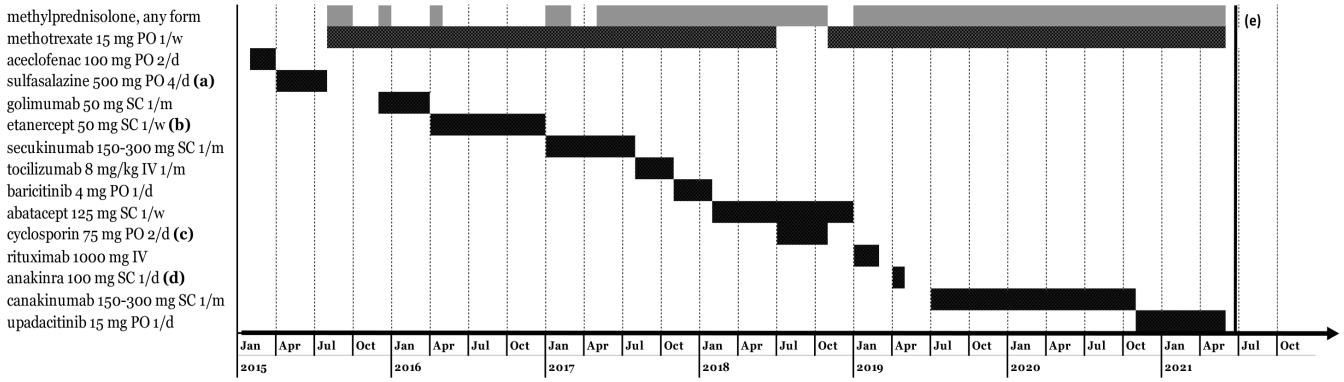
Supplementary material



Supplementary Fig. S1. Overview of treatments received before HSCT in June 2021.
Horizontally, the timeline from presentation until stem cell transplantation on 21st June 2021 is visualised. Vertically, all treatments with dose are listed. The patient was almost continuously treated with methylprednisolone and methotrexate, in combination with a third therapy. (**a**) Sulfasalazine was ceased in August 2015 because of intolerance (nausea, constipation, anorexia). (**b**) Etanercept was stopped because of development of chronic inflammatory demyelinating polyneuropathy (CIDP) possibly due to anti-TNF-therapy, for which plasmapheresis was initiated. (1, 2) (**c**) Due to absence of clinical response to abatacept and because of intense T-cell proliferation on synovial biopsy, cyclosporin was added in July 2018; the patient developed gingivitis and cyclosporin was switched to methotrexate in November 2018. (**d**) Anakinra induced an erythematous rash and was rapidly stopped; methylprednisolone 80 mg PO in slow tapering scheme was started. (**e**) Allogeneic haematopoietic stem cell transplantation was performed on 21st June 2021.
HSCT: haematopoeitic stem cell transplantation; IV: intravenous; PO: peroral; SC: subcutaneous.

References

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Supplementary Table S1. Reported cases of allogeneic HSCT in RA patients.

First author, reference, year of publication [a]	Sex	Age	RF and ACPA status	Indication for HSCT	Year of HSCT	Donor type	Donor RA status	Number of HLA alleles predisposing to RA [g]	Level of evidence for RA diagnosis	Lines of therapy received before HSCT [h]	RA duration before haematological disease [i] (years)	RA duration before HSCT (years)
Baldwin 1977 [b] (1)	F	34	+/?	aplastic anaemia	1974	MSD	?	?	Probable	2	4	4
McKendry 1996 (2)	F	53	+/?	aplastic anaemia	1986	MSD	No	2	Definite	≥1	8	8
Nelson 1997 [c] (3)	F	30	-/?	aplastic anaemia?	1975	MSD	No	?	Definite	1	0.2	2
Snowden 1998 [d] (4)	F	34	+/?	aplastic anaemia	1982	MSD	No	1?	Definite	3	<1	1
Tapprich 2003 (5)	F	54	+/?	multiple myeloma	2001	MSD	No[k]	1[m]	Probable	2	≤1[o]	6
Burt 2004 (6)	F	52	+/?	RA	?	MSD	?[l]	?	Definite	≥5	NA	?
Lowenthal 2006 [e] Pt 1 (7)	F	27	?/?	aplastic anaemia	1984	MSD	?	2?	Definite	≥2	6	6
Lowenthal 2006 [f] Pt 2 (7)	F	30	+/?	aplastic anaemia	1986	MSD	?	0	Definite	2	9	9
Itamura 2012 (8)	F	48	+/?	haemophagocytic lymphohistiocytosis	?	MMCB	?	0	Probable	2	>1	>1
Atoui 2020 (9)	F	37	-/-	peripheral T-cell lymphoma	2015	Haplo	?	0[n]	Definite	≥2	?	?
Bettag 2020, Pt 1 (10)	M	70	+/+	follicular lymphoma	2014	MSD[j]	No	2	Definite	1	7	9
Bettag 2020, Pt 2 (10)	M	64	+/+	myelodysplastic syndrome	2017	MSD[j]	No	2	Definite	1	7	13
Shifa 2021 (UPN 154) (11)	M	44	-/?	AML	1993	MMSD	No	1-2	Probable	4	3	3
Shifa 2021 (UPN 655) (11)	M	59	?/?	myelodysplastic syndrome	2003	MUD	No	1	Probable	2	0.5	1
Van Compernolle submitted	F	26	-/-	RA	2021	Haplo	No	0	Definite	9	NA	6

