Supplementary: Outcomes of first-line therapy after CD19-CAR-T failure in large B-cell lymphoma

Contents

Supplementary Tables

Table S1. Definitions

Best response	Best response denotes the best response achieved up to 100 days following CD19-CAR-T cells infusion.
Pre-treatment lactate dehydrogenase (LDH)	Pre-treatment LDH was defined as the highest LDH level in the 15 days preceding first therapy after CAR-T.
Cell of origin	Defined according to Hans algorithm. (Hans et al, Blood 103:275-282, 2004)

Table S2. Flow cytometry panels and methodology

B cell panel up to 10/2020
surface Kappa FITC
surface Lambda PE
CD10 PC5
CD20 PC7
CD38 APC
CD22 APC-A700
CD45 APC-H7
CD19 BV421
CD5 BV510
B cell panel after 10/2020
surface Kappa FITC
surface Lambda PE
CD25 PE-Dazzle 594
CD22 PC5.5
CD19 PC7
CD10 APC
CD45 APC-H7
CD5 BV421
CD38 BV480
CD279 (PD1) BV605
CD20 BV650
CD3 BUV737
CD14 BUV805

Reference ranges were established using CD19 intensity on normal samples. The expression was classified as "dim" if the mean fluorescence intensity (MFI) was < ½ of the mean of the reference range; expression was classified as "negative" if < 20% of the cells showed expression above the negative internal reference (T cells)

Table S3. Grade of CRS and ICANS and responses by CAR-T product

Characteristic	Overall, N = 305[1]	Axicabtagene ciloleucel n = 116[1]	Tisagenlecleucel n = 83[1]	POC-CAR-T n= 78[1]	Lisocabtagene maraleucel, n = 28[1]
Maximum CRS grade					
0	73 (24%)	16 (14%)	28 (34%)	13 (17%)	16 (57%)
1	132 (43%)	43 (37%)	30 (36%)	49 (63%)	10 (36%)
2	69 (23%)	42 (36%)	18 (22%)	8 (10%)	1 (4%)
3	23 (8%)	11 (9%)	6 (7%)	6 (8%)	0 (0%)
4	7 (2%)	4 (3%)	0 (0%)	2 (3%)	1 (4%)
5	1 (0%)	0 (0%)	1 (1%)	0 (0%)	0 (0%)
Maximum ICANS grade					
0	209 (69%)	68 (59%)	67 (81%)	49 (63%)	25 (89%)
1	27 (9%)	10 (9%)	8 (10%)	8 (10%)	1 (4%)
2	14 (5%)	7 (6%)	3 (4%)	4 (5%)	0 (0%)
3	48 (16%)	28 (24%)	5 (6%)	14 (18%)	1 (4%)
4	6 (2%)	3 (3%)	0 (0%)	3 (4%)	0 (0%)
5	1 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
Best response by day 100					
Complete response	147 (48%)	67 (58%)	36 (43%)	30 (38%)	14 (50%)
Partial response	59 (19%)	23 (20%)	11 (13%)	16 (21%)	9 (32%)
Stable /Progressive disease	92 (30%)	25 (22%)	33 (40%)	29 (37%)	5 (18%)
Unevaluable	7 (2%)	1 (1%)	3 (4%)	3 (4%)	0 (0%)

[1] n (%)

Abbreviations: Point-of-Care CD19-CAR-T cell (POC), Cytokine release syndrome (CRS), Immune effector cell-associated neurotoxicity syndrome (ICANS).

