Allogeneic transplant following CAR T-cell therapy for large B-cell lymphoma

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Received: April 13, 2022.
Accepted: July 6, 2022.
Prepublished: July 14, 2022.

https://doi.org/10.3324/haematol.2022.281242

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Table S1. Participating Academic Medical Centers[1]

Institution	City, State
Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, The Ohio State University	Columbus, OH
Carbone Comprehensive Cancer Center, University of Wisconsin	Madison, WI
City of Hope, Department of Hematology and Hematopoietic Cell Transplantation[2]	Duarte, CA
Dana-Farber Cancer Institute, Department of Medical Oncology	Boston, MA
Fred Hutchinson Cancer Research Center and University of Washington	Seattle, WA
H. Lee Moffitt Cancer Center & Research Institute	Tampa, FL
Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern	Dallas, TX
Hollings Cancer Center, Medical University of South Carolina,	Charleston, SC
John Theurer Cancer Center at Hackensack Meridian Health	Piscataway, NJ
Levine Cancer Institute/Atrium Health	Charlotte, NC
Mayo Clinic, Division of Hematology-Oncology and Blood and Marrow Transplantation and Cellular Therapy Program	Jacksonville, FL
Medical College of Wisconsin Cancer Center	Milwaukee, WI
Memorial Sloan Kettering Cancer Center	New York, NY
Sylvester Comprehensive Cancer Center, Division of Transplantation and Cellular Therapy,	Miami, FL
University of Kansas Medical Center, Division of Hematologic Malignancies & Cellular Therapeutics	Westwood, KS
University of Texas MD Anderson Cancer Center, Department of Stem Cell Transplantation, Division of Cancer Medicine	Houston, TX
Vanderbilt-Ingram Cancer Center, Division of Hematology and Oncology	Nashville, TN
Wilmot Cancer Institute, University of Rochester Medical Center	Rochester, NY

[1] Sites listed in alphabetical order by institution

[2] Primary coordinating site

Table S2: Additional methodology details

Variables considered in model building for Cox model multivariate analysis
Age at alloHCT (≤60 versus [vs] >60 years)
Ethnicity (White vs Hispanic vs other)
MYC rearrangement (yes vs no)
Lines of therapy between CAR-T and alloHCT (0 vs 1 vs ≥2)
History of prior autologous HCT (yes vs no)
Receipt of radiation therapy between CAR-T and alloHCT (yes vs no)
Disease status prior to alloHCT (CR vs PR vs SD/PD)
Conditioning regimen (MAC vs RIC/NMA)
Donor type (MRD vs MUD vs other [haploidentical, cord, mismatched unrelated donor])
Details regarding administrative truncation time
All outcomes were administratively truncated at no later than 36 months due to the low number of patients followed beyond that time-point.
Short-term outcomes, such as neutrophil/platelet engraftment and aGVHD were truncated at shorter timeframes (33, 100, and 180 days, respectively), to focus on the relevant risk period.

Table S3. Treatment regimens given across multiple lines between CAR-T and allogeneic hematopoietic cell transplantation

Treatment Category	No. (n=142)	Response rate(s)
Chemotherapy[1]	31	ORR 60% (CR 33%) 1 pt unknown response
Polatuzumab + bendamustine + rituximab[2]	23	ORR 91% (CR 74%)
Radiation[3]	18	ORR 56% (CR 17%)
PD-1 inhibitor	12	ORR 58% (CR 17%)
IMiD +/- anti-CD20 antibody	9	ORR 56% (CR 33%)
Axi-cel	6	ORR 83% (CR 33%)
Investigational CAR-T	6	ORR 33% (CR 17%)
Polatuzumab + rituximab +/- radiation[4]	5	ORR 100% (CR 40%)
CD3, CD20 bispecific antibody	4	ORR 50% (CR 50%)
BTKi +/- anti-CD20 antibody	4	ORR 25% (CR 25%)
Lenalidomide + PD-1 inhibitor +/- anti-CD20 antibody	3	ORR 100% (CR 0%)
Ibrutinib + anti-CD20 antibody + lenalidomide	3	ORR 0%
Surgery	2	ORR 50% (50% CR)
Other	16	Regimens with n=1 noted below[5]

Abbreviations: alloHCT, allogeneic hematopoietic cell transplant; CAR-T, chimeric antigen receptor T-cell; CR, complete response; DLBCL, diffuse large B-cell lymphoma; n, number; No., number; PD, progressive disease; PD-1, PMBL, primary mediastinal B-cell lymphoma; PR, partial response; SD, stable disease

[1] n=1 had concurrent radiation
[2] n=1 had concurrent radiation
[3] n=1 had concurrent steroids + radiation
[4] n=2 had concurrent radiation
[5] The following regimens had an n=1: Steroids alone (n=1, 1 SD); IMiD + BTKi + ipilimumab + nivolumab (n=1, 1 PR), tafasitamab + lenalidomide (n=1; 1 CR), investigational PD-L1 inhibitor (n=1; 1 PD); rituximab (n=1; 1 PD), investigational ADC (n=1, 1 PD), clinical trial unspecified (n=1; 1 CR), anti-CD20 bispecific antibody + polatuzumab (n=1; 1 PR), PD-1 inhibitor + vorinostat (n=1; 1 CR), anti-CD52 antibody (n=1; 1 PD), brentuximab vedotin (n=1; 1 PR), lenalidomide + polatuzumab + rituximab (n=1; 1 CR), obinutuzumab + venetoclax (n=1, 1 CR), chemotherapy + PD-L1 inhibitor (n=1; 1 PD), BET inhibitor + venetoclax (n=1; 1 PD), loncastuximab tesirine (n=1; 1 PR)

