

REVIEW ARTICLE

Hematopoietic stem cell transplantation in Wiskott–Aldrich syndrome: A systematic review and meta-analysis

Supplementary Files

Table S1. Newcastle-Ottawa Scale quality assessment of observational cohort studies ($n=21$)

Studies	Selection				Comparability	Outcome			Overall quality
	1	2	3	4	1	1	2	3	
Yamaguchi <i>et al.</i> (2002) ¹	★	NA	★	★	NA	★	★	★	Poor
Pai <i>et al.</i> (2006) ²	★	NA	★	★	NA	★	★	★	Poor
Tsuji <i>et al.</i> (2006) ³	★	★	★	★	NA	★	★	★	Poor
Muñoz <i>et al.</i> (2007) ⁴	★	NA	★	★	NA	★	★	★	Poor
Ozsahin <i>et al.</i> (2007) ⁵	★	★	★	★	NA	★	★	★	Poor
Al-Ghonaïum <i>et al.</i> (2008) ⁶	★	NA	★	NA	NA	★	NA	NA	Poor
Friedrich <i>et al.</i> (2009) ⁷	★	NA	★	NA	NA	★	★	NA	Poor
Mahlaoui <i>et al.</i> (2013) ⁸	★	NA	★	★	NA	★	★	★	Poor
Mitchell <i>et al.</i> (2013) ⁹	★	NA	★	★	NA	★	★	★	Poor
Stepensky <i>et al.</i> (2013) ¹⁰	★	★	★	★	NA	★	★	★	Poor
Oshima <i>et al.</i> (2015) ¹¹	★	NA	★	★	NA	★	★	★	Poor
Ngwube <i>et al.</i> (2017) ¹²	★	★	★	★	NA	★	★	★	Poor
Uppuluri <i>et al.</i> (2018) ¹³	★	NA	★	★	NA	★	★	★	Poor
Balaschov <i>et al.</i> (2018) ¹⁴	★	★	★	★	★★	★	★	★	Good
Iguchi <i>et al.</i> (2019) ¹⁵	★	★	★	★	★★	★	★	★	Good
Burroughs <i>et al.</i> (2020) ¹⁶	★	★	★	★	NA	★	★	★	Poor
Fernandes <i>et al.</i> (2020) ¹⁷	★	★	★	★	★★	★	★	★	Good
Haskoğlu, <i>et al.</i> (2020) ¹⁸	★	NA	★	★	NA	★	★	★	Poor
Bildik <i>et al.</i> (2021) ¹⁹	★	NA	★	★	NA	★	★	★	Poor
Raj <i>et al.</i> (2021) ²⁰	★	NA	★	★	NA	★	★	★	Poor
Albert <i>et al.</i> (2022) ²¹	★	NA	★	★	★★	★	★	★	Good

Table S2. ROBANS score for quality assessment of clinical trial studies ($n = 3$)

Items assessed	Braun <i>et al.</i> (2014) ²²	Ferrua <i>et al.</i> (2019) ²³	Magnani <i>et al.</i> (2022) ²⁴
1. Comparability of target groups	Unclear	Unclear	Unclear
2. Target group selection	Low	Low	High
3. Confounding variables	High	High	High
4. Measurement of intervention (exposure)	Low	Low	Low
5. Blinding of outcome assessors	High	High	High
6. Outcome assessment	Low	Low	Low
7. Incomplete outcome data	Low	Low	Unclear
8. Selective outcome reporting	Low	Low	Unclear
Score	High	High	High

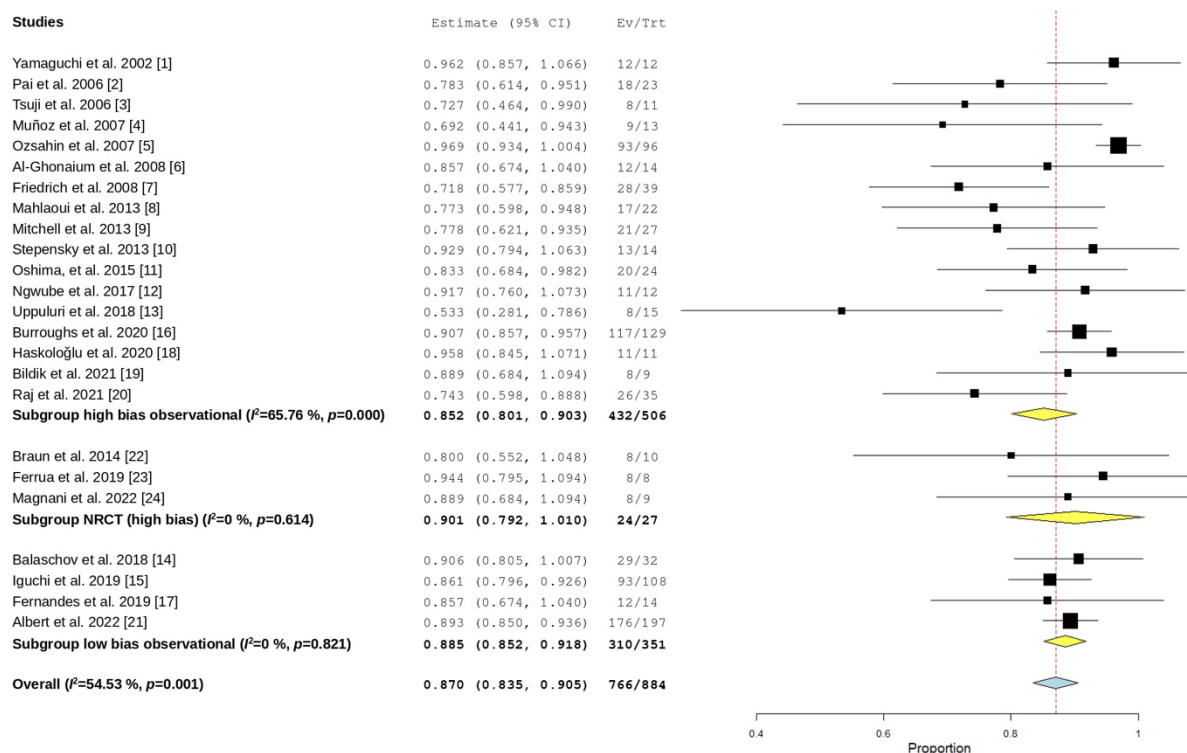


Figure S1. Pooled prevalence of overall survival in patients receiving hematopoietic stem cell transplantation