Table S4. Comparisons between refractory to CAR-T patients and those who responded to CAR-T and relapsed

Characteristic	Overall, N = 182[1]	CAR-T refractory, n = 92[1]	Post-CAR-T relapse, n = 90[1]	p-value[2]
Age (years) at CAR-T infusion	62 (52 - 70)	61 (52 - 69)	64 (52 - 70)	0.37
LBCL type				0.053
De novo	115 (64%)	65 (71%)	50 (57%)	
Transformed low-grade	65 (36%)	27 (29%)	38 (43%)	
Unknown	2	0	2	
Cell of origin				0.33
Germinal Center B cells	69 (44%)	31 (40%)	38 (48%)	
Non- Germinal Center B cells	89 (56%)	47 (60%)	42 (52%)	
Unknown	24	14	10	
Double/triple hit cytogenetics translocations	20 (15%)	10 (15%)	10 (15%)	>0.99
Unknown	48	25	23	
Number of prior lines of therapy				0.49
2 lines	54 (30%)	31 (34%)	23 (26%)	
3 lines	54 (30%)	28 (30%)	26 (29%)	
4-5 lines	54 (30%)	23 (25%)	31 (34%)	
6+ lines	20 (11%)	10 (11%)	10 (11%)	
Prior autologous transplantation	42 (23%)	19 (21%)	23 (26%)	0.43
Bulky disease at apheresis	29 (16%)	18 (20%)	11 (12%)	0.18
Primary refractory disease up to apheresis	85 (47%)	53 (58%)	32 (36%)	0.003
Patient received bridging	109 (60%)	55 (60%)	54 (60%)	0.98
Pre-CAR-T LDH				0.37
Normal range	67 (38%)	31 (34%)	36 (41%)	
> ULN	111 (62%)	59 (66%)	52 (59%)	
Unknown	4	2	2	
Disease status at the time of CAR-T infusion				0.83
Complete response	3 (2%)	1 (1%)	2 (2%)	

Characteristic	Overall, N = 182[1]	CAR-T refractory, n = 92[1]	Post-CAR-T relapse, n = 90[1]	p-value[2]
Partial response	33 (18%)	16 (18%)	17 (19%)	
Stable /Progressive disease	143 (80%)	73 (81%)	70 (79%)	
Unknown	3	2	1	
Maximal ICANS grade				0.66
0-1	146 (80%)	75 (82%)	71 (79%)	
≥ 2	36 (20%)	17 (18%)	19 (21%)	
Maximal CRS grade				0.93
0-1	132 (73%)	67 (73%)	65 (72%)	
≥ 2	50 (27%)	25 (27%)	25 (28%)	
Median Pre- next line treatment LDH	298 (208 - 456)	325 (221 - 558)	282 (187 - 419)	0.21
Unknown	66	38	28	
Pre- next line treatment LDH				0.57
Normal range	44 (38%)	19 (35%)	25 (40%)	
> ULN	72 (62%)	35 (65%)	37 (60%)	
Unknown	66	38	28	
Disease stage at relapse/progression				0.066
Stage I	29 (18%)	10 (13%)	19 (23%)	
Stages II-IV	135 (82%)	73 (87%)	62 (77%)	
Unknown	18	9	9	
Days from CAR-T to next treatment	83 (53 - 130)	51 (37 - 66)	123 (92 - 236)	<0.001
No subsequent treatment	47	32	15	
PET-avid sites at relapse/ progression				0.017
Previously involved	127 (78%)	58 (70%)	69 (86%)	
New involvement	35 (22%)	24 (30%)	11 (14%)	
Unknown	20	10	10	
CD19 antigen expression by flow at relapse/progression				0.88
Normal	35 (67%)	10 (71%)	25 (66%)	
Diminished (Dim)	14 (27%)	3 (21%)	11 (29%)	
Negative	3 (6%)	1 (7%)	2 (5%)	

Characteristic	Overall, N = 182[1]	CAR-T refractory, n = 92[1]	Post-CAR-T relapse, n = 90[1]	p-value[2]
Unknown	130	78	52	
CD19 Median fluorescence index (MFI)	10,249 (6,972 - 17,504)	11,924 (7,863 - 16,957)	9,638 (6,614 - 17,381)	0.65
Unknown	130	78	52	
CD19 MFI ratio	0.64 (0.42 - 1.10)	0.75 (0.48 - 1.01)	0.60 (0.43 - 1.14)	0.60
Unknown	130	78	52	