Table S4. Treatment Regimens Given After CAR-T To Achieve a Complete Response Prior to AlloHCT Across Multiple Lines

Category	No. (%)	Specific regimens (No.)
Polatuzumab-containing	19 (42)	Polatuzumab + bendamustine + rituximab (15) Polatuzumab + rituximab (2) Polatuzumab + rituximab + radiation (1) Polatuzumab + lenalidomide + rituximab + radiation therapy (1)
Chemotherapy	10 (22)	Gemcitabine + cisplatin + dexamethasone + rituximab (R-GDP) (2) Gemcitabine + oxaliplatin + rituximab (2) R-HyperCVAD part A only (1) HyperCVAD part B only (1) Rituximab + cyclophosphamide + doxorubicin + vincristine + prednisone (R-CHOP) (1) Ifosfamide + etoposide + cytarabine (IVAC) (1) High dose methotrexate and cytarabine with intrathecal chemotherapy (1) Obinutuzumab + Ifosfamide + carboplatin + etoposide (ICE) (1)
Lenalidomide + anti-CD20 antibody	3 (7)	Lenalidomide + ofatumumab (2) Lenalidomide + obinutuzumab (1)
CAR-T	3 (7)	Second axicabtagene (1) Other CAR-T (2)
Bispecific antibodies	2 (4)	Investigational anti-CD3, anti-CD20 bispecific antibody (2)
Checkpoint inhibitor	2 (4)	Pembrolizumab (1) (patient with PMBL) PD-1 inhibitor, unspecified (1) (patient with DLBCL)
Radiation alone	2 (4)	Radiation therapy (2)
Other	4 (9)	Surgery (1) Clinical trial, unspecified (1) Pembrolizumab + vorinostat (1) (patient with PMBL) Obinutuzumab + venetoclax (1)

Abbreviations: alloHCT, allogeneic hematopoietic cell transplant; CAR-T, chimeric antigen receptor T-cell; CR, complete response; DLBCL, diffuse large B-cell lymphoma; No., number; PMBL, primary mediastinal B-cell lymphoma

Table S5. Incidence of acute and chronic GVHD stratified by receipt of PD-1 inhibitor between CAR-T and alloHCT

Cumulative incidence of acute GVHD grade II-IV	**At 100 days, % (95% CI)**	**At 180 days % (95% CI)**
PD-1 inhibitor	22% (10% - 49%)	22% (10% - 49%)
No PD-1 inhibitor	37% (27% - 51%)	40% (30% - 54%)
Cumulative incidence of chronic GVHD	At 12 months, % (95% CI)	At 24 months, % (95% CI)
PD-1 inhibitor	40% (22% - 72%)	40% (22% - 72%)
No PD-1 inhibitor	27% (18% - 41%)	39% (28% - 56%)

Abbreviations: alloHCT, allogeneic hematopoietic cell transplantation; CAR-T, chimeric antigen receptor T-cell therapy; GVHD, graft-versus-host disease

Table S6. Univariate analysis of survival outcomes

Overall survival			
	HR	95% CI	P-value
Age at alloHCT (grouped)			0.27
≤60	—	—	
>60	1.46	0.75, 2.81	
Race/ethnicity			0.068
White	—	—	
Hispanic	2.13	1.07, 4.21	
Other	0.69	0.21, 2.31	
cMYC+ on FISH			0.59
No	—	—	
Yes	1.24	0.57, 2.67	
Lines of therapy between CAR-T and alloHCT			0.064
0	—	—	
1	0.45	0.18, 1.10	
2+	0.94	0.39, 2.29	
Did patient get radiation after CAR-T infusion and before conditioning for alloHCT?			0.19
No	—	—	
Yes	1.58	0.81, 3.08	
Autologous HCT prior to CAR-T infusion?			0.80
No	—	—	
Yes	1.10	0.53, 2.27	
Time to progression after CAR-T			0.29
<90 days	—	—	
≥90 days	0.95	0.47, 1.92	
Disease status prior alloHCT (grouped)			0.030
CR	—	—	
PR	2.74	1.32, 5.70	
SD/PD	1.56	0.70, 3.47	
Conditioning regimen intensity			0.19
MAC	—	—	
RIC/NMA	0.61	0.30, 1.24	
Donor type (grouped)			0.15
MUD	—	—	
MRD	0.67	0.27, 1.65	
Other	1.55	0.77, 3.16	
Progression-free survival			
	HR	95% CI	P-value
Age at alloHCT (grouped)			0.82
≤60	—	—	
>60	1.07	0.59, 1.93	
Race/ethnicity			0.12
White	—	—	