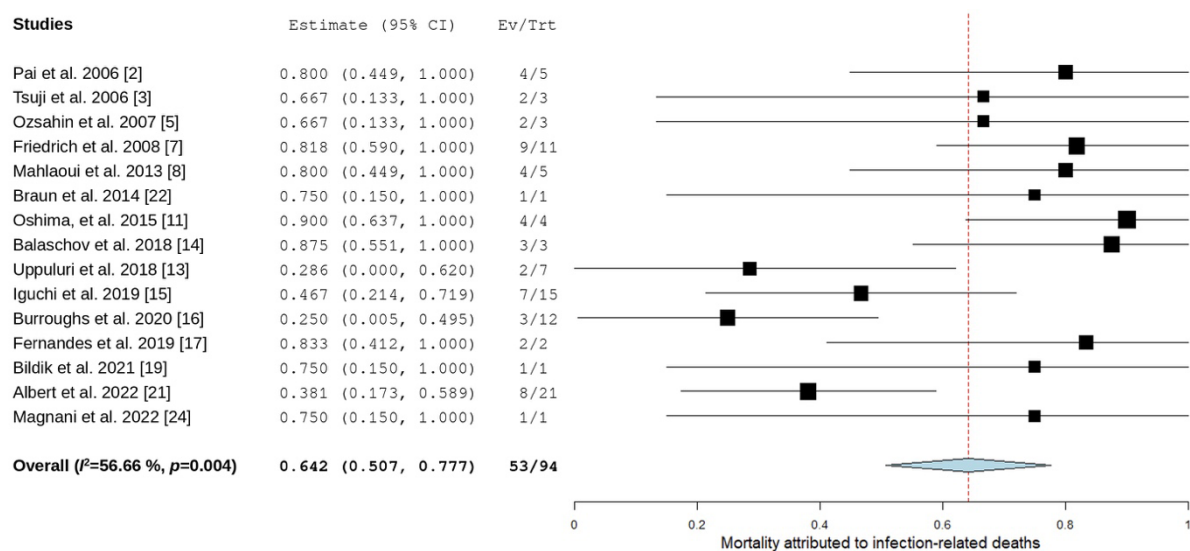


Figure S2. Mortality attributed to infection-related deaths

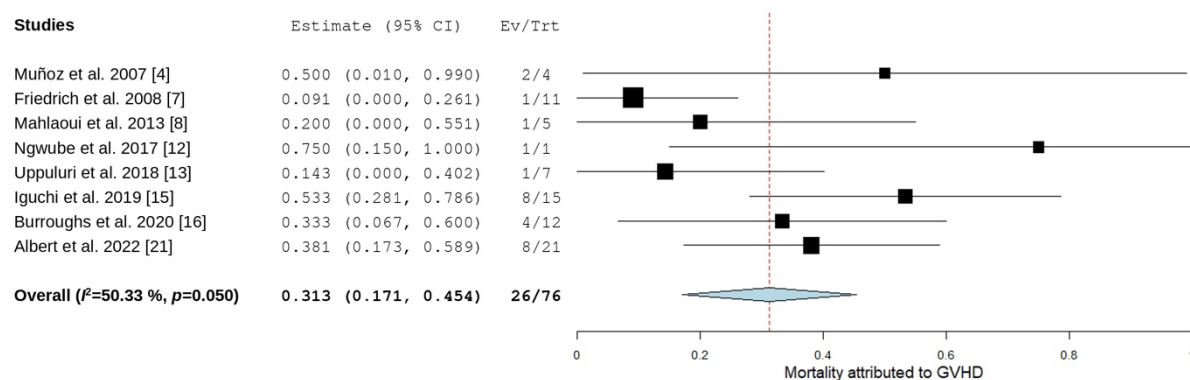


Figure S3. Mortality attributed to graft-versus-host disease (GVHD)

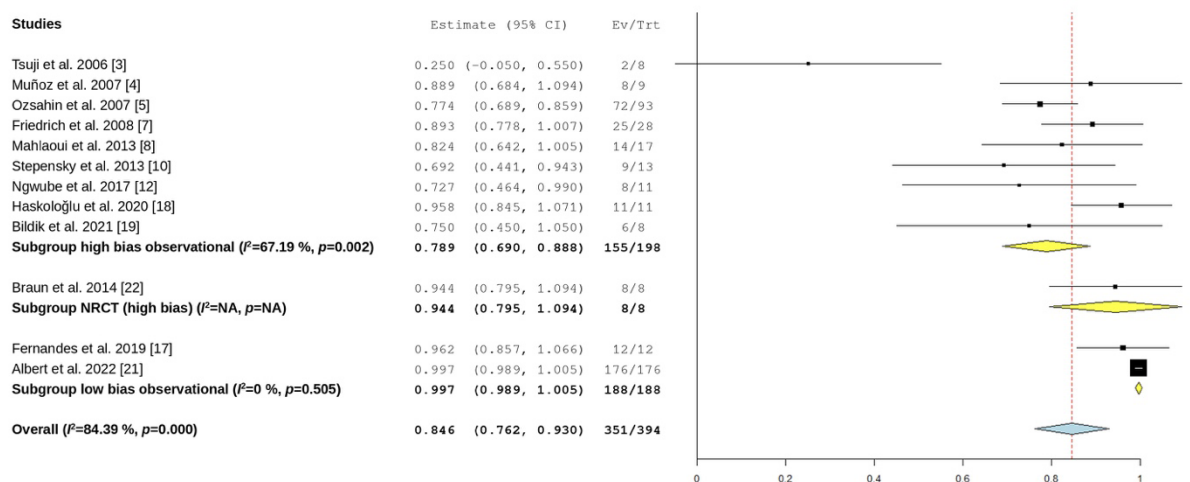


Figure S4. Pooled prevalence of event-free survivals

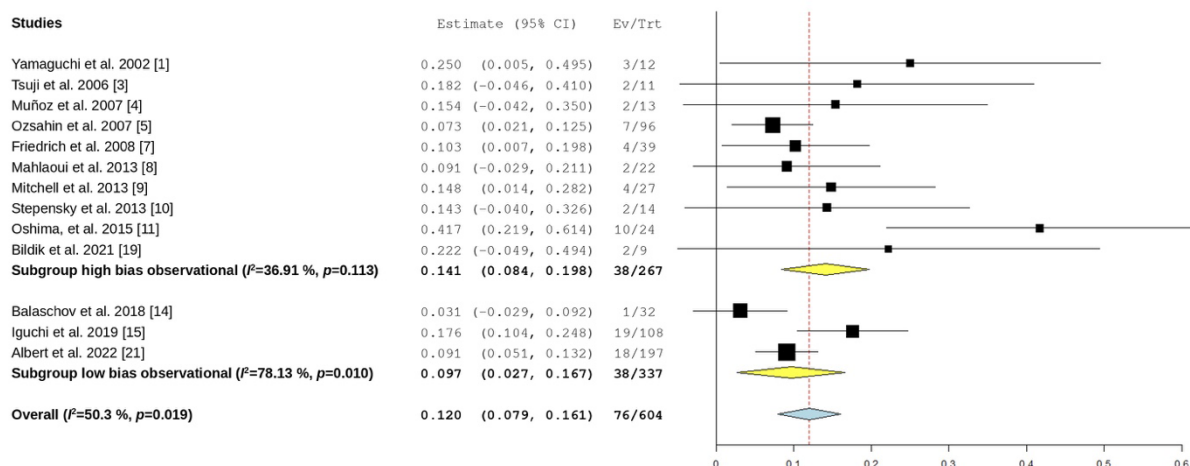


Figure S5. Pooled prevalence of chronic graft-versus-host disease (GVHD)