[1]Median (IQR); n (%)
[2] Pearson's Chi-squared test; Fisher's exact test; Wilcoxon rank sum exact test; Wilcoxon rank sum test
[3]Double/ triple hit is defined by two or three recurrent chromosome translocations; *MYC*/8q24 loci in combination with the t (14; 18) (q32; q21) bcl-2 gene or/and BCL6/3q27 chromosomal translocation.
Abbreviations: Large B cell lymphoma (LBCL), Lactate dehydrogenase (LDH), Upper Limit of Normal (ULN), Point-of-Care CD19-CAR-T cell (POC), Immune effector cell-associated neurotoxicity syndrome (ICANS), Cytokine release syndrome (CRS), Central Nervous System (CNS) Immunohistochemistry (IHC).

Table S5. Comparison of features by anti-cancer treatment status after CAR-T therapy

Characteristic	Treatment post CAR-T n = 135[1]	No anti-cancer treatment n=47[1]	p-value[2]
Age at CAR-T infusion (y)	60 (49 - 69)	65 (57 - 72)	0.029
Patient sex			0.53
Female	50 (37%)	15 (32%)	
Male	85 (63%)	32 (68%)	
LBCL origin			0.72
De novo	86 (65%)	29 (62%)	
Transformed from low-grade	47 (35%)	18 (38%)	
Unknown	2	0	
Cell of origin			0.26
Germinal Center B cells	55 (46%)	14 (36%)	
non- Germinal Center B cells	64 (54%)	25 (64%)	
Unknown	16	8	
Double/triple hit cytogenetic translocations[3]	16 (16%)	4 (11%)	0.45
Unknown	37	11	
Number of prior lines of therapy (pre-apheresis)			0.34
2 lines	41 (30%)	13 (28%)	
3 lines	36 (27%)	18 (38%)	
4-5 lines	44 (33%)	10 (21%)	
6+ lines	14 (10%)	6 (13%)	
Primary refractory disease (pre-apheresis)	58 (43%)	27 (57%)	0.087
Prior autologous transplantation	36 (27%)	6 (13%)	0.051
Prior allogeneic transplantation	9 (7%)	0 (0%)	0.11
Bulky disease at apheresis	16 (12%)	13 (28%)	0.011
Patient received bridging	76 (56%)	33 (70%)	0.094
Pre-CAR-T LDH			0.079
Normal range	55 (41%)	12 (27%)	
> ULN	78 (59%)	33 (73%)	
Unknown	2	2	
Disease status at the time of CAR-T infusion			0.086
Complete response	1 (1%)	2 (5%)	
Partial response	28 (21%)	5 (11%)	
Stable /Progressive disease	106 (79%)	37 (84%)	
Unknown	0	3	
CAR-T product			0.41

Characteristic	Treatment post CAR-T n = 135[1]	No anti-cancer treatment n=47[1]	p-value[2]
Axicabtagene ciloleucel	42 (31%)	18 (38%)	
Lisocabtagene maraleucel	17 (12%)	2 (4%)	
POC CAR-T	32 (24%)	12 (26%)	
Tisagenlecleucel	44 (33%)	15 (32%)	
Maximal ICANS grade			
0-1	114 (84%)	32 (68%)	
≥ 2	21 (16%)	15 (32%)	
Maximal CRS grade			0.43
0-1	100 (74%)	32 (68%)	
≥ 2	35 (26%)	15 (32%)	
Overall response to CAR-T			0.005
Responder	75 (56%)	15 (32%)	
No responder	60 (44%)	32 (68%)	
Best response to CAR T (day 100)			0.017
Complete response	43 (32%)	10 (21%)	
Partial response	32 (24%)	5 (11%)	
Stable /Progressive disease	60 (44%)	32 (68%)	
Disease stage at relapse or progression			0.034
Stage I	26 (21%)	3 (10%)	
Stages II-IV	99 (79%)	36 (90%)	
Unknown	10	8	
PET-avid sites at relapse or progression			0.12
Previously involved	99 (81%)	28 (70%)	
New involvement	24 (19%)	11 (28%)	
Unknown	12	8	

