Appendix 2 Excluded references

Table of contents

1 Studies excluded on relevance

Study	Reason for exclusion
Atidarsagene autotemcel (LIBMELDY®) in metachromatic leukodystrophy. Prescrire International. 2022;31(243):289-90.	Study design
Al-Saady ML, Galabova H, Schoenmakers DH, Beerepoot S, Lindemans C, van Hasselt PM, et al. Longitudinal volumetric analysis of gray matter atrophy in metachromatic leukodystrophy. Journal of Inherited Metabolic Disease. 2024;47(4):792-804. Available from: https://doi.org/10.1002/jimd.12725	Outcomes
Antony JS, Daniel-Moreno A, Lamsfus-Calle A, Raju J, Kaftancioglu M, Ureña-Bailén G, et al. A Mutation-Agnostic Hematopoietic Stem Cell Gene Therapy for Metachromatic Leukodystrophy. CRISPR Journal. 2022;5(1):66-79. Available from: https://doi.org/10.1089/crispr.2021.0075	Intervention
Armstrong N, Olaye A, Noake C, Pang F. A systematic review of clinical effectiveness and safety for historical and current treatment options for metachromatic leukodystrophy in children, including atidarsagene autotemcel. Orphanet Journal of Rare Diseases. 2023;18(1). Available from: https://doi.org/10.1186/s13023-023-02814-2	Study design
Aubourg P. Gene therapy for leukodystrophy: Progress, challenges and opportunities. Expert Opinion on Orphan Drugs. 2016;4(4):359-67. Available from: https://doi.org/10.1517/21678707.2016.1151352	Study design
Bekri S, Bley A, Brown HA, Chanson C, Church HJ, Gelb MH, et al. Higher precision, first tier newborn screening for metachromatic leukodystrophy using 16:1-OH-sulfatide. Molecular Genetics and Metabolism. 2024;142(1). Available from: https://doi.org/10.1016/j.ymgme.2024.108436	Index test
Beschle J, Doring M, Kehrer C, Raabe C, Bayha U, Strolin M, et al. Early clinical course after hematopoietic stem cell transplantation in children with juvenile metachromatic leukodystrophy. Mol.	Comparator

2020;7(1):12. Available from: https://doi.org/10.1186/s40348-020-00103-7	
Bredius RGM, Laan LAEM, Lankester AC, Poorthuis BJHM, van Tol MJD, Egeler RM, et al. Early marrow transplantation in a pre-symptomatic neonate with late infantile metachromatic leukodystrophy does not halt disease progression [2]. Bone Marrow Transplantation. 2007;39(5):309-10. Available from: https://doi.org/10.1038/sj.bmt.1705581	Outcomes
Cable C, Finkel RS, Lehky TJ, Biassou NM, Wiggs EA, Bunin N, et al. Unrelated umbilical cord blood transplant for juvenile metachromatic leukodystrophy: A 5-year follow-up in three affected siblings. Molecular Genetics and Metabolism. 2011;102(2):207-9. Available from: https://doi.org/10.1016/j.ymgme.2010.10.002	Comparator
Calbi V, Fumagalli F, Consiglieri G, Penati R, Acquati S, Redaelli D, et al. Use of Defibrotide to help prevent post-transplant endothelial injury in a genetically predisposed infant with metachromatic leukodystrophy undergoing hematopoietic stem cell gene therapy. Bone Marrow Transplantation. 2018;53(7):913-7. Available from: https://doi.org/10.1038/s41409-017-0085-1	Comparator
Corre G, Galy A. Evaluation of diversity indices to estimate clonal dominance in gene therapy studies. Molecular Therapy Methods and Clinical Development. 2023;29:418-25. Available from: https://doi.org/10.1016/j.omtm.2023.05.003	Study design
Corrigan-Curay J, Cohen-Haguenauer O, O'Reilly M, Ross SR, Fan H, Rosenberg N, et al. Challenges in vector and trial design using retroviral vectors for long-term gene correction in hematopoietic stem cell gene therapy. Molecular Therapy. 2012;20(6):1084-94. Available from: https://doi.org/10.1038/mt.2012.93	Study design
Dangouloff T, Boemer F, Servais L. Newborn screening of neuromuscular diseases. Neuromuscular Disorders. 2021;31(10):1070-80. Available from: https://doi.org/10.1016/j.nmd.2021.07.008	Study design
Groeschel S, Köhl JS, Bley AE, Kehrer C, Weschke B, Döring M, et al. Long-Term outcome of allogeneic hematopoietic stem cell transplantation in patients	Comparator