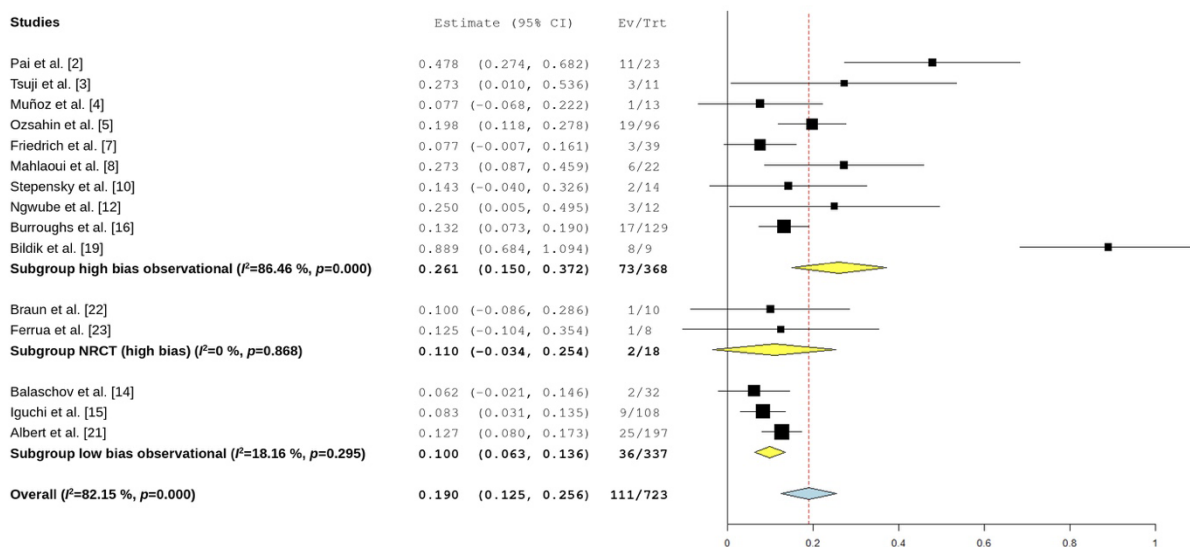


Figure S6. Pooled prevalence of autoimmune complications

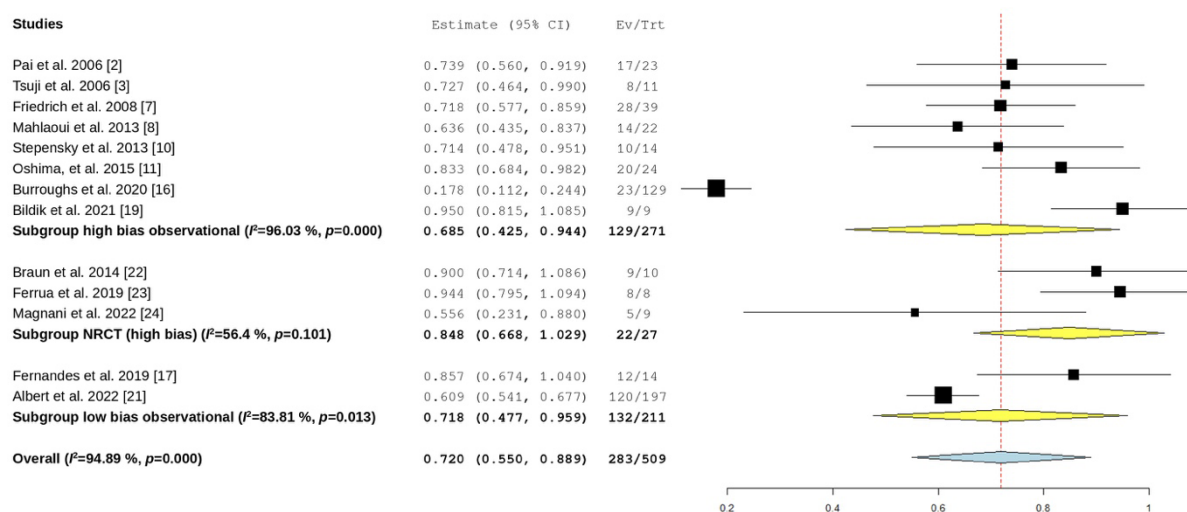


Figure S7. Pooled prevalence of symptomatic recovery

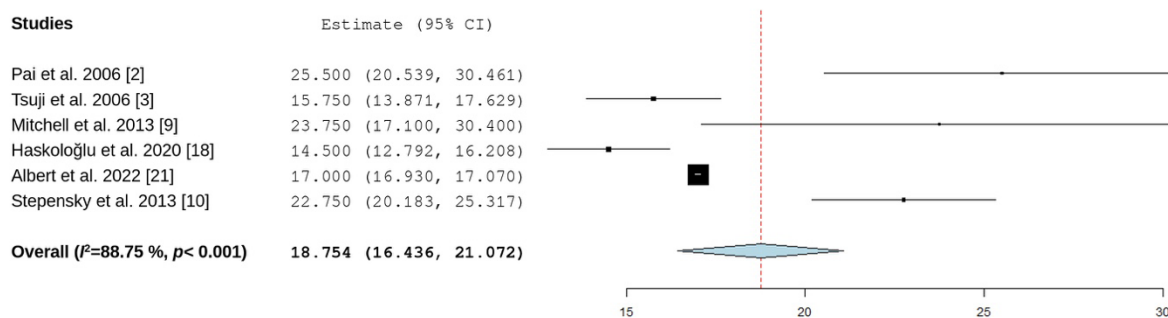


Figure S8. Pooled mean of days to neutrophil engraftment post-hematopoietic stem cell transplantation