[1]Median (IQR); n (%)

[2] Pearson's Chi-squared test; Fisher's exact test; Wilcoxon rank sum exact test; Wilcoxon rank sum test

[3]Double/ triple hit is defined by two or three recurrent chromosome translocations; *MYC*/8q24 loci in combination with the t (14; 18) (q32; q21) bcl-2 gene or/and BCL6/3q27 chromosomal translocation.

Abbreviations: Large B cell lymphoma (LBCL), Lactate dehydrogenase (LDH), Upper Limit of Normal (ULN), Point-of-Care CD19-CAR-T cell (POC), Immune effector cell-associated neurotoxicity syndrome (ICANS), Cytokine release syndrome (CRS), Central Nervous System (CNS) Immunohistochemistry (IHC).

Table S6. Post-CAR-T Treatment strategies

Treatment group	Specific treatment strategies
Lenalidomide-based (n=15)	Lenalidomide monotherapy (n=8) Lenalidomide plus Tafasitamab(n=5) Lenalidomide Ibrutinib (n=2)
Standard chemotherapy strategies - anthracycline and platinum-based (n =17)	Etoposide, doxorubicin, vincristine, cyclophosphamide, prednisone (EPOCH +/- dose adjusted) (n= 2) Gemcitabine, oxaloplatin GEMOX (n= 3) Cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) (n= 1) Ifosfamide, carboplatin, and etoposide ICE (n= 3) Ifosphamide, etoposide, epirubicin IVE (n= 3) Mesna, ifosfamide, mitoxantrone, etoposide MINE (n= 2) BCNU, etoposide, ara-c (cytarabine), melphalan (mini-BEAM: not auto-conditioning) (n= 3)
Polatuzumab-based strategies (n=29)	Polatuzumab monotherapy (n= 3) Polatuzumab Bendamustine Pola BR (n= 23) Polatuzumab Bendamustine and ISRT (n= 2) Polatuzumab Bendamustine and Ibrutinib (n= 1)
BTKi-based (n=14)	Ibrutinib monotherapy (n= 3) Ibrutinib Venetoclax (n= 1) Ibrutinib Bendamustine (n= 8) Ibrutinib Selinexor (n= 1) Loxo 305 (n= 1)
Immune checkpoint inhibitors (n=10)	Pembrolizumab (n= 7) Nivolumab (n= 1) Nivolumab + Ibrutinib (n= 1) Tazametostat atezolizumab (n= 1)
ISRT(n=15)	ISRT monotherapy
Investigational/other (n=35)	Investigational (n=23) Selinexor (n=1) High Dose MTX (n=3) High dose Cytarabine(n=1) Allogeneic transplantation (n=3) 2nd CD19 CAR T Therapy: Lisocabtagene Maraleucel (n=3) Single agent Rituximab (n=1)

