

Long-term management of leukocyte adhesion deficiency type III without hematopoietic stem cell transplantation

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SUPPLEMENTAL MATERIAL

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Supplemental Table: Complications, therapeutic management and outcome of previously reported LAD-III patients

FERMT3 alteration	Gender (M / F)	HSCT Age at conditioning, donor, conditioning regimen, complications, outcome	Bleeding complications		Infections		Survival (Y / N)	Supplemental references
			Description	Management	Description	Management		
c.48G>A p.W16X	M	Yes	Mucosal bleedings, CNS bleeding	RBC TF	Lymphadenitis, Recurrent infections	NA	Y	1
c.48G>A p.W16X	F	Yes	Mucocutaneous bleedings, CNS bleeding	Platelet TF	Recurrent infections	NA	Y	1

c.687G>A p.W229X	NA	Yes, †	Moderate bleeding tendency	NA	NA	NA	N	2,3

c.687G>A p.W229X	M	6 years, MMRD, RIC (alemtuzumab/Bu/Flu/Mel), †	Mucocutaneous bleedings Life-threatening bleedings	Platelet and RBC TF, Tranexamic acid	Omphalitis, Recurrent soft tissue infections, Bacteremia (Staphylococcus), Osteomyelitis, CMV viremia, Disseminated fungal infection (†)	ATB therapy, granulocyte TF, surgical debridement, ATB prophylaxis, ganciclovir, antifungal treatment	N	4,5
c.687G>A p.W229X	F	21 and 51 months, MMUCBD 5/6 and MMUD 8/10, MAC (Bu/Cy/ATG) and RIC (Flu/Treo/TT/ATG), GvHD (Grade IV), good outcome	Mucocutaneous bleedings, Gastrointestinal bleedings	Platelet and RBC TF	Pneumocystis pulmonary infection, Recurrent CMV viremia	ATB therapy, ganciclovir	Y	5

c.687G>A p.W229X	M	12 months, MRD, RIC (Flu/Treo/TT/Alemtuzumab), no GvHD, good outcome	Cutaneous bleeding	Platelet and RBC TF	Recurrent pulmonary infections, Cellulitis, Gangrene, Deep-seated abscesses, Intestinal infection, Bacteremia (Pseudomonas, Klebsiella)	ATB therapy, amputation	Y	5

c.[922G>A;1287delT] p.[G308R;E430Rfs*3]	F	8 months, MMUCBD 5/6, RIC (Flu/Bu/Cy/rabbit ATG), skin and gut GvHD (Grade III), good outcome	Gastrointestinal bleedings, Traumatic hematomas	Platelet and RBC TF	Necrotizing enterocolitis, RSV pulmonary infection, Urinary tract infection (E. coli, P. aeruginosa), Bacteremia (S. aureus)	ATB therapy, Partial bowel resection	Y	6,7

c.1324-1G>A splice variant	F	No HSCT	Joint bleedings (knee, elbow), Mucocutaneous bleedings	NA	Pulmonary infection, Otitis media, Arthritis, Recurrent CMV viremia	ATB therapy, ganciclovir	Y	8
c.1438C>T p.Q480X	M	8 months, MRD, Good outcome	Mucosal bleedings	NA	Omphalitis, Urachal duct cyst infection, Soft tissue infection, Bacteremia (Staphylococcus), Pneumocystis pulmonary infection, Oral candidiasis; Urinary tract infection	ATB therapy	Y	9-11
c.1438C>T p.Q480X	M	15 weeks, Good outcome	Cutaneous bleedings	NA	Oral candidiasis, Omphalitis, Bacteremia (Staphylococcus)	ATB therapy	Y	9
c.1537C>T p.R513X	F	MUD, GvHD (†)	Gastrointestinal bleedings, Hematuria, Mucosal bleedings	Platelet and RBC TF	Recurrent pulmonary infections, Bacteremia (†)	NA	N	12
c.1537C>T p.R513X	M	Good outcome	Gastrointestinal bleedings, Hematuria, Mucosal bleedings	Platelet and RBC TF	Recurrent pulmonary infections	NA	Y	12
c.1537C>T p.R513X	M	No HSCT	Severe mucocutaneous bleedings	Platelet and RBC TF	Bacteremia and fungemia	NA	N	13
c.1537C>T p.R513X	M	No HSCT	Cutaneous bleedings, Pulmonary hemorrhage (†)	NA	Recurrent pulmonary infections, Intestinal infection, Bacteremia (P. aeruginosa), Oral candidiasis	NA	N	13,14
c.1537C>T p.R513X	F	3.5 years, MMRD x 2, RIC (Flu/Mel/TT/rabbit ATG) and MAC (Bu/Cy/TLNI), no engraftment	Severe bleeding tendency	Platelet and RBC TF	Recurrent pulmonary infections, buccal infection (P. aeruginosa)	ATB therapy	Y	13-15
c.1537C>T p.R513X	F	No HSCT	Mucocutaneous bleedings, Pulmonary hemorrhage (†)	Platelet and RBC TF	Pulmonary infections, Otitis media, Bacteremia (†)	ATB therapy	N	13,14
c.1537C>T p.R513X	M	13 years, MUD, †	Mucosal bleedings, Postoperative thoracic bleeding	Platelet and RBC TF	Perianal abscesses, Pulmonary infection, Bacteremia (P. aeruginosa), Mediastinal mass	ATB therapy, ATB prophylaxis, Ig replacement therapy, granulocyte TF, voriconazole	N	2,3,16,17