Hispanic	1.89	1.00, 3.55	
Other	0.81	0.31, 2.07	
cMYC+ on FISH			0.56
No	—	—	
Yes	1.23	0.62, 2.44	
Lines of therapy between CAR-T and alloHCT			0.16
0	—	—	
1	0.64	0.27, 1.51	
2+	1.14	0.49, 2.66	
Did patient get radiation after CAR-T infusion and before conditioning for alloHCT?			0.33
No	—	—	
Yes	1.35	0.75, 2.44	
Autologous HCT prior to CAR-T infusion?			0.95
No	—	—	
Yes	1.02	0.54, 1.91	
Time to progression after CAR-T			0.75
<90 days	—	—	
≥90 days	0.96	0.53, 1.75	
Disease status prior alloHCT (grouped)			0.074
CR	—	—	
PR	2.08	1.09, 3.95	
SD/PD	1.61	0.81, 3.19	
Conditioning regimen intensity			0.37
MAC	—	—	
RIC/NMA	0.74	0.39, 1.41	
Donor type (grouped)			0.31
MUD	—	—	
MRD	0.81	0.39, 1.69	
Other	1.39	0.75, 2.59	
Relapse/progression			
	HR	95% CI	P-value
Age at alloHCT (grouped)			0.43
≤60	—	—	
>60	1.32	0.66, 2.61	
Race/ethnicity			0.98
White	—	—	
Hispanic	1.08	0.49, 2.39	
Other	1.04	0.36, 3.01	
cMYC+ on FISH			0.15
No	—	—	
Yes	1.71	0.82, 3.58	
Lines of therapy between CAR-T and alloHCT			0.14
0	—	—	
1	0.47	0.21, 1.05	
2+	0.49	0.22, 1.12	

Did patient get radiation after CAR-T infusion and before conditioning for alloHCT?			0.96
No	—	—	
Yes	0.98	0.48, 2.02	
Autologous HCT prior to CAR-T infusion?			0.31
No	—	—	
Yes	1.41	0.72, 2.74	
Time to progression after CAR-T			0.40
<90 days	—	—	
≥90 days	1.15	0.55, 2.40	
Disease status prior alloHCT (grouped)			0.29
CR	—	—	
PR	1.17	0.54, 2.53	
SD/PD	1.87	0.86, 4.06	
Conditioning regimen intensity			0.58
MAC	—	—	
RIC/NMA	1.25	0.56, 2.80	
Donor type (grouped)			0.75
MUD	—	—	
MRD	1.05	0.45, 2.48	
Other	1.30	0.63, 2.68	
NRM			
	HR	95% CI	P-value
Age at alloHCT (grouped)			0.68
≤60	—	—	
>60	0.82	0.32, 2.13	
Race/ethnicity			0.12
White	—	—	
Hispanic	2.20	0.90, 5.35	
Other	0.46	0.06, 3.37	
cMYC+ on FISH			0.41
No	—	—	
Yes	0.53	0.12, 2.40	
Lines of therapy between CAR-T and alloHCT			0.12
0	—	—	
1	1.63	0.23, 11.8	
2+	3.68	0.55, 24.8	
Did patient get radiation after CAR-T infusion and before conditioning for alloHCT?			0.31
No	—	—	
Yes	1.59	0.64, 3.94	
Autologous HCT prior to CAR-T infusion?			0.34
No	—	—	
Yes	0.55	0.16, 1.86	
Time to progression after CAR-T			0.94
<90 days	—	—	

≥90 days	0.85	0.34, 2.15	
Disease status prior alloHCT (grouped)			0.10
CR	—	—	
PR	2.39	0.94, 6.05	
SD/PD	0.80	0.22, 2.92	
Conditioning regimen intensity			0.15
MAC	—	—	
RIC/NMA	0.51	0.20, 1.28	
Donor type (grouped)			0.53
MUD	—	—	
MRD	0.55	0.15, 2.06	
Other	1.17	0.47, 2.94	
GVHD-free relapse-free survival (GRFS)			
	HR	95% CI	P-value
Age at alloHCT (grouped)			0.84
≤60	—	—	
>60	1.06	0.61, 1.85	
Race/ethnicity			
White	—	—	
Hispanic	1.79	0.97, 3.31	
Other	1.30	0.60, 2.81	
cMYC+ on FISH			0.66
No	—	—	
Yes	1.17	0.60, 2.29	
Lines of therapy between CAR-T and alloHCT			0.26
0	—	—	
1	0.71	0.31, 1.66	
2+	1.13	0.49, 2.63	
Did patient get radiation after CAR-T infusion and before conditioning for alloHCT?			0.22
No	—	—	
Yes	1.43	0.82, 2.51	
Autologous HCT prior to CAR-T infusion?			0.58
No	—	—	
Yes	0.84	0.45, 1.56	
Time to progression after CAR-T			0.68
<90 days	—	—	
≥90 days	0.97	0.55, 1.68	
Disease status prior alloHCT (grouped)			0.16
CR	—	—	
PR	1.84	1.00, 3.39	
SD/PD	1.27	0.65, 2.45	
Conditioning regimen intensity			0.26
MAC	—	—	
RIC/NMA	0.69	0.37, 1.29	
Donor type (grouped)			0.52

MUD	—	—	
MRD	0.83	0.42, 1.64	
Other	1.23	0.68, 2.22	

Abbreviations: alloHCT, allogeneic hematopoietic cell transplant; CAR-T, chimeric antigen receptor T-cell; CR, complete response; HCT, hematopoietic cell transplant; MAC, myeloablative conditioning; MRD, matched related donor; MTX, methotrexate; MUD, matched unrelated donor; NMA/RIC, non-myeloablative/reduced intensity conditioning; No., number; PD, progressive disease; PR, partial response; SD, stable disease

Table S7. Demographic and clinical characteristics of patients based on disease status at time of alloHCT