with juvenile metachromatic leukodystrophy compared with nontransplanted control patients. JAMA Neurology. 2016;73(9):1133-40. Available from: https://doi.org/10.1001/jamaneurol.2016.2067	
Han M, Jun SH, Lee YJ, Eun BL, Lee SJ, Seong MW, et al. Biochemical and Genetic Analysis of Seven Korean Individuals With Suspected Metachromatic Leukodystrophy. Annals of laboratory medicine. 2015;35(4):458-62. Available from: https://doi.org/10.3343/alm.2015.35.4.458	Comparator
Hong X, Kumar AB, Daiker J, Yi F, Sadilek M, De Mattia F, et al. Leukocyte and Dried Blood Spot Arylsulfatase A Assay by Tandem Mass Spectrometry. Anal Chem. 2020;92(9):6341-8. Available from: https://doi.org/10.1021/acs.analchem.9b05274	Index test
Horgan C, Watts K, Ram D, Rust S, Hutton R, Jones S, et al. A retrospective cohort study of Libmeldy (atidarsagene autotemcel) for MLD: What we have accomplished and what opportunities lie ahead. JIMD rep. 2023;64(5):346-52. Available from: https://doi.org/10.1002/jmd2.12378	Study design
Horovenko NH, Ol'khovych NV. Differentiation between arylsulfatase A deficiency and pseudo-deficiency. Ukrainskii biokhimicheskii zhurnal. 2003;75(5):106-11.	Language
Kahn JM, Brazauskas R, Tecca HR, Bo-Subait S, Buchbinder D, Battiwala M, et al. Subsequent neoplasms and late mortality in children undergoing allogeneic transplantation for nonmalignant diseases. Blood Advances. 2020;4(9):2084-94. Available from: https://doi.org/10.1182/bloodadvances.2019000839	Population
Leboulch P. Gene therapy: primed for take-off. Nature. 2013;500(7462):280-2. Available from: https://doi.org/10.1038/500280a	Study design
Lum SH, Will A, Church HJ, Mercer J, Tylee KL, Poulton K, et al. A decade of excellent transplant survival in children with inherited metabolic diseases: A report from a single metabolic transplant centre in Europe. Blood Cell Ther. 2019;2(2):31-5. Available from: https://doi.org/10.31547/bct-2018-012	Comparator