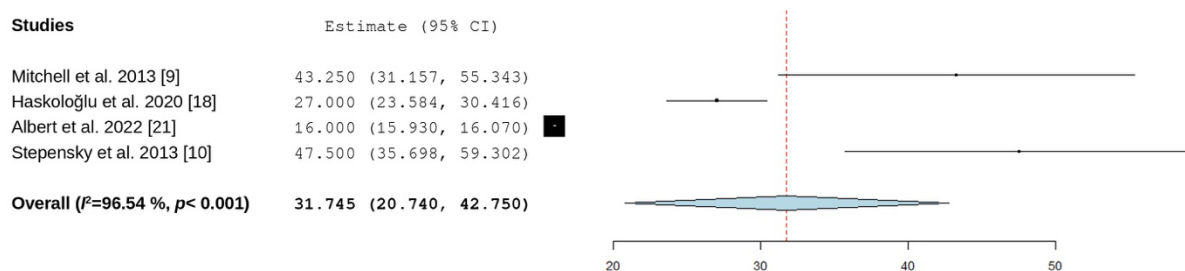


Figure S9. Pooled mean of days to platelet engraftment post-hematopoietic stem cell transplantation

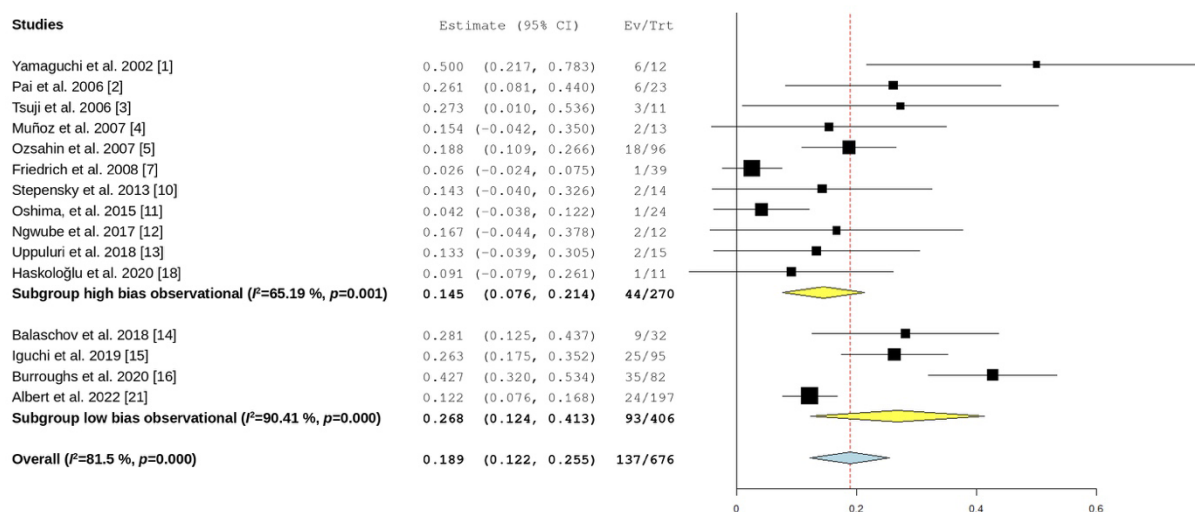


Figure S10. Pooled prevalence of mixed chimerism

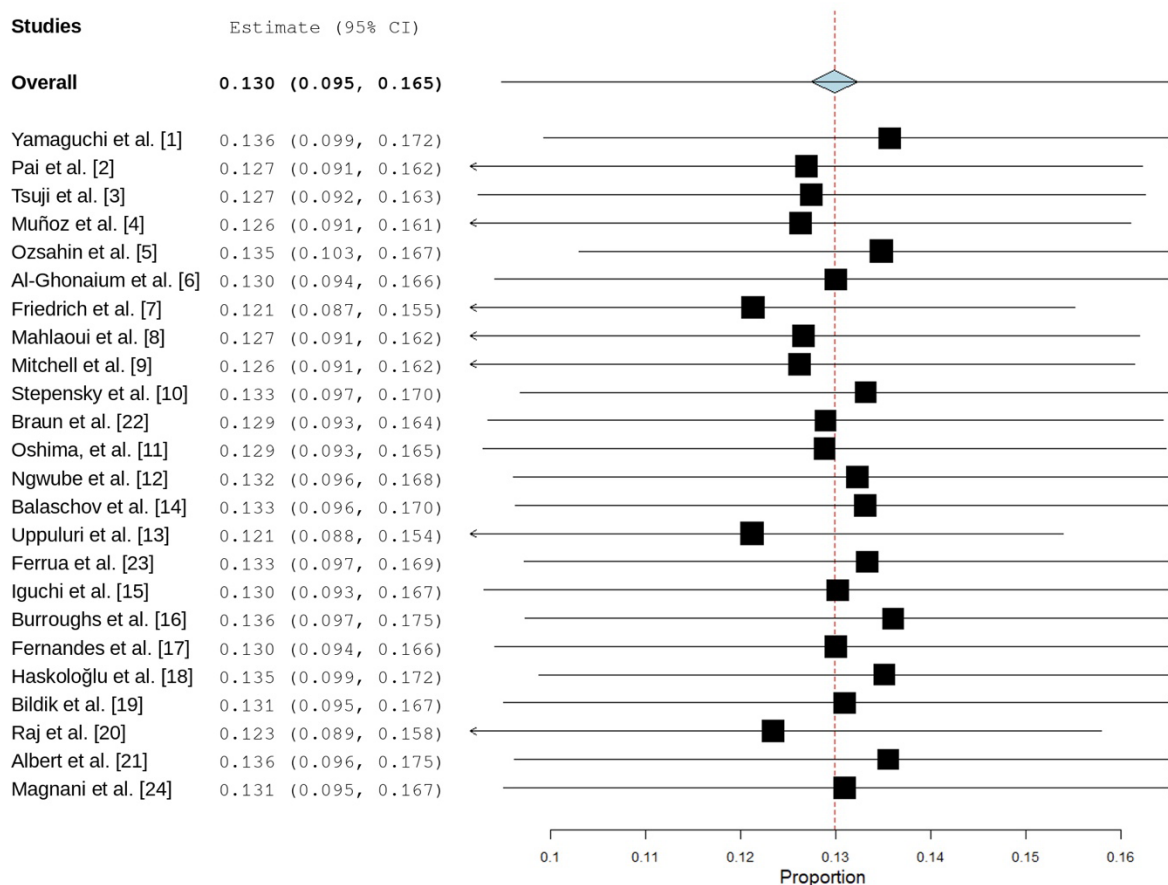


Figure S11. Mortality leave-one-out sensitivity analyses

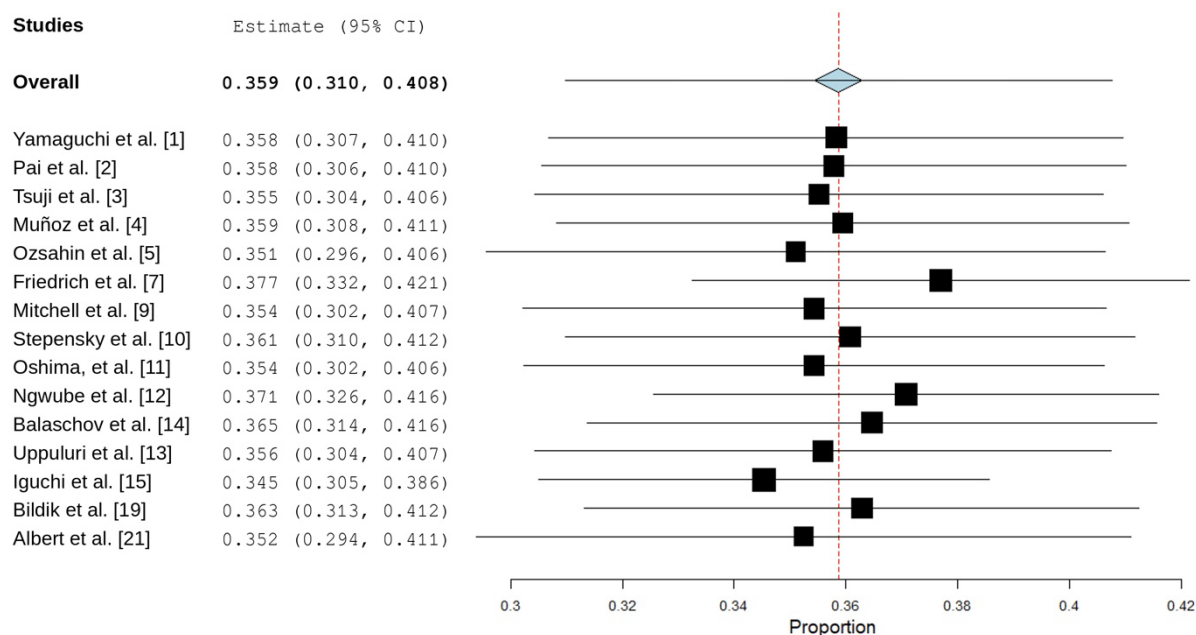


Figure S12. Incidence of acute graft-versus-host disease leave-one-out sensitivity analyses