Characteristic	CR, N = 45[1]	PR, N = 22[1]	SD/PD, N = 21[1]
Age at time of alloHCT, years	53 (19 - 70)	52 (19 - 67)	55 (27 - 72)
Male Sex	29 (64%)	15 (68%)	19 (90%)
Race			
White	33 (73%)	12 (55%)	13 (62%)
Hispanic	5 (11%)	8 (36%)	5 (24%)
Black	3 (6.7%)	2 (9.1%)	1 (4.8%)
Asian	4 (8.9%)	0 (0%)	1 (4.8%)
American Indian or Alaska Native	0 (0%)	0 (0%)	1 (4.8%)
Chemorefractory disease prior to CAR-T infusion	29 (64%)	17 (77%)	18 (86%)
Best response to CAR-T			
CR	22 (49%)	4 (18%)	5 (24%)
PR	16 (36%)	10 (45%)	6 (29%)
SD/PD	7 (16%)	8 (36%)	10 (48%)
Stage at time of CAR-T relapse/progression			
1	14 (32%)	7 (37%)	5 (25%)
2	6 (14%)	1 (5.3%)	2 (10%)
3/4	24 (53%)	11 (50%)	13 (62%)
Unknown	1	3	1
Extranodal involvement at time of CAR-T relapse/progression	27 (60%)	8 (42%)	14 (67%)
Unknown	0	3	0
No. of days between CAR-T infusion and day 0 of alloHCT	300 (141 - 753)	196 (63 - 708)	171 (64 - 431)
Unknown	1	0	0
No. of lines of therapy between CAR-T infusion and alloHCT	2 (1 - 6)	1 (0 - 7)	1 (0 - 4)
Lines of therapy between CAR-T and alloHCT			
0	0 (0%)	5 (23%)	4 (19%)
1	21 (47%)	11 (50%)	10 (48%)
2+	24 (53%)	6 (27%)	7 (33%)
Conditioning regimen intensity			
MAC	7 (16%)	4 (18%)	9 (43%)
NMA/RIC	38 (84%)	18 (82%)	12 (57%)
Graft source			
Peripheral blood	37 (82%)	19 (86%)	20 (95%)
Bone marrow	6 (13%)	3 (14%)	1 (4.8%)

Cord	2 (4.4%)	0 (0%)	0 (0%)
Donor type			
MUD	24 (53%)	5 (23%)	5 (24%)
Haploidentical	9 (20%)	11 (50%)	6 (29%)
MRD	9 (20%)	5 (23%)	9 (43%)
MMUD	1 (2.2%)	1 (4.5%)	1 (4.8%)
Cord	2 (4.4%)	0 (0%)	0 (0%)
[1] **n (%); Median (Range)**			

Abbreviations: alloHCT, allogeneic hematopoietic cell transplant; CAR-T, chimeric antigen receptor T-cell; CR, complete response; HCT, hematopoietic cell transplant; MAC, myeloablative conditioning; MRD, matched related donor; MUD, matched unrelated donor; n, number; NMA/RIC, non-myeloablative/reduced intensity conditioning; No., number; PD, progressive disease; PR, partial response; SD, stable disease

Figure S1. Cumulative incidence of neutrophil and platelet recovery

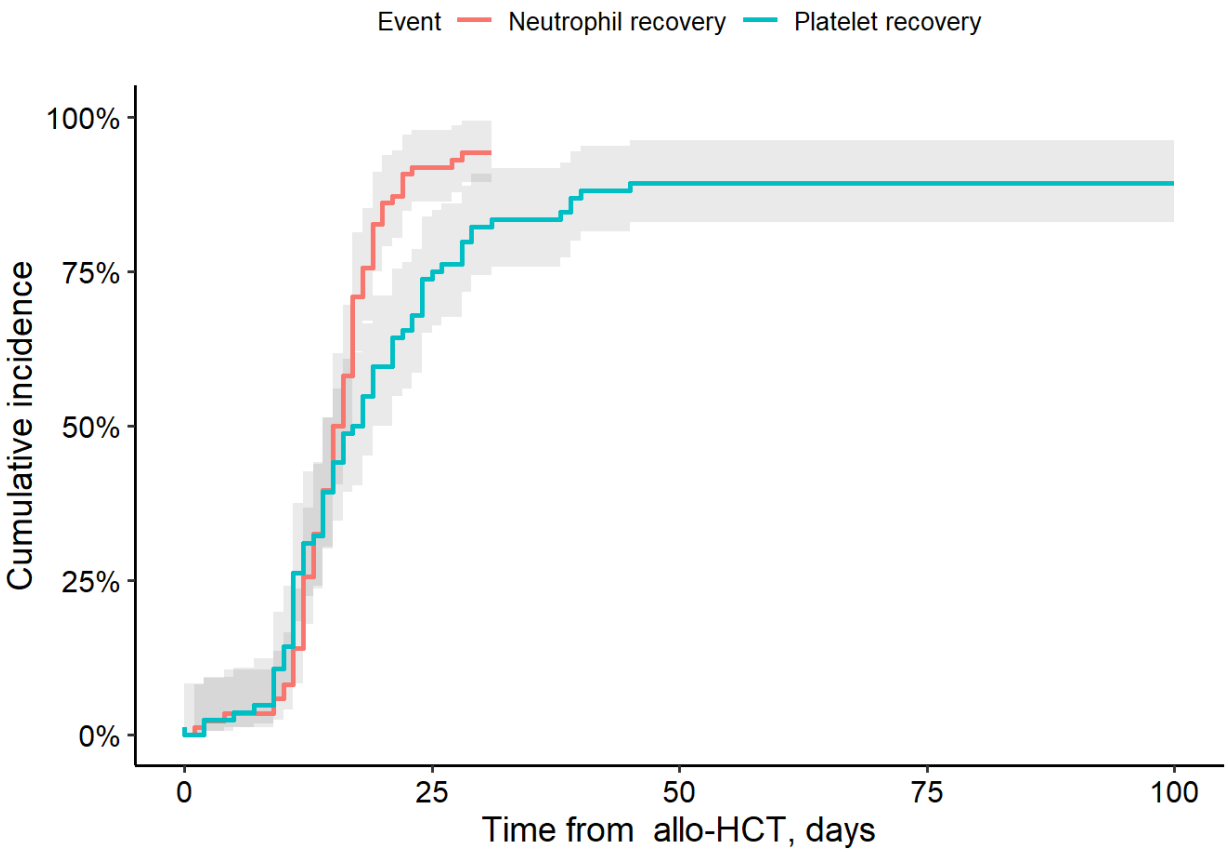
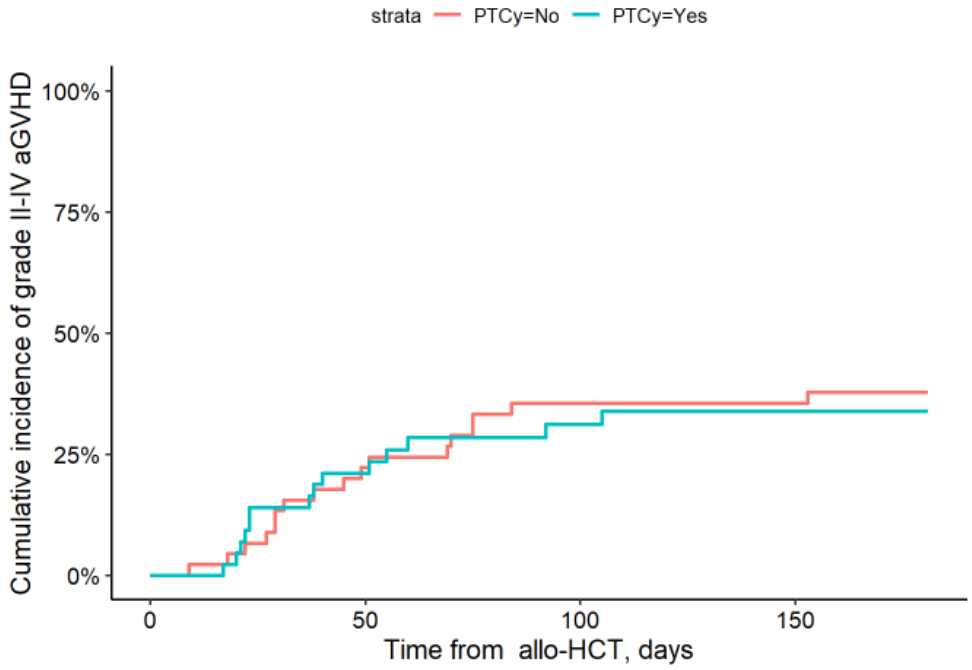