First author, reference, year of publication [a]	Chemo or immuno-suppressive therapy pre-HSCT [p]	Conditioning intensity	Relapse of RA post-HSCT [q]	Time from HSCT to IST stop (years)	Follow-up for RA since HSCT (years)	Duration of RA remission since stop of IST (years)	Duration of RA remission since HSCT (years)	GVHD	Serotherapy for GVHD prophylaxis	Chimerism (pre-relapse of RA, Last available if no RA relapse)
Baldwin 1977 [b] (1)	No	?	**No**[r]	?	2	?	2	Yes	?	?
McKendry 1996 (2)	No	reduced intensity	**Yes** [s]	?	13.0	?	2	Yes	None	Complete [ff]
Nelson 1997 [c] (3)	No	reduced intensity	**No** [t]	<2	20	18	20	Yes	?	?
Snowden 1998 [d] (4)	No	reduced intensity	**Yes** [u]	1.0	14	1.0	2	Yes	None	?
Tapprich 2003 (5)	Yes	reduced intensity	**Yes** [v]	2.5	2.5	0	0.8	Yes	None	Complete [gg]
Burt 2004 (6)	No	reduced intensity	**No** [w]	0.8	5[cc]	4	5	No	Alemtuzumab	Mixed [hh]
Lowenthal 2006 [e] Pt 1 (7)	No	reduced intensity	**No** [x]	2	21	19	21	Yes	None	Complete [ii]
Lowenthal 2006 [f] Pt 2 (7)	No	reduced intensity	**No** [y]	≤3	19	16	19	Yes	None	Complete [jj]
Itamura 2012 (8)	No	reduced intensity	**No** [z]	0.3	8 [dd]	~8	~8	?	None	Complete [kk]
Atoui 2020 (9)	Yes	myeloablative	**No**	0.3	8	7.7	8	No	ATG	Complete [ll]
Bettag 2020, Pt 1 (10)	Yes	myeloablative	**Yes** [aa]	?	5	?	1.3	Yes	?	Complete
Bettag 2020, Pt 2 (10)	No	reduced intensity	**Yes** [bb]	N	1.6	?	0.8	Yes	?	Complete
Shifa 2021 (UPN 154) (11)	Yes	myeloablative	**No**	0.5	0.5	0	0.5	Yes	None	?
Shifa 2021 (UPN 655) (11)	No	myeloablative	**Yes**	0.6	1.9	0.4	1 [ee]	No	ATG	Complete [mm]

Supplementary Table S1 summarises the most important figures about the reported cases. Shaded rows denote highly informative cases, defined as in Shifa *et al*. (11). Briefly, for patients with relapsed RA, follow-up data had to be available for >1 year beyond the discontinuation of immunosuppressive therapy. For patients with relapsed RA, their donor had to be known not to have RA. The table is adapted from Shifa *et al*. with permission of the authors (11).
ACPA: anti-citrullinated peptide antibody; AML: acute myeloid leukaemia; ATG: antithymocyte globulin; GVHD: graft-versus-host disease; Haplo: haploidentical relative; HSCT: haematopoietic stem cell transplant; MMCB: HLA mismatched cord blood; MMSD: HLA mismatched sibling donor; MSD: HLA matched sibling donor; NA: not applicable; RA: rheumatoid arthritis; RF: rheumatoid factor; UPN: unique patient number.