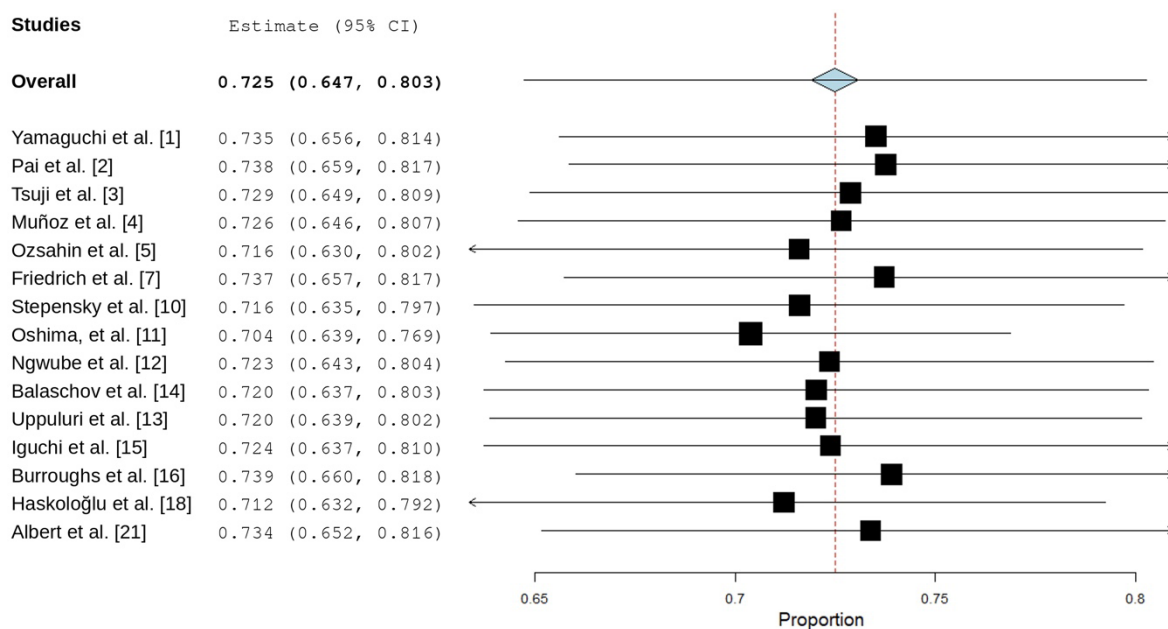


Figure S13. Full chimerism leave-one-out sensitivity analyses

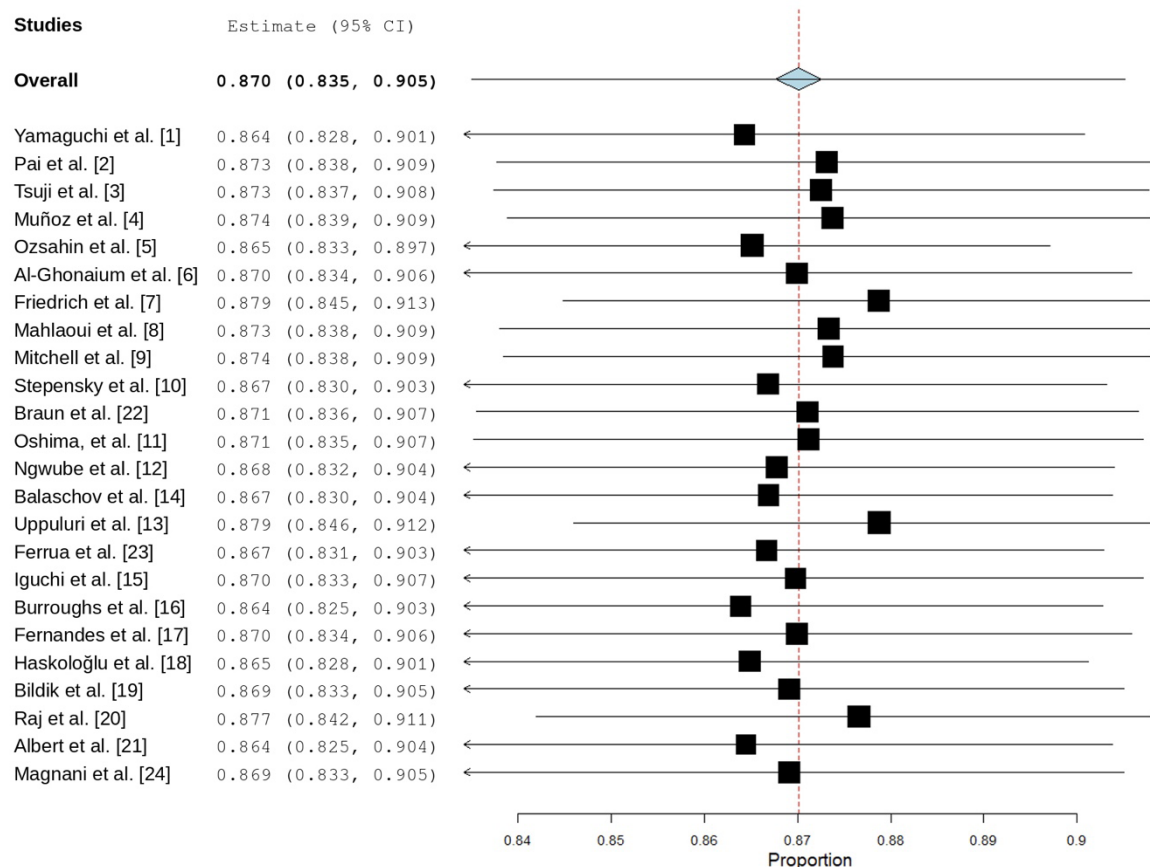


Figure S14. Overall survival leave-one-out sensitivity analyses

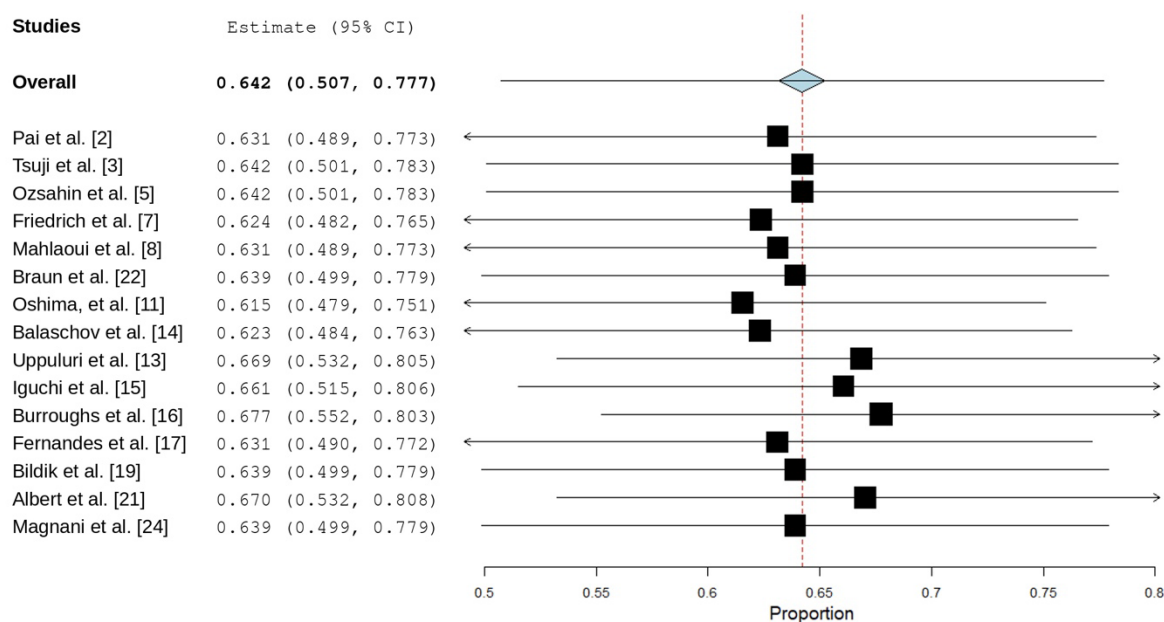