Table S7. Patient characteristics by post-CAR-T treatment groups

Characteristic	Investigational/other /allogeneic HCT n = 35[1]	Polatuzumab-based n=29[1]	Chemo Based n=17[1]	ISRT Monotherapy n=15[1]	Lenalidomide based n=15[1]	BTKi based n=14[1]	Checkpoint inhibitors n=10[1]
Age at treatment (years)	65 (58 - 72)	57 (45 - 68)	60 (55 - 66)	63 (58 - 70)	69 (56 - 72)	52 (35 - 67)	46 (39 - 62)
≤ 65	17 (49%)	19 (66%)	12 (71%)	9 (60%)	5 (33%)	10 (71%)	8 (80%)
> 65	18 (51%)	10 (34%)	5 (29%)	6 (40%)	10 (67%)	4 (29%)	2 (20%)
LBCL origin							
De novo	18 (53%)	16 (55%)	14 (82%)	10 (67%)	10 (67%)	9 (69%)	9 (90%)
Transformed from low-grade	16 (47%)	13 (45%)	3 (18%)	5 (33%)	5 (33%)	4 (31%)	1 (10%)
Unknown	1	0	0	0	0	1	0
Cell of origin							
Germinal center B cells	14 (41%)	15 (58%)	5 (33%)	9 (69%)	6 (40%)	5 (38%)	1 (33%)
non-Germinal center B cells	20 (59%)	11 (42%)	10 (67%)	4 (31%)	9 (60%)	8 (62%)	2 (67%)
Unknown	1	3	2	2	0	1	7
Double/triple HIT	6 (21%)	4 (19%)	2 (15%)	2 (15%)	1 (8%)	1 (12%)	0 (0%)
Unknown	7	8	4	2	3	6	7
Number of pre-apheresis lines of therapy							
2 lines	7 (20%)	15 (52%)	3 (18%)	4 (27%)	2 (13%)	6 (43%)	4 (40%)
3 lines	11 (31%)	4 (14%)	7 (41%)	5 (33%)	3 (20%)	5 (36%)	1 (10%)
4-5 lines	13 (37%)	7 (24%)	4 (24%)	4 (27%)	9 (60%)	3 (21%)	4 (40%)
6+ lines	4 (11%)	3 (10%)	3 (18%)	2 (13%)	1 (7%)	0 (0%)	1 (10%)
Primary refractory disease (pre-apheresis)	12 (34%)	13 (45%)	10 (59%)	5 (33%)	5 (33%)	7 (50%)	6 (60%)

Characteristic	Investigational/other /allogeneic HCT n = 35[1]	Polatuzumab-based n=29[1]	Chemo Based n=17[1]	ISRT Monotherapy n=15[1]	Lenalidomide based n=15[1]	BTKi based n=14[1]	Checkpoint inhibitors n=10[1]
Prior platinum therapy	30 (86%)	26 (90%)	12 (71%)	13 (87%)	11 (73%)	10 (71%)	9 (90%)
Prior ISRT	7 (20%)	7 (24%)	5 (29%)	3 (20%)	5 (33%)	5 (36%)	1 (10%)
Prior lenalidomide exposure	3 (9%)	0 (0%)	5 (29%)	3 (20%)	2 (13%)	0 (0%)	0 (0%)
Prior checkpoint inhibitors	6 (17%)	1 (3%)	2 (12%)	0 (0%)	0 (0%)	1 (7%)	2 (20%)
Prior BTKi	0	0	0	0	0	0	0
Prior Polatuzumab	4 (11%)	1 (3%)	0 (0%)	1 (7%)	3 (20%)	0 (0%)	1 (10%)
Prior autologous HCT	11 (31%)	6 (21%)	4 (24%)	3 (20%)	3 (20%)	5 (33%)	4 (40%)
Prior allogeneic HCT	2 (6%)	1 (3%)	4 (24%)	1 (7%)	0 (0%)	0 (0%)	1 (10%)
Bulky disease at apheresis	4 (11%)	3 (10%)	4 (24%)	1 (7%)	0 (0%)	2 (14%)	2 (20%)
Bridging treatment	21 (60%)	20 (69%)	8 (47%)	9 (60%)	8 (53%)	6 (43%)	4 (40%)
Pre-CAR-T LDH							
Normal range	15 (43%)	10 (34%)	6 (35%)	7 (47%)	11 (73%)	2 (15%)	4 (44%)
> ULN	20 (57%)	19 (66%)	11 (65%)	8 (53%)	4 (27%)	11 (85%)	5 (56%)
Unknown	0	0	0	0	0	1	1
Disease status at the time of CAR-T infusion							
Complete response	0 (0%)	0 (0%)	1 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Partial response	9 (26%)	5 (17%)	3 (18%)	3 (20%)	3 (20%)	3 (21%)	2 (20%)
Stable /Progressive disease	26 (74%)	24 (83%)	13 (76%)	12 (80%)	12 (80%)	11 (79%)	8 (80%)
CART product							
Axicabtagene ciloleucel	11 (31%)	9 (31%)	2 (12%)	5 (33%)	8 (53%)	2 (14%)	5 (50%)
Lisocabtagene maraleucel	5 (14%)	1 (3%)	2 (12%)	6 (40%)	1 (7%)	1 (7%)	1 (10%)
POC CAR-T	6 (17%)	6 (21%)	9 (53%)	0 (0%)	1 (7%)	6 (43%)	4 (40%)
Tisagenlecleucel	13 (37%)	13 (45%)	4 (24%)	4 (27%)	5 (33%)	5 (36%)	0 (0%)