c.1537C>T p.R513X	M	4 years, Good outcome	Severe bleeding tendency, Cutaneous bleedings	Platelet and RBC TF	Perianal abscesses, Candidiasis	NA	Y	2,3,16
c.1537C>T p.R513X	M	1 year, Sinusoidal obstruction syndrome (†)	Severe bleeding tendency, CNS bleeding	Platelet and RBC TF	Pulmonary aspergillosis	Amphotericin B	N	2,3,16
c.1537C>T p.R513X	M	No HSCT	Severe bleeding tendency	Platelet and RBC TF	Omphalitis, Fungemia (F. oxysporum), Soft tissue infection, Bacteremia (P. aeruginosa) (†)	ATB therapy, Amphotericin B, flucytosine, granulocytes TF	N	2,3,16
c.1537C>T p.R513X	M	No HSCT	Severe traumatic epistaxis (†)	Platelet and RBC TF	Bacterial infections	NA	N	2,3,16
c.1537C>T p.R513X	M	Yes	Severe bleeding tendency, CNS bleeding	Platelet and RBC TF	Omphalitis, Perianal abscesses, CMV infections	ATB therapy	Y	2,3,16
c.1537C>T p.R513X	F	No HSCT	Moderate bleeding tendency	Platelet and RBC TF	NA	NA	Y	2,3,16
c.1537C>T p.R513X	F	No HSCT	Moderate bleeding tendency	Platelet and RBC TF	NA	NA	Y	2,3,16
c.1537C>T p.R513X	M	No HSCT	Moderate bleeding tendency Mucocutaneous bleedings	Platelet and RBC TF	Sepsis, CMV infection	NA	Y	2,3,16
c.1537C>T p.R513X	F	No HSCT	Hematuria, Gastrointestinal bleedings, Cutaneous bleedings	RBC TF	Cutaneous ulcers, Cellulitis, Bacteremia	NA	Y	18
c.1597C>T p.Q533X	F	5 months, MUD, RIC (Bu/Flu/TT), no GvHD, Good outcome	Gastrointestinal bleedings, Vaginal bleedings	Platelet and RBC TF	Presumed amnion infection	ATB therapy	Y	19

c.1683-2A>G splice variant	F	Yes, Good outcome	Antenatal CNS bleeding, Cutaneous bleeding	Platelet TF, Tranexamic acid	Recurrent infections, Cutaneous ulcers	ATB therapy, ATB prophylaxis	Y	7,18,20
c.1729C>T p.R577X	M	7 years, MUD, MAC (Bu/Flu/Cy/Rabbit ATG), GvHD (grade II), Good outcome	Buccal bleedings, Epistaxis	Platelet and RBC TF	Recurrent infections, Pulmonary infections, bacteremia (<i>S. pneumoniae</i>)	ATB therapy	Y	21
c.1729C>T p.R577X	M	3.5 years, MUD, MAC (Bu/Flu/Cy), Chronic lung GvHD (grade I)	Mucosal bleedings	NA	Recurrent infection, Pulmonary infections	ATB therapy	Y	21
c.1729C>T p.R577X	NA	No HSCT	Moderate bleeding tendency	NA	NA	NA	Y	2,3
c.1796A>C p.Q599P	F	No HSCT	Mild bleeding tendency	NA	Recurrent pulmonary infections (<i>A.</i> <i>baumanii</i> , <i>S. mitis</i> , <i>E. coli</i>), Bacteremia (<i>P.</i> <i>aeruginosa</i>), Mucocutaneous candidiasis, Intestinal infection (<i>Salmonella</i>), Urinary tract infection	ATB therapy, Ig replacement therapy	Y	22–24
c.1802delA p.N601Mfs*?	F	2 months, MUUCBD, RIC (Flu/Treo/TT/rabbit ATG), Liver and skin GvHD (grade III)	Cutaneous bleedings	NA	Pulmonary candidiasis, CMV viremia	NA	Y	25
c.1857delG p.A620Pfs*?	NA	14 months, MUUCBD, good outcome	Cutaneous bleeding, Epistaxis	NA	Pneumocystis pulmonary infection	NA	Y	26,27

FERMT3 variants were numbered according to the reference sequence NM_178443. The conditioning regimen intensity was defined as previously described.²⁸ The affected families are separated using dotted lines. Abbreviations: †: death; ATB: antibiotic; ATG: anti-thymocyte globulin; Bu: busulfan; CMV: cytomegalovirus; CNS: central nervous system; Cy: cyclophosphamide; F: female; Flu: fludarabine; GvHD: graft versus host disease; HSCT: hematopoietic stem cell transplantation; Ig: immunoglobulin; M: male; MAC: myeloablative conditioning; Mel: melphalan; MMRD: mismatched related donor; MMUUCBD mismatched unrelated umbilical cord blood donor; MRD: matched related donor; MUD: matched unrelated donor; MUUCBD: matched unrelated umbilical cord blood donor; N: no; NA: not available; RBC: red blood cells; RIC: reduced intensity conditioning; RSV: respiratory syncytial virus; TF: infusion; TLNI: total lymph node irradiation; Treo: treosulfan; TT thiotepa; Y: yes.

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