Figure S2. Cumulative incidence of acute and chronic graft-versus-host disease stratified by receipt of post-transplant cyclophosphamide based GVHD prophylaxis

A. Cumulative incidence of grade II-IV acute GVHD for patients who received versus did not receive PTCy-based GVHD prophylaxis



B. Cumulative incidence of chronic GVHD for patients who received versus did not receive PTCy-based GVHD prophylaxis

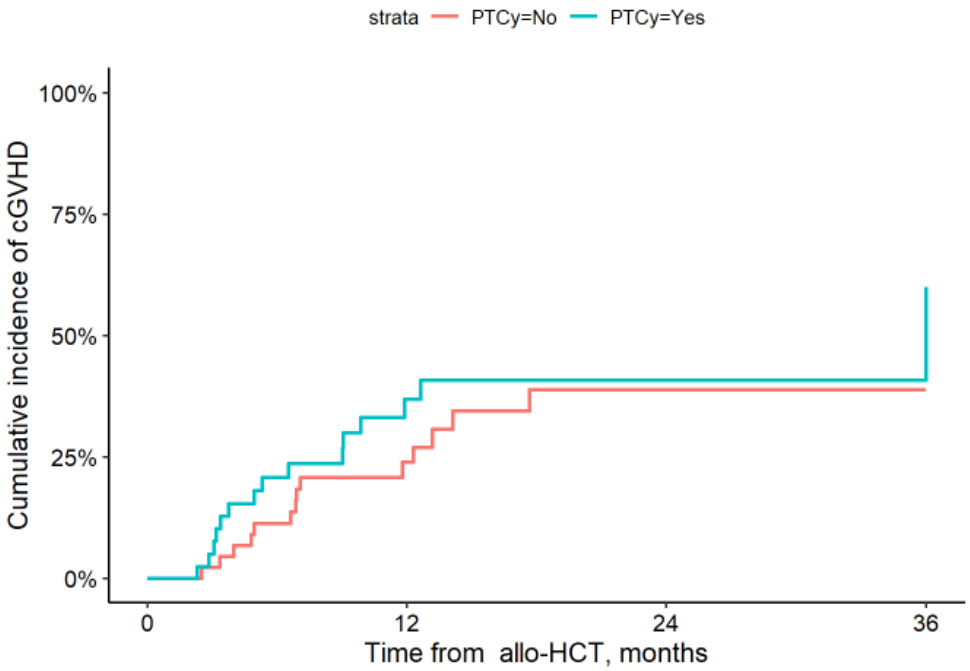
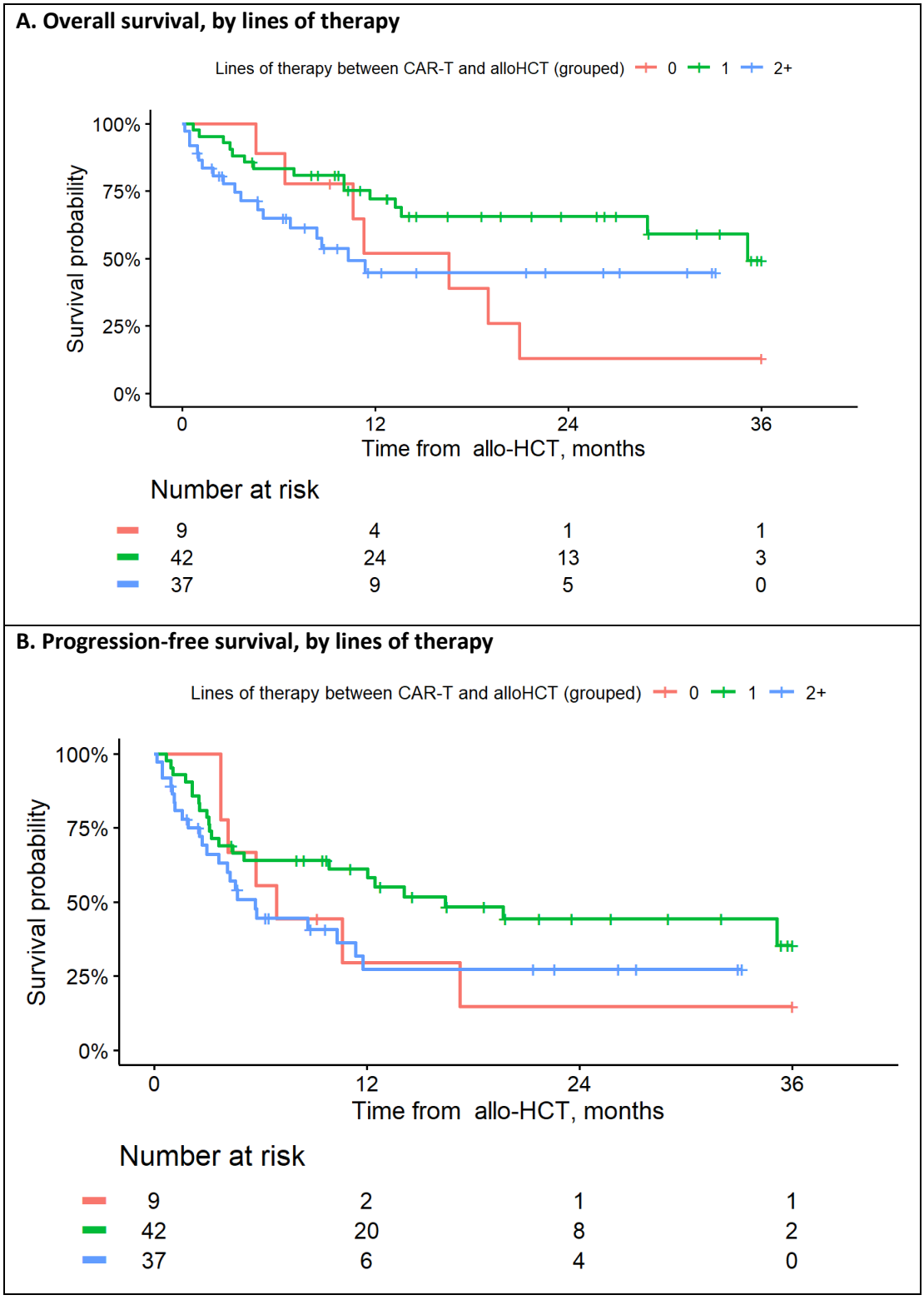
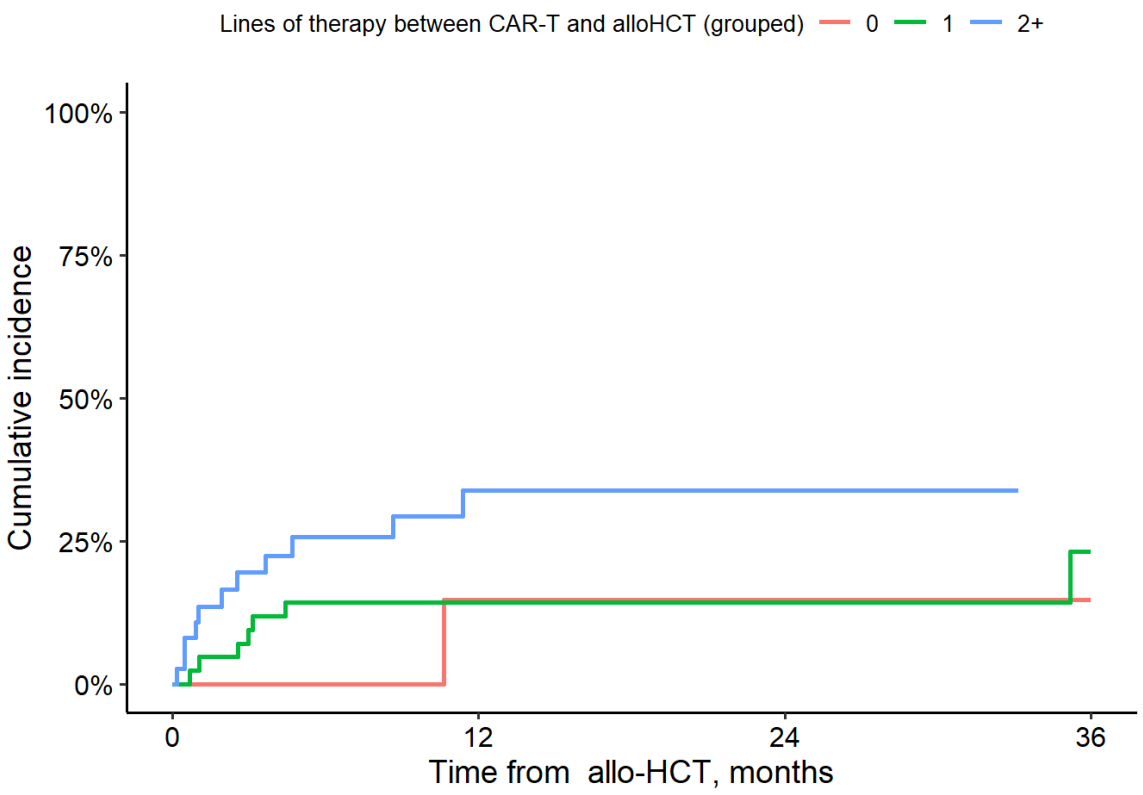