Figure S15. Mortality attributed to infection-related deaths: leave-one-out sensitivity analyses

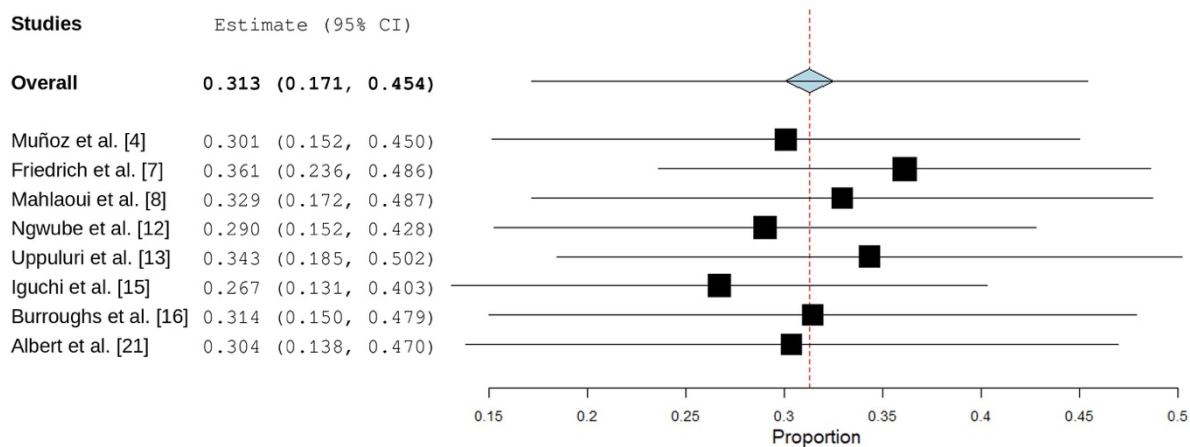


Figure S16. Mortality attributed to graft-versus-host disease: leave-one-out sensitivity analyses

