LETTER TO THE EDITOR

Impact of high-risk disease on the efficacy of chimeric antigen receptor T-cell therapy for multiple myeloma: a meta-analysis of 723 patients

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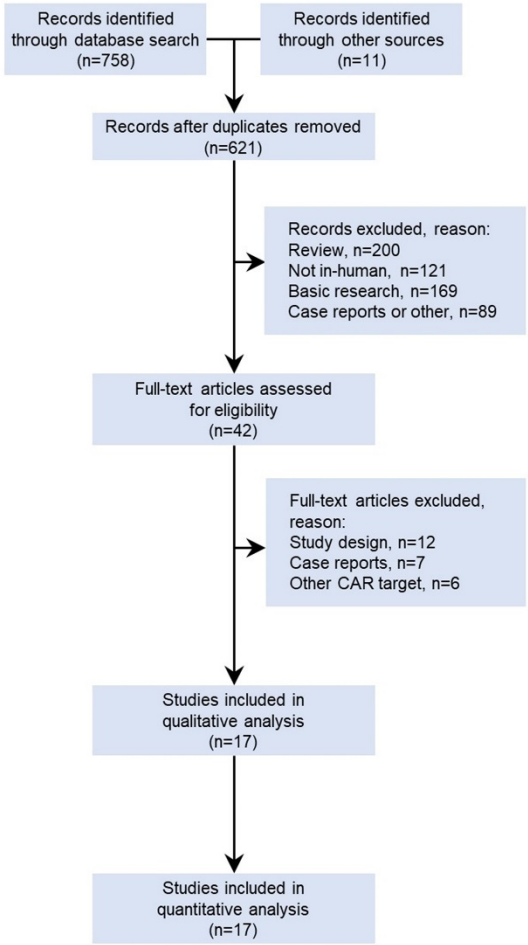
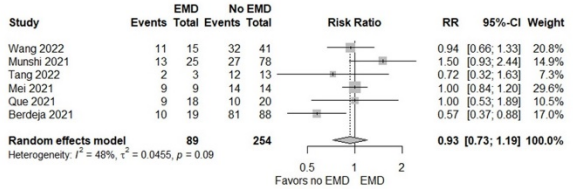
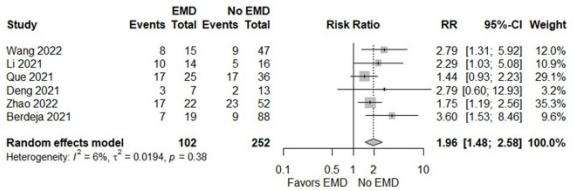
Figure S1. PRISMA flow diagram of study selection and meta-analysis.



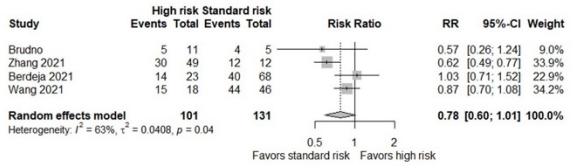
A. Meta-analysis for measurable residual disease in patients with or without extramedullary disease.



B. Meta-analysis for overall survival in patients with or without extramedullary disease.



C. Meta-analysis for measurable residual disease in patients with high-risk or standard-risk cytogenetics.



D. Meta-analysis for overall survival in patients with high-risk or standard-risk cytogenetics.

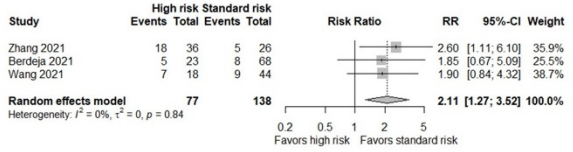


Table S1. Characteristics of included studies.