Characteristic	Investigational/other /allogeneic HCT n = 35[1]	Polatuzumab-based n=29[1]	Chemo Based n=17[1]	ISRT Monotherapy n=15[1]	Lenalidomide based n=15[1]	BTKi based n=14[1]	Checkpoint inhibitors n=10[1]
Maximal ICANS grade							
0-1	28 (80%)	25 (86%)	15 (88%)	13 (87%)	12 (80%)	13 (93%)	8 (80%)
≥ 2	7 (20%)	4 (14%)	2 (12%)	2 (13%)	3 (20%)	1 (7%)	2 (20%)
Maximal CRS grade							
0-1	27 (77%)	21 (72%)	15 (88%)	11 (73%)	7 (47%)	12 (86%)	7 (70%)
≥ 2	8 (23%)	8 (28%)	2 (12%)	4 (27%)	8 (53%)	2 (14%)	3 (30%)
Best response to CAR-T (day 100)							
Complete response (CR)	16 (46%)	10 (34%)	4 (24%)	4 (27%)	6 (40%)	1 (7%)	2 (20%)
Partial response (PR)	10 (29%)	5 (17%)	2 (12%)	5 (33%)	4 (27%)	4 (29%)	2 (20%)
Stable /Progressive disease SD/PD	9 (26%)	14 (48%)	11 (65%)	6 (40%)	5 (33%)	9 (64%)	6 (60%)
Disease stage at relapse/progression							
Stage I	7 (22%)	3 (12%)	2 (12%)	9 (60%)	2 (13%)	1 (9%)	2 (20%)
Stages II-IV	25 (78%)	23 (88%)	15 (88%)	6 (40%)	13 (87%)	10 (91%)	8 (80%)
Unknown	3	3	0	0	0	3	0
PET-avid sites at relapse/ progression							
Previously involved	30 (94%)	17 (71%)	9 (53%)	14 (93%)	13 (87%)	8 (73%)	9 (90%)
New involvement	2 (6%)	7 (29%)	8 (47%)	1 (7%)	2 (13%)	3 (27%)	1 (10%)
Unknown	3	5	0	0	0	3	0
Pre-next-line treatment LDH	306 (234 - 423)	327 (252 - 651)	364 (252 - 702)	250 (164 - 385)	208 (186 - 285)	320 (247 - 421)	270 (205 - 453)
Normal range	11 (33%)	6 (29%)	4 (25%)	6 (60%)	9 (60%)	4 (31%)	4 (50%)
> ULN	22 (67%)	15 (71%)	12 (75%)	4 (40%)	6 (40%)	9 (69%)	4 (50%)
Unknown	2	8	1	5	0	1	2

Characteristic	Investigational/other /allogeneic HCT n = 35[1]	Polatuzumab-based n=29[1]	Chemo Based n=17[1]	ISRT Monotherapy n=15[1]	Lenalidomide based n=15[1]	BTKi based n=14[1]	Checkpoint inhibitors n=10[1]
Days from CAR-T to next treatment	112 (84 - 200)	80 (60 - 111)	45 (27 - 138)	80 (56 - 278)	98 (56 - 194)	47 (34 - 69)	65 (53 - 77)

[1]Median (IQR); n (%)

[2] Double/ triple hit is defined by two or three recurrent chromosome translocations; *MYC*/8q24 loci in combination with the t (14; 18) (q32; q21) bcl-2 gene or/and BCL6/3q27 chromosomal translocation.