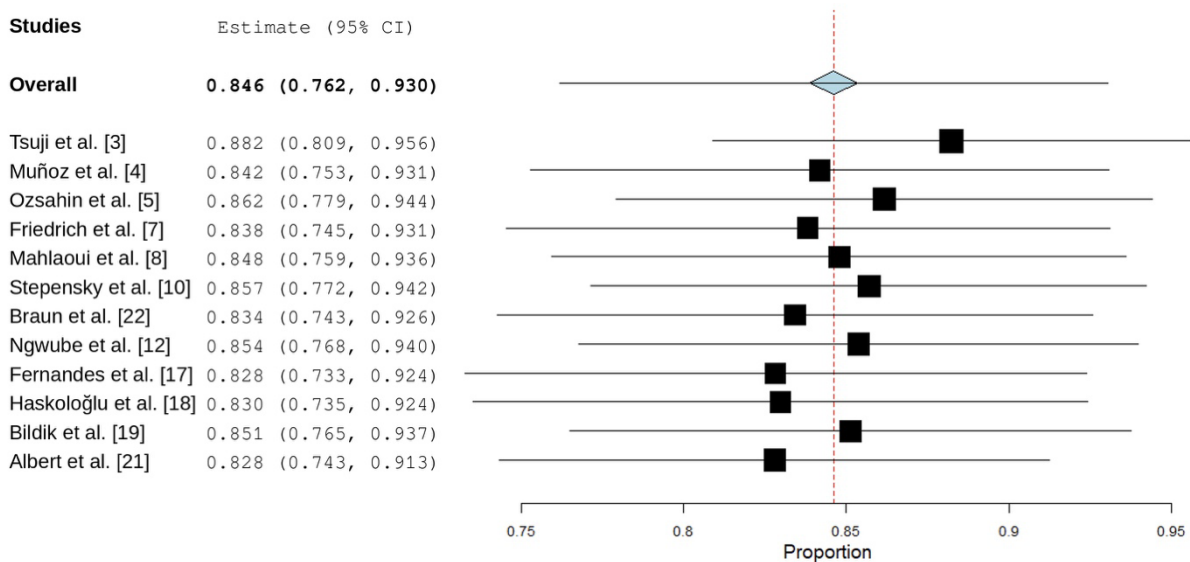


Figure S17. Event-free survival leave-one-out sensitivity analyses

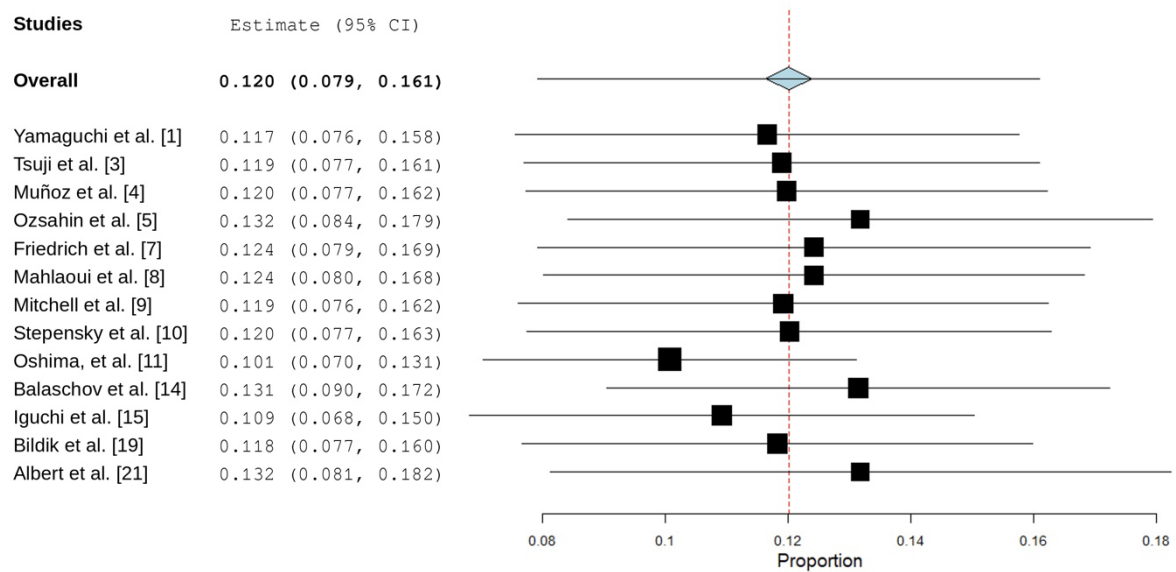


Figure S18. Chronic graft-versus-host disease leave-one-out sensitivity analyses

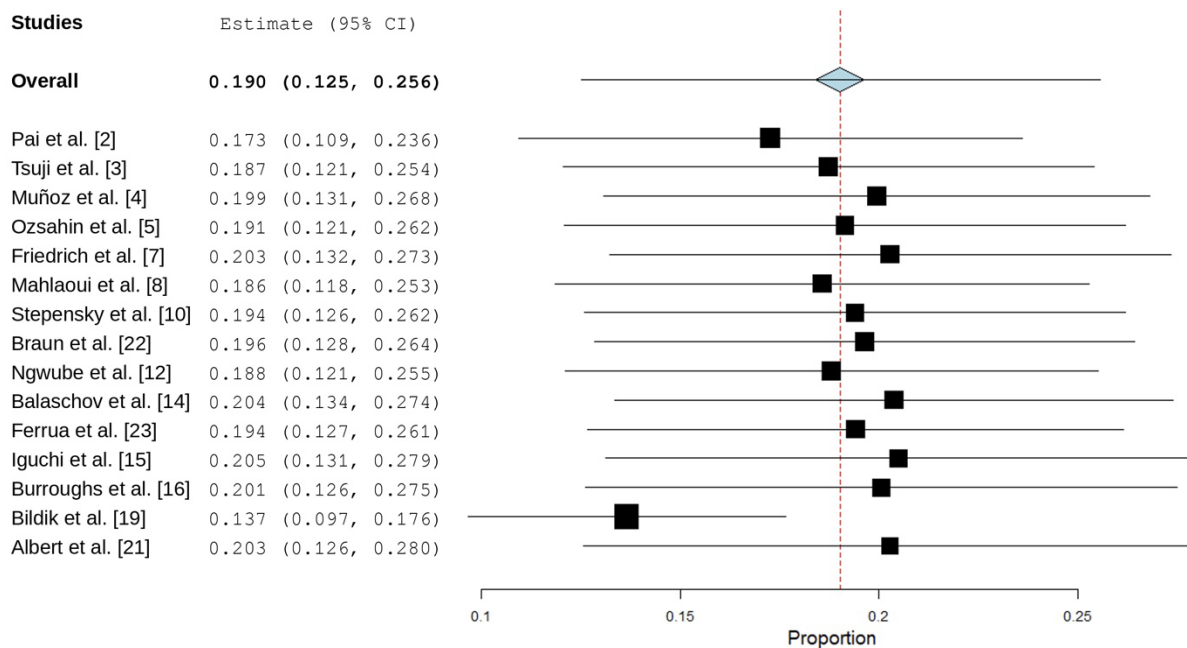


Figure S19. Autoimmune complications leave-one-out sensitivity analyses

References

1. Yamaguchi K, Ariga T, Yamada M, *et al.* Mixed chimera status of 12 patients with Wiskott–Aldrich syndrome (WAS) after hematopoietic stem cell transplantation: Evaluation by flow cytometric analysis of intracellular WAS protein expression. *Blood*. 2002;100(4):1208–1214.
doi: 10.1182/blood-2002-01-0211
2. Pai SY, DeMartis D, Forino C, *et al.* Stem cell transplantation for the Wiskott–Aldrich syndrome: a single-center experience confirms efficacy of matched unrelated donor transplantation. *Bone Marrow Transplant*. 2006;38(10):671–679.
doi: 10.1038/sj.bmt.1705512
3. Tsuji Y, Imai K, Kajiura M, *et al.* Hematopoietic stem cell transplantation for 30 patients with primary immunodeficiency diseases: 20 years' experience of a single team. *Bone Marrow Transplant*. 2006;37(5):469–477.
doi: 10.1038/SJ.BMT.1705273
4. Muñoz A, Olivé T, Martínez A, *et al.* Allogeneic hematopoietic stem cell transplantation (HSCT) for Wiskott–Aldrich syndrome: A report of the Spanish Working Party for Blood and Marrow Transplantation in Children (GETMON). *Pediatric Hematol Oncol*. 2007;24(6):393–402.
doi: 10.1080/08880010701454404
5. Ozsahin H, Cavazzana-Calvo M, Notarangelo LD, *et al.* Long-term outcome following hematopoietic stem-cell transplantation in Wiskott–Aldrich syndrome: Collaborative study of the European Society for Immunodeficiencies and European Group for Blood and Marrow Transplantation. *Blood*. 2008;111(1):439–445.
doi: 10.1182/BLOOD-2007-03-076679
6. Al-Ghoni A. Stem cell transplantation for primary immunodeficiencies: King Faisal Specialist Hospital experience from 1993 to 2006. *Bone Marrow Transplant*. 2008;42(S1):S53–S56.
doi: 10.1038/BMT.2008.115
7. Friedrich W, Schütz C, Schulz A, Benninghoff U, Hönig M. Results and long-term outcome in 39 patients with Wiskott–Aldrich syndrome transplanted from HLA-matched and -mismatched donors. *Immunol Res*. 2009;44(1–3):18–24.
doi: 10.1007/s12026-008-8063-8
8. Mahlaoui N, Pellier I, Mignot C, *et al.* Characteristics and outcome of early-onset, severe forms of Wiskott–Aldrich syndrome. *Blood*. 2013;121(9):1510–1516.
doi: 10.1182/blood-2012-08-448118
9. Mitchell R, Nivison-Smith I, Anazodo A, *et al.* Outcomes of Hematopoietic Stem Cell Transplantation in Primary Immunodeficiency: A Report from the Australian and New Zealand Children's Hematology Oncology Group and the Australasian Bone Marrow Transplant Recipient Registry. *Biol Blood Marrow Transplant*. 2013;19(3):338–343.
doi: 10.1016/j.bbmt.2012.11.619
10. Stepensky P, Krauss A, Goldstein G, *et al.* Impact of conditioning on outcome of hematopoietic stem cell transplantation for Wiskott–Aldrich syndrome. *J Pediatric Hematol/Oncol*. 2013;35(6):e234–e238.
doi: 10.1097/MPH.0B013E318279CBFC
11. Oshima K, Imai K, Albert MH, *et al.* Hematopoietic Stem Cell Transplantation for X-Linked Thrombocytopenia With Mutations in the WAS gene. *J Clin Immunol*. 2015;35(1):15–21.
