Graft-Versus-Host Disease Prophylaxis: A Systematic Review and Meta-Analysis

Jaap Jan Boelens, MD[1], *Andrew Bodiford, PharmD*[2], *Francois Bourhis, MSc*[3], *Marie Baccara-Dinet, MD MSc*[4], *Lauren Rota, PhD*[5], *Michaela Lysikova, MD PhD*[6]

[1] Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY
[2] Sanofi, Bridgewater, Bridgewater, MA
[3] Sanofi, Chilly-Mazarin, France
[4] Sanofi, Montpellier, France
[5] Sanofi, Bridgewater
[6] Sanofi, s.r.o, Czech Republic

*Introduction:*Graft-versus-host disease (GVHD) is a serious complication after allogeneic hematopoietic stem cell transplant (HSCT), limiting its success. Meta-analyses have confirmed clinical efficacy and safety of several types of anti-thymocyte globulins (ATGs) in GVHD prophylaxis; however, there are no meta-analyses assessing the efficacy of rabbit anti-thymocyte globulin (rATG; Thymoglobulin ®) in particular. This study assessed the effectiveness and safety of rATG relative to non-ATG prophylaxis regimens for acute GVHD (aGVHD) or chronic GVHD (cGVHD) based on randomized controlled trials (RCTs) and observational studies.

*Methods:*A literature search was conducted in MEDLINE, Embase, Cochrane Central, and the Web of Science using the PICOS framework to identify studies published until June 2022 focusing on the prophylaxis use of rATG in GVHD. The United States and European Union clinical trial registry databases were also searched to identify unpublished data from studies. Efficacy outcomes included incidences of aGVHD (Grade II-IV and Grade III-IV), cGVHD (mild to severe and moderate to severe) and overall survival. Safety outcomes included the incidence of relapse, cytomegalovirus (CMV) infection, and Epstein-Barr virus (EBV) reactivation. Pre-specified subgroups of interest included donor type, and stem cell source (an unrelated peripheral blood [PB]/bone marrow [BM] transplant, a related PB/BM transplant, or a mixed unrelated and related PB/BM transplant). All analyses present the overall effect, the effect by subgroups, and the percentage contributing to the overall effect.

Results: Overall, 4295 records were retrieved from the databases and hand searching (1000 from PubMed, 1700 from Embase, 1419 from the Web of Science, 155 from the Cochrane Central, 20 from the clinical trial registry databases and 1 from hand searching). After screening, 45 studies (6 RCTs, 35 retrospective studies and 4 prospective observational studies) published between 2001 and June 2022 were included in this review. Among the 45 studies, 39 reported aGVHD Grade II-IV, 33 reported aGVHD Grade III-IV, 33 reported mild to severe cGVHD, 31 reported moderate to severe cGVHD, and 41 reported overall survival (**Table**). Use of rATG for GVHD prophylaxis resulted in a significant 24% reduction in Grade II-IV aGVHD (RR=0.76; 95% CI: 0.68-0.85) and a significant 43% reduction in Grade III-IV aGVHD (RR=0.57; 95% CI: 0.49-0.65) compared with non-ATG arm across all donor types. Similarly, a 35% reduction was observed in mild to severe cGVHD (RR=0.65; 95%CI: 0.57-0.74) and a significant 48% reduction (RR=0.52; 95% CI: 0.45-0.60) was observed in moderate to severe cGVHD across all donor types. Use of rATG decreased overall mortality by 9% (RR=0.91; 95% CI: 0.85-0.99). Among the subgroups, the decrease in mortality was statistically significant in unrelated PB/BM transplant donors. The incidence of relapse was reported in 36 studies, with an overall 18% increase (RR=1.18; 95% CI: 1.08-1.30) for patients treated with rATG. However, among the subgroups, the incidence of relapse was comparable between rATG and non-ATG prophylaxis arms for all types of donors. rATG and non-ATG prophylaxis regimens were comparable in terms of CMV infection (RR=1.00; 95% CI: 0.88-1.15). The incidence of EBV infection was significantly higher in the rATG arm (RR=2.53; 95% CI: 1.54-4.17) than that in the non-ATG arm.

Conclusions: This meta-analysis provides useful information to support patients and health-care providers in making treatment decisions for the prevention of aGVHD or cGVHD after allogeneic HSCT. rATG demonstrated significant reductions in the incidence of both aGVHD and cGVHD and increased the overall survival across donor types and stem cell sources despite slightly increased risk of relapse in rATG arm versus non-ATG arm.

Disclosures Boelens: *Sobi:* Consultancy, Honoraria; *Sanofi:* Consultancy, Honoraria; *Immusoft:* Consultancy, Honoraria; *Advanced Clinical:* Honoraria; *Bluebird Bio:* Honoraria; *SmartImmune:* Consultancy, Honoraria; *Omeros:* Consultancy, Honoraria; *Bluerock:* Consultancy, Honoraria.

Endpoint	N Study	rATG		Non-ATG		Risk ratio	p-value	I^2
		N event	N patient	N event	N patient			
aGVHD Grade II–IV	39	984	2763	4163	10,488	0.76 [0.68; 0.85]	<0.001	60%
aGVHD Grade III–IV	33	254	2477	2235	12,437	0.57 [0.49; 0.65]	<0.001	11%
Mild to severe cGVHD	33	766	2402	2671	5988	0.65 [0.57; 0.74]	<0.001	61%
Moderate to severe cGVHD	31	351	2270	2945	11,496	0.52 [0.45; 0.60]	<0.001	39%
Mortality	41	1284	3219	5227	13,080	0.91 [0.85; 0.99]	0.021	35%
Relapse	36	725	2695	2231	9295	1.18 [1.08; 1.30]	<0.001	7%
CMV infection	22	458	1227	464	1427	1.00 [0.88; 1.15]	0.951	43%
EBV infection	12	221	843	72	963	2.53 [1.54; 4.17]	<0.001	72%

ATG, anti-thymocyte globulin; aGVHD, acute GVHD; cGVHD, chronic GVHD; CMV, cytomegalovirus; EBV, Epstein-Barr virus; GVHD, graft versus host disease; rATG, rabbit ATG

Figure 1

https://doi.org/10.1182/blood-2023-181836