Study	Country	N	Median age	Lines of Prior treatment	ASCT before CAR-T	LD	Antigen	Follow-up, months	Reference
Brudno 2018	US	26	(18-70)	10	85%	Flu/Cy: 30mg/m^2 /300mg/m^2 daily on day -5 to -3	BCMA	5	Brudno JN, Maric I, Hartman SD, et al. T Cells Genetically Modified to Express an Anti-B-Cell Maturation Antigen Chimeric Antigen Receptor Cause Remissions of Poor-Prognosis Relapsed Multiple Myeloma. J Clin Oncol 2018;36:2267–80.
Tang 2022	China	16	57	3	20%	Flu/Cy: 25mg/m^2 and 250mg/m^2 days -4 to -2	BCMA and CD38	12	Tang Y, Yin H, Zhao X, et al. High efficacy and safety of CD38 and BCMA bispecific CAR-T in relapsed or refractory multiple myeloma. J Exp Clin Cancer Res 2022;41:2.
Mei 2021	China	23	59	4	13%	Flu/Cy: 25mg/m^2 and 250mg/m^2 days -5 to -3	BCMA and CD38	9	Mei H, Li C, Jiang H, et al. A bispecific CAR-T cell therapy targeting BCMA and CD38 in relapsed or refractory multiple myeloma. J Hematol Oncol 2021;14:161.
Berdeja 2021	US, Europe	113	61	6	90%	Flu/Cy: 30mg/m^2 and 300mg/m^2 for 3 days	BCMA	12	Berdeja JG, Madduri D, Usmani SZ, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. The Lancet 2021;398:314–24.
Shi 2021	China	10	54	NA	100%	NA	BCMA	42	Shi X, Yan L, Shang J, et al. Anti-CD19 and anti-BCMA CAR T cell therapy followed by lenalidomide maintenance after autologous stem-cell transplantation for high-risk newly diagnosed multiple myeloma. Am J Hematol 2022;97:537–47.
Li 2021	China	28	55	4	37%	Flu/Cy: 25mg/m^2 and 20mg/kg days -4 to -2	BCMA	13	Li C, Cao W, Que Y, et al. A phase I study of anti-BCMA CAR T cell therapy in relapsed/refractory multiple myeloma and plasma cell leukemia. Clin Transl Med 2021;11:e346.
Munshi 2021	US, Europe	128	61	6	94%	Flu/Cy: 30mg/m^2 and 300mg/m^2 days -5 to -3	BCMA	13	Munshi NC, Anderson LD, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med 2021;384:705–16.
Deng 2021	China	13	58	9	33%	Flu/Cy: 30mg/m^2 and 400mg/m^2 days -4 to -2	BCMA	10	Deng H, Liu M, Yuan T, et al. Efficacy of Humanized Anti-BCMA CAR T Cell Therapy in Relapsed/Refractory Multiple Myeloma Patients With and Without Extramedullary Disease. Front Immunol 2021;12:720571.
Du 2021	China	49	57	4	29%	Flu/Cy: 30mg/m^2 and 300mg/m^2 days -4 to -2	BCMA	15	Du J, Wei R, Jiang S, et al. CAR-T cell therapy targeting B cell maturation antigen is effective for relapsed/refractory multiple myeloma, including cases with poor performance status. Am J Hematol 2022;97:933–41.
Cohen 2019	US	25	58	7	92%	Cy: 1.5g/m^2 or no LD	BCMA	13	Cohen AD, Garfall AL, Stadtmauer EA, et al. B cell maturation antigen-specific CAR T cells are clinically active in multiple myeloma. J Clin Invest 2019;129:2210–21.
Garfall 2018	US	10	61	6	100%	Melphalan: 140-200 mg/m^2	CD19	5	Garfall AL, Stadtmauer EA, Hwang W-T, et al. Anti-CD19 CAR T cells with high-dose melphalan and autologous stem cell transplantation for refractory multiple myeloma. JCI Insight 2018;3.
Zhao 2021	China	74	54	3	24%	Flu/Cy: 30mg/m^2 and 300mg/m^2 days -5 to -3	BCMA	24	Zhao W-H, Wang B-Y, Chen L-J, et al. Four-year follow-up of LCAR-B38M in relapsed or refractory multiple myeloma: a phase 1, single-arm, open-label, multicenter study in China (LEGEND-2). J Hematol Oncol 2022;15:86.

Que 2021	China	61	54	4	33%	Flu/Cy: 25mg/m^2 and 20mg/kg days -4 to -2	BCMA	28	Que Y, Xu M, Xu Y, et al. Anti-BCMA CAR-T Cell Therapy in Relapsed/Refractory Multiple Myeloma Patients With Extramedullary Disease: A Single Center Analysis of Two Clinical Trials. Front Immunol 2021;12:755866.
Wang 2022	China	69	58	4	27%	Flu/Cy: 30mg/m^2 for 3 days and 750mg/m^2 for 1 day	CD19 and BCMA	21	Wang Y, Cao J, Gu W, et al. Long-Term Follow-Up of Combination of B-Cell Maturation Antigen and CD19 Chimeric Antigen Receptor T Cells in Multiple Myeloma. J Clin Oncol 2022;40:2246–56.
Xu 2019	China	17	55	5	47%	Flu/Cy: 25 mg/m^2 and 250 mg/m^2 days -5 to -3	BCMA	15	Xu J, Chen L-J, Yang S-S, et al. Exploratory trial of a biepitopic CAR T-targeting B cell maturation antigen in relapsed/refractory multiple myeloma. Proc Natl Acad Sci U S A 2019;116:9543–51.
Zhang 2021	China	61	59	3	39%	Flu 30mg/m² days -4 to -2, Cy 500 mg/m² days -3 to -2	BCMA	21	Zhang M, Zhou L, Zhao H, et al. Risk Factors Associated with Durable Progression-Free Survival in Patients with Relapsed or Refractory Multiple Myeloma Treated with Anti-BCMA CAR T-cell Therapy. Clin Cancer Res 2021;27:6384–92.

Table S2. Results of heterogeneity across comparisons and outcomes.

Outcomes	Heterogeneity	P
Overall response		
EMD vs no EMD	2%	0.43
High vs standard risk	69%	<0.01
Measurable residual disease		
EMD vs no EMD	48%	0.09
High vs standard risk	63%	0.04
Progression-free survival		
EMD vs no EMD	0%	0.50
High vs standard risk	0%	0.79
Overall survival		
EMD vs no EMD	6%	0.38
High vs standard risk	0%	0.84