Notes

[a] If ≥2 patients were reported in one paper, the patients are identified by unique patient number (UPN) or the sequence of patients in the paper (e.g. Pt 1 means Patient no. 1).
[b] Case no. 2 in that paper (Baldwin 1997) (1)
[c] Patient no. 1 in Nelson 1997 (3)
[d] Patient no. 1 in Snowden *et al*. 1998 (4) is also reported in Jacobs *et al*. 1986 (12)
[e] Patient no. 1 in Lowenthal *et al*. 2006 (7) is also reported in Snowden *et al*. 1998 (4) as patient no. 2 and in Lowenthal *et al*.1993 (13) as patient no. 1
[f] Patient no. 2 in Lowenthal *et al*. 2006 (7) is also reported in Snowden *et al*. 1998 (4) as patient no. 3, and in Lowenthal *et al*. 1993 (13) as patient no. 2
[g] HLA DRB1*01:01, 01:02, 04:01, 04:04, 04:05, 04:08, or 10:01, or, in case of serological typing, HLA DR/DRB1*01, 04, or 10. The number in parentheses denotes the number of the predisposing DRB1 alleles. If only serological typing was done, the number of predisposing alleles is marked with a question mark. In the cases of UPN154 (11) and Itamura 2012 (8), the mismatch was at a locus other than DRB1, so only one case was DRB1-mismatched.
[h] Number of lines of therapy (other than analgesics/NSAIDs or topical therapy) used to treat RA before HCT.
[i] Duration of RA before the diagnosis of the haematological disease that needed HCT. Negative values indicate that RA was diagnosed after the diagnosis of the haematological disease. For most patients, the figures are approximate.
[j] Both cases were homozygous for DRB1 1001
[k] Donor had mildly elevated rheumatoid factor (17 U/ml) but no symptoms of RA
[l] RF in donor blood was negative.
[m] Both donor and recipient had DRB1*04:01 and 04:05. This information was kindly provided by Dr Guido Kobbe, Heinrich Heine University, Düsseldorf, Germany
[n] Donor HLA DRB1 was 03:01 and 11:04. Recipient DRB1 was 11:04 and 13:01. Additional information was kindly provided by Dr Ali Bazarbachi (American University of Beirut, Lebanon).
[o] Despite of the short interval between RA diagnosis and MM diagnosis, the case is considered highly informative as no association between RA and MM has been described (11)
[p] Immunosuppressive therapy (IST) as given for diseases other than RA before HCT conditioning (*e.g*. chemotherapy for leukaemia or antithymocyte globulin for aplastic anaemia).
[q] Autoantibodies were not used for relapse determination. If autoantibody status was reported both pre- and post-HCT in non-relapse cases, the status is given in a footnote
[r] RF was positive pre-HCT and negative on several determinations post-HCT (specific time was not reported).
[s] RF was positive pre-HCT and negative in clinical RA remission early post-HCT. It became positive multiple times when relapse occured at 3-13 years post-HCT.
[t] RF was negative at RA diagnosis and at 1 month, 1 year, and 15 years post-HCT.
[u] RF was positive pre-HCT and became negative when in clinical RA remission early post-HCT. At relapse 2 years post-HCT, it again became positive. The patient received DMARDs at 2-4 years post-HCT and was afterwards in clinical RA remission at 4-14 years post-HCT with borderline RF positivity.
[v] RF was positive pre-HCT and became negative when in clinical RA remission early post-HCT. RF again became positive at relapse at 10-20 months post-HCT.
[w] RF was high pre-HCT and became undetectable by 1 year post-HCT.
[x] RF was not reported pre-HCT and was negative at 1 ½, 4, 10, and 21 years post-HCT.
[y] RF was positive between 6 years and 1 year pre-HCT, but not immediately pre-HCT. RF was negative at 10 and 18 years post-HCT.
[z] RF was high (164 IU/ml) pre-HCT and was undetectable at 6 months post-HCT.
[aa] The patient was seropositive pre-HCT, with high ACPA (491 U/ml, normal <17) and RF (474 IU/ml, normal <17) at relapse. After rituximab, clinical and serologic remission was achieved lasting until end of follow-up three years post-rituximab.
[bb] The patient was seropositive pre-HCT, with high ACPA (37, normal <5) and RF (178 IU/ml, normal <17) at relapse, after starting prednisone. After rituximab, clinical and serologic remission was achieved lasting until end of follow-up two months post-rituximab.
[cc] Updated follow-up retrieved from Snowden *et al*. 2008 (14)
[dd] Updated follow-up kindly provided by Dr Noriyasu Fukushima, Hiroshima University, Japan
[ee] RA relapse occurred one year after HCT and was treated with prednisone 0.5 mg/day.
[ff] >98.4% donor among WBC, time not reported
[gg] At 10 months post-HCT, cell type not reported
[hh] 70% donor CD3 (T) cells and 50% donor CD 33 (myeloid) cells at 1-year post-HCT
[ii] 100% donor assumed given ABO type only donor at 1 year post-HCT
[jj] >98.4% donor among WBC and blood T cells, time not reported
[kk] Complete donor chimerism among marrow nucleated cells at 60 days post-HCT
[ll] 99% donor among marrow nucleated cells at 3 months post-HCT
[mm] >95% donor among bone marrow nucleated cells at 11 months post-HCT

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