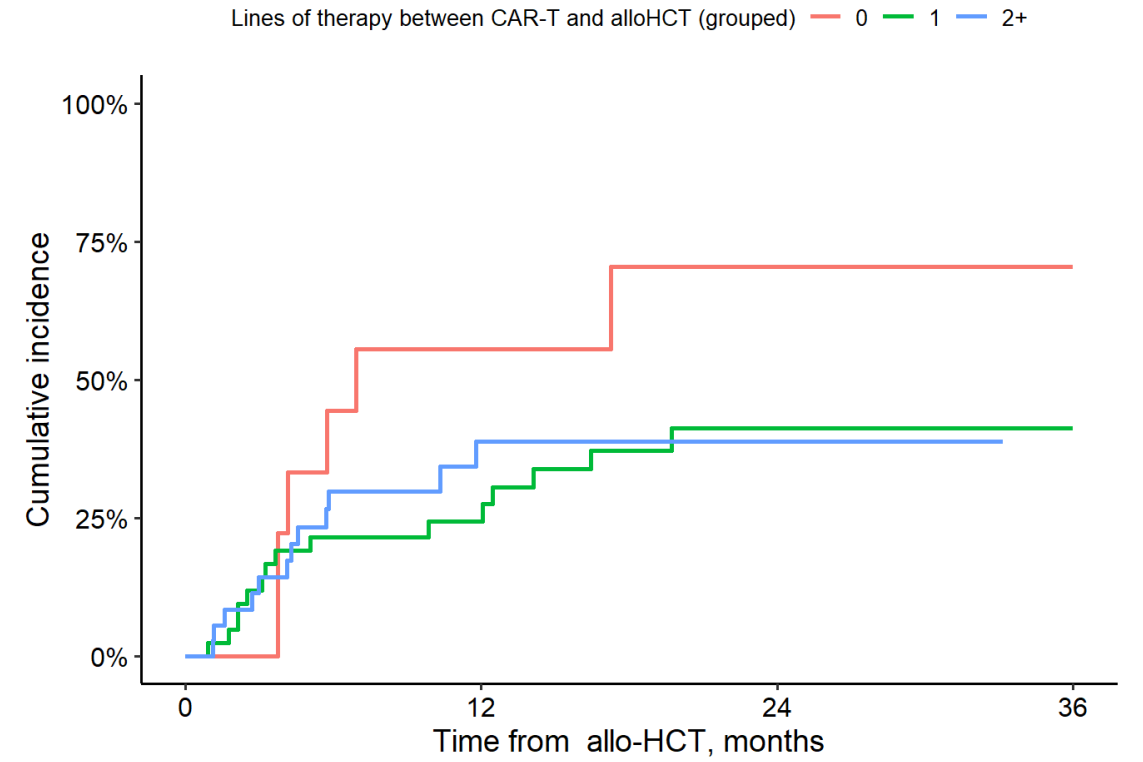
Figure S3. Survival outcomes, non-relapse mortality and progression/relapse and based on lines of therapy between CAR-T and alloHCT