doi: 10.1007/S10875-014-0105-5
12. Ngwube A, Hanson IC, Orange J, *et al.* Outcomes after Allogeneic Transplant in Patients with Wiskott–Aldrich Syndrome. *Biol Blood Marrow Transplant*. 2018;24(3):537–541.
doi: 10.1016/J.BBMT.2017.11.019
13. Uppuluri R, Jayaraman D, Sivasankaran M, *et al.* Hematopoietic Stem Cell Transplantation for Primary Immunodeficiency Disorders: Experience from a Referral Center in India. *Indian Pediatrics*. 2018;55(8):661–664.
doi: 10.1007/s13312-018-1354-9
14. Balashov D, Laberko A, Shcherbina A, *et al.* A Conditioning Regimen with Plerixafor Is Safe and Improves the Outcome of TCRαβ + and CD19 + Cell-Depleted Stem Cell Transplantation in Patients with Wiskott–Aldrich Syndrome. *Biol Blood Marrow Transplant*. 2018;24(7):1432–1440.
doi: 10.1016/J.BBMT.2018.03.006
15. Iguchi A, Cho Y, Yabe H, *et al.* Long-term outcome and chimerism in patients with Wiskott–Aldrich syndrome treated by hematopoietic cell transplantation: a retrospective nationwide survey. *Int J Hematol*. 2019;110(3):364–369.
doi: 10.1007/s12185-019-02686-y
16. Burroughs LM, Petrovic A, Brazauskas R, *et al.* Excellent outcomes following hematopoietic cell transplantation for Wiskott–Aldrich syndrome: a PIDTC report. *Blood*. 2020;135(23):2094–2105.
doi: 10.1182/BLOOD.2019002939
17. Fernandes JF, Nichele S, Arcuri LJ, *et al.* Outcomes after Haploidentical Stem Cell Transplantation with Post-Transplantation Cyclophosphamide in Patients with Primary Immunodeficiency Diseases. *Biol Blood Marrow Transplant*. 2020;26(10):1923–1929.
doi: 10.1016/j.bbmt.2020.07.003
18. Haskoğlu Ş, Öztürk A, Öztürk G, *et al.* Clinical features and outcomes of 23 patients with Wiskott–Aldrich syndrome: A single-center experience. *Turk J Hematol*. 2020;37(4):271–281.

- doi: 10.4274/tjh.galenos.2020.2020.0334
19. Bildik HN, Cagdas D, Ozturk Kura A, Oskay Halacli S, Sanal O, Tezcan I. Clinical, Laboratory Features and Clinical Courses of Patients with Wiskott–Aldrich Syndrome and X-linked Thrombocytopenia–A single-center study. *Immunol Investig*. 2022;51(5):1272-1283.
doi: 10.1080/08820139.2021.1933516
20. Raj R, Aboobacker FN, Yadav SP, *et al*. Multicenter Outcome of Hematopoietic Stem Cell Transplantation for Primary Immune Deficiency Disorders in India. *Front Immunol*. 2021;11.
doi: 10.3389/FIMMU.2020.606930
21. Albert MH, Slatter MA, Gennery AR, *et al*. Hematopoietic stem cell transplantation for Wiskott–Aldrich syndrome: an EBMT Inborn Errors Working Party analysis. *Blood*. 2022;139(13):2066-2079.
doi: 10.1182/BLOOD.2021014687
22. Braun CJ, Boztug K, Paruzynski A, *et al*. Gene therapy for Wiskott–Aldrich syndrome–long-term efficacy and genotoxicity. *Sci Transl Med*. 2014;6(227).
doi: 10.1126/SCITRANSLMED.3007280
23. Ferrua F, Cicalese MP, Galimberti S, *et al*. Lentiviral hemopoietic stem/progenitor cell gene therapy for treatment of Wiskott–Aldrich syndrome: interim results of a non-randomized, open-label, phase 1/2 clinical study. *Lancet Haematol*. 2019;6(5):e239-e253.
doi: 10.1016/S2352-3026(19)30021-3
24. Magnani A, Semeraro M, Adam F, *et al*. Long-term safety and efficacy of lentiviral hematopoietic stem/progenitor cell gene therapy for Wiskott–Aldrich syndrome. *Nature Med*. 2022;28(1):71-80.
doi: 10.1038/s41591-021-01641-x