Maaswinkel-Mooij PD, Poorthuis BJHM, Hoogerbrugge PM, Brouwer OF, Vossen JMJJ. Allogeneic bone marrow transplantation in the treatment of (lysosomal) storage diseases. Nederlands Tijdschrift voor Geneeskunde. 1998;142(4):169-74.	Language
Mallhi KK, Smith AR, DeFor TE, Lund TC, Orchard PJ, Miller WP. Allele-Level HLA Matching Impacts Key Outcomes Following Umbilical Cord Blood Transplantation for Inherited Metabolic Disorders. Biology of Blood and Marrow Transplantation. 2017;23(1):119-25. Available from: https://doi.org/10.1016/j.bbmt.2016.10.019	Population
Malm G, Ringdén O, Winiarski J, Gröndahl E, Uvebrant P, Eriksson U, et al. Clinical outcome in four children with metachromatic leukodystrophy treated by bone marrow transplantation. Bone Marrow Transplantation. 1996;17(6):1003-8.	Comparator
Martin PL, Carter SL, Kernan NA, Sahdev I, Wall D, Pietryga D, et al. Results of the Cord Blood Transplantation Study (COBLT): Outcomes of unrelated donor umbilical cord blood transplantation in pediatric patients with lysosomal and peroxisomal storage diseases. Biology of Blood and Marrow Transplantation. 2006;12(2):184-94. Available from: https://doi.org/10.1016/j.bbmt.2005.09.016	Population
Mitchell R, Nivison-Smith I, Anazodo A, Tiedemann K, Shaw PJ, Teague L, et al. Outcomes of haematopoietic stem cell transplantation for inherited metabolic disorders: a report from the Australian and New Zealand Children's Haematology Oncology Group and the Australasian Bone Marrow Transplant Recipient Registry. Pediatr Transplant. 2013;17(6):582-8. Available from: https://doi.org/10.1111/petr.12109	Comparator
Morena F, Argentati C, Acquati S, DeWall S, Kelly F, Calbi V, et al. Toward Reference Intervals of ARSA Activity in the Cerebrospinal Fluid: Implication for the Clinical Practice of Metachromatic Leukodystrophy. The journal of applied laboratory medicine. 2021;6(2):354-66. Available from: https://doi.org/10.1093/jalm/jfaa108	Outcomes
Musolino PL, Lund TC, Pan J, Escolar ML, Paker AM, Duncan CN, et al. Hematopoietic stem cell transplantation in the leukodystrophies: A systematic	Study design

review of the literature. Neuropediatrics. 2014;45(3):169-74. Available from: https://doi.org/10.1055/s-0033-1364179	
Nct. UCB Transplant of Inherited Metabolic Diseases With Administration of Intrathecal UCB Derived Oligodendrocyte-Like Cells. https://clinicaltrialsgov/show/NCT02254863. 2014.	Study design
Nct. MT2013-31: allo HCT for Metabolic Disorders and Severe Osteopetrosis. https://clinicaltrialsgov/show/NCT02171104. 2014.	Study design
Ohashi T, Eto Y, Learish R, Barranger JA. Correction of deficiency in metachromatic leukodystrophy fibroblssts by retroviral-mediated transfer of the human arylsulphtase A gene. Journal of Inherited Metabolic Disease. 1993;16(5):881-5.	Study design
Qureshi AA, Shaikh B, Aswad AS, Saeed AH, Tabassum H, Tahir MF, et al. 'Lenmeldy (OTL-200) in MLD: FDA's validation of advanced therapy'. Ann Med Surg (Lond). 2024;86(11):6376-80. Available from: https://doi.org/10.1097/MS9.0000000000002580	Study design
Ringdén O, Remberger M, Svahn BM, Barkholt L, Mattsson J, Aschan J, et al. Allogeneic hematopoietic stem cell transplantation for inherited disorders: Experience in a single center. Transplantation. 2006;81(5):718-25. Available from: https://doi.org/10.1097/01.tp.0000181457.43146.36	Study design
Sanpakit K. Overview in pediatric hematopoietic stem cell transplantation. Journal of the Medical Association of Thailand. 2005;88(8):1147-52.	Study design
Saute JAM, De Souza CFM, De Oliveira Poswar F, Donis KC, Campos LG, Deyl AVS, et al. Neurological outcomes after hematopoietic stem cell transplantation for cerebral X-linked adrenoleukodystrophy, late onset metachromatic leukodystrophy and hurler syndrome. Arquivos de Neuro-Psiquiatria. 2016;74(12):953-66. Available from: https://doi.org/10.1590/0004-282x20160155	Comparator
Sevin C, Mochel F. Hematopoietic stem cell transplantation in leukodystrophies. Handbook of clinical neurology. 2024;204:355-66. Available from:	Study design