C. Non-relapse mortality, by lines of therapy



D. Progression/relapse, by lines of therapy



E. Graft-versus-host disease relapse-free survival, by lines of therapy

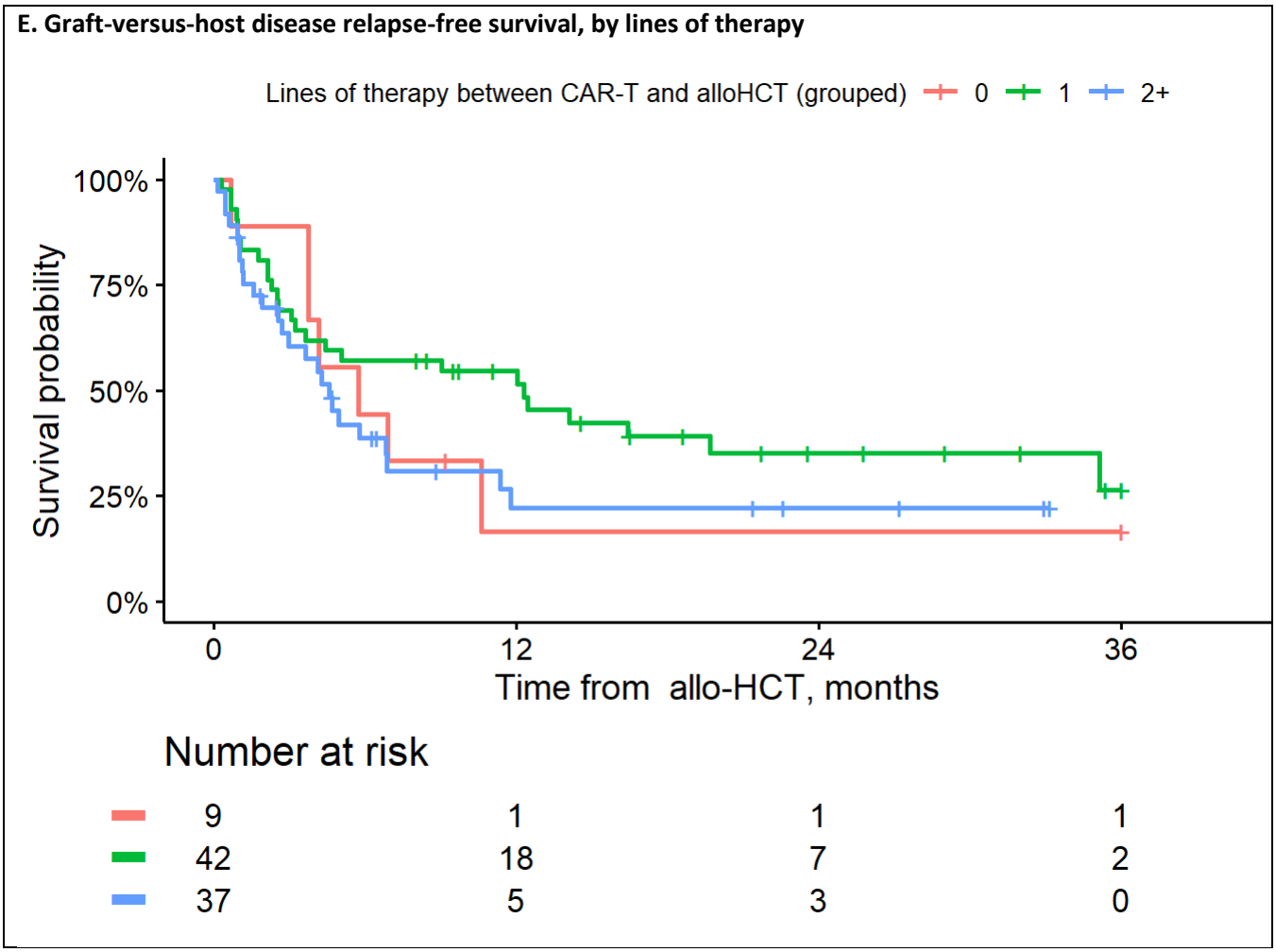


Figure S4. Overall survival by both disease status and number of lines of therapy

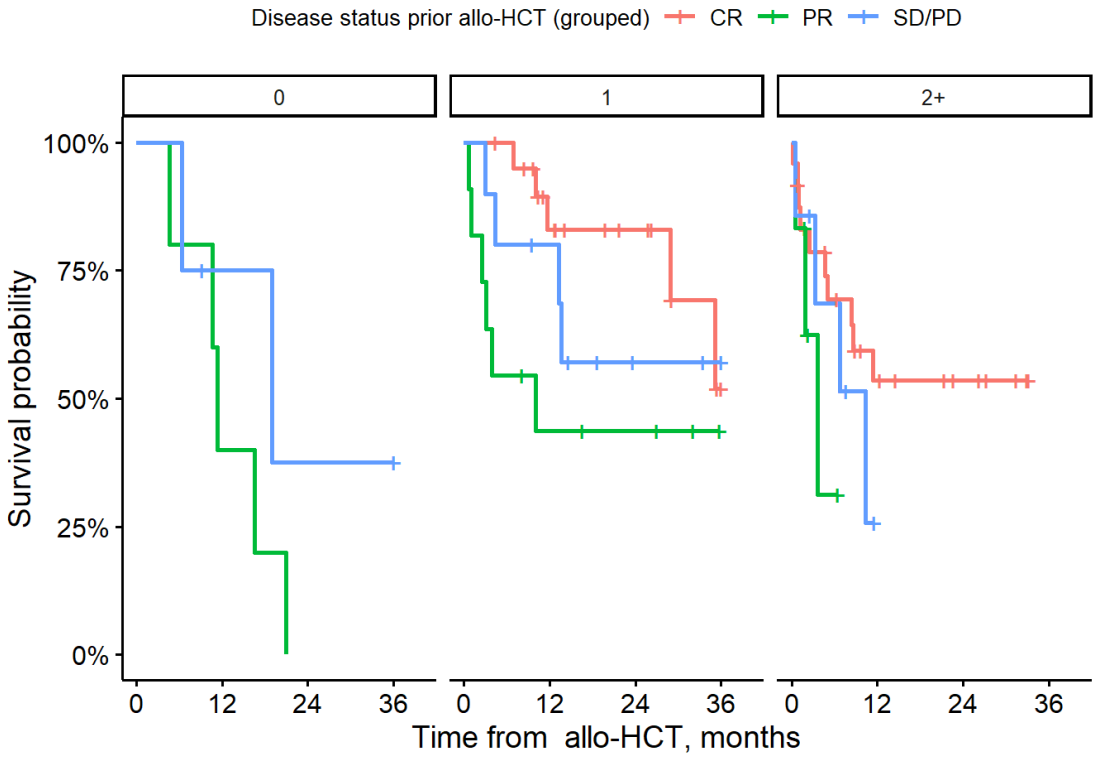


Figure S5. Progression-free survival by both disease status and number of lines of therapy