Abbreviations: Hematopoetic stem cell transplantation (HCT), Chemotherapy (chemo), Involved site radiation therapy (ISRT), Bruton tirosin Kinasa inhibitors (BTKi), Large B cell lymphoma (LBCL), Lactate dehydrogenase (LDH), Upper Limit of Normal (ULN), Point-of-Care CD19-CAR-T cell (POC), Immune effector cell-associated neurotoxicity syndrome (ICANS), Cytokine release syndrome (CRS), Central Nervous System (CNS) Immunohistochemistry (IH

Table S8. Response rates to first-line treatment post CAR T therapy

Characteristic	Investigational/other /allogeneic HCT n = 35[1]	Polatuzumab-based n=29[1]	Chemo Based n=17[1]	ISRT Monotherapy n=15[1]	Lenalidomide based n=15[1]	BTKi based n=14[1]	Checkpoint inhibitors n=10[1]
CR	5 (14%)	10 (34%)	0 (0%)	4 (27%)	5 (33%)	1 (7%)	2 (20%)
PR	5 (14%)	4 (14%)	7 (41%)	4 (27%)	0 (0%)	5 (36%)	0 (0%)
SD/PD/NE	25 (71%)	15 (52%)	10 (59%)	7 (47%)	10 (67%)	8 (57%)	8 (80%)

[1]n (%)

Abbreviations: Hematopoetic stem cell transplantation (HCT), Chemotherapy (chemo), Involved site radiation therapy (ISRT), Bruton tirosin Kinasa inhibitors (BTKi), Complete response (CR), Partial response (PR), Stable disease (SD), Progressive disease (PD), Response not evaluated (NE)

Table S9. 1-year probability of overall survival by treatment strategies

Treatment strategies	12 months
Checkpoint inhibitors	------ (-----, -----)
BTKi-based	21% (7.9%, 58%)
Chemotherapy based approaches	25% (11%, 59%)
Polatuzumab-based	37% (22%, 63%)
Lenalidomide-based	69% (48%, 100%)

Table S10. Multivariable Cox regression model comparing overall survival between the most frequent treatment groups after CAR-T

Characteristic	n	HR[1]	95% CI[1]	p-value
Age at post-CAR-T treatment (years)	65			
≤ 65		—	—	
>65		2.40	1.15, 5.00	0.019
Overall response to CAR-T	65			
Responder		—	—	
No responder		1.36	0.56, 3.32	0.50
Pre-next line treatment LDH	65			
Normal range		—	—	
> ULN		3.68	1.64, 8.28	0.002
Treatment strategies	65			
Chemotherapy based		—	—	
BTKi-based		0.63	0.26, 1.52	0.30
Lenalidomide-based		0.25	0.07, 0.85	0.027
Polatuzumab-based		0.60	0.26, 1.34	0.21

[1]HR = Hazard Ratio, CI = Confidence Interval

Abbreviations: Lactate dehydrogenase (LDH), Upper Limit of Normal (ULN), Bruton Tyrosine Kinase Inhibitor (BTKi)

Supplementary Figures

Figure 1. Individual patient trajectories following treatment after CD19-CAR-T. Swimmer plot depicting the clinical outcomes of the four most common treatment groups for non-localized disease. Bars are color-coded by best response to the first treatment after CAR-T.

CR – complete response; PR – partial response; SD/PD – stable disease/progressive disease.

1. Hans CP, Weisenburger DD, Greiner TC, et al: Confirmation of the molecular classification of diffuse large B-cell lymphoma by immunohistochemistry using a tissue microarray. Blood 103:275-282, 2004

Supplemental Figure 1