https://doi.org/10.1016/B978-0-323-99209-1.00017-X	
Sok-Fedele P, Galambrun C, Bourgues F, Naudet F, Gandemer V, Michel G. Unrelated cord blood transplants in childhood metabolic diseases: A real health benefit for Hurler syndrome. Revue d'Oncologie Hematologie Pediatrique. 2013;1(1):32-40. Available from: https://doi.org/10.1016/j.oncohp.2013.05.003	Language
Stanchi KMC, Böhringer J, Strölin M, Groeschel S, Lenglinger K, Treuner C, et al. Hematopoietic Stem Cell Transplantation with Mesenchymal Stromal Cells in Children with Metachromatic Leukodystrophy. Stem Cells and Development. 2022;31(7-8):163-75. Available from: https://doi.org/10.1089/scd.2021.0352	Intervention
Swaminathan VV, Meena S, Varla H, Chandar R, Jayakumar I, Ramakrishnan B, et al. Hematopoietic Stem Cell Transplantation for Children With Inborn Errors of Metabolism: Single Center Experience Over Two Decades. Indian Pediatrics. 2022;59(9):699-702. Available from: https://doi.org/10.1007/s13312-022-2597-z	Comparator
Tolar J, Scott Baker K, Orchard PJ. Hematopoietic stem cell transplantation for metabolic storage diseases. Cellular Therapy and Transplantation. 2010;2(7).	Outcomes
Tricoli L, Sase S, Hacker J, Pham V, Smith S, Chappell M, et al. Effective Gene Therapy for Metachromatic Leukodystrophy Achieved with Minimal Lentiviral Genomic Integrations. bioRxiv. 2024;14:14. Available from: https://doi.org/10.1101/2024.03.14.584404	Study design
Van Til NP, Wagemaker G. Lentiviral gene transduction of mouse and human hematopoietic stem cells. 2014. p. 311-9.	Setting
Wadhwa A, Chen Y, Holmqvist A, Wu J, Ness E, Parman M, et al. Late Mortality after Allogeneic Blood or Marrow Transplantation for Inborn Errors of Metabolism: A Report from the Blood or Marrow Transplant Survivor Study-2 (BMTSS-2). Biology of Blood and Marrow Transplantation. 2019;25(2):328-	Comparator

34. Available from: https://doi.org/10.1016/j.bbmt.2018.09.035	
Wolf NI, Breur M, Plug B, Beerepoot S, Westerveld ASR, van Rappard DF, et al. Metachromatic leukodystrophy and transplantation: remyelination, no cross-correction. Annals of Clinical and Translational Neurology. 2020;7(2):169-80. Available from: https://doi.org/10.1002/acn3.50975	Setting
Yabe H, Koike T, Yamamoto S, Otsuka K, Nakajima J, Shibata M, et al. Allogeneic stem cell transplantation for inherited metabolic disorders: 35 years' experience at a single institution. International Journal of Hematology. 2024;120(3):365-74. Available from: https://doi.org/10.1007/s12185-024-03810-3	Population
Yamada M, Inui K. Metachromatic leukodystrophy. Ryōikibetsu shōkōgun shirīzu. 2001(34 Pt 2):178-9.	Study design
Zhang Z, Jiang H, Huang L, Liu S, Zhou X, Cai Y, et al. Lentivirus-modified hematopoietic stem cell gene therapy for advanced symptomatic juvenile metachromatic leukodystrophy: A long-term follow-up pilot study. Protein & cell. 2024. Available from: https://doi.org/10.1093/procel/pwae037	Comparator

2 Study excluded after risk of bias-evaluation

Guffon N, Souillet G, Maire I, Dorche C, Mathieu M, Guibaud P. Juvenile metachromatic leukodystrophy: neurological outcome two years after bone marrow transplantation. J Inherit Metab Dis. 1995;18(2):159-61. Available from: https://doi.org/10.1007/bf00711755	Undefined outcome data, follow up and confounding