

Supplementary table 1. Clinical outcomes of trials using CAR-T-cell therapy in B-cell malignancy

Centre	Authors	Year	N	Disease (median age/age range)	Cond. Reg.	Gene trans- fer	Target/ scFV	Costim. Domain	Cell dose	Response
B-ALL										
MKSCC [24, 53, 55]	Park et al.	2015	46	Adult ALL (45/ 22-74)	Cy	Gamma Retrovirus	CD19/ SJ25C1	CD28	1-3x10E6/kg	CR: 37/45 (82%) MRD-: 30/36 (83%) OS: 65% (all) and 80% (MRD- CR patients) at 6 mo
FHCRC [46]	Turtle et al.	2016	30	Adult ALL (40/ 20-73)	Cy or Cy/Eto or Flu/Cy	Lentivirus	CD19/ FMC63	4-1BB	2x10E5, 2x10E6 and 2x10E7/kg	CR: 27/29 (93%) MRD-: 25/29 (86%)
Multi-centre (ZUMA-3) [74]	Shah et al.	2017	11	Adult ALL (≥18 eligible)	Flu/Cy	Gamma Retrovirus	CD19/FMC63	CD28	1x10E6/kg	MRD- CR: 6/8 (75%)
CHOP/UPenn [43, 52]	Grupp et al.	2015	53	Paed. ALL (11/ 4-24)	Per discreti- on of treating physician	Lentivirus	CD19/ FMC63	4-1BB	1.07-17.36x10E6	CR: 50/53 (94.3%) MRD-: 45/50 (90%) OS: 78% at 12 mo LFS: 45% at 12 mo CR: 14/20 (70%) MRD-: 12/20 (60%) OS: 52% at 7.8 mo LFS: 79% at 4.8 mo (MRD- only)
NCI [31]	Lee et al.	2015	20	Paed. ALL (13 / 5-27)	Flu/Cy	Gamma Retrovirus	CD19/ FMC63	CD28	1-3x10E6/kg	CR: 40/43 (93%) (MRD- only) OS: 69.5% at 12 mo LFS: 50.8% at 12 mo
SRI [32]	Gardner et al.	2017	45	Paed. ALL (12.2/ 1.3-25.3)	Flu/Cy vs. non-Flu/Cy	Lentivirus	CD19	4-1BB	0.5-10x10E6/kg	
B-NHL and CLL										
NCI [22]	Kochenderfer et al.	2012	8	Adult CLL and B- NHL (55/ 47-63)	Flu/Cy	Gamma Retrovirus	CD19/ FMC63	CD28	0.3-3x1036	ORR: 6/8 (75%) CR: 1/8 (13%) PR: 5/8 (63%)
NCI [75]	Kochenderfer et al.	2015	15	Adult B-NHL (56/ 38-68)	Flu/Cy	Gamma Retrovirus	CD19/ FMC63	CD28	1-5x10E6/kg	CR: 4/7 (57%, refractory DLBCL), 4/6 (67%, Indolent B-NHL)
FHCRC [35]	Turtle et al.	2015	28	Adult B-NHL and CLL B-NHL: (59/ 36- 70) CLL: (60/ 54-64)	Cy or Flu/CY	Lentivirus	CD19/ FMC63	4-1BB	2x10E5, 2x10E6 and 2x10E7/kg	Cy cohort: ORR: 6/12 (50%), CR: 1/12 (8%), PR: 5/12 (42%) Flu/Cy cohort: ORR: 8/12 (67%) CR: 5/12 (42%) PR: 3/12 (25%)
UPenn [76]	Schuster et al.	2015	24	Adult B-NHL (56/ 25-77)	Per discreti- on of treating physician	Lentivirus	CD19/ FMC63	4-1BB	3.08 - 8.87x 10E6/kg	ORR: 15/22 (68%) (DLBCL, 7/13; FL, 7/7, MCL: 1/2)1) PFS: 62% at 11.7 mo
MKSCC [77]	Sauter et al.	2015	8	Adult DLBCL (61.5/ 34-68)	HD-BEAM+ ASCT	Gamma Retrovirus	CD19/ SJ25C1	CD28	5x10E6/kg, 1x107/kg	CR: 5/8 (63%) at 10-18 months PD: 2/8, death due to NRM: 1/8
UPenn [21, 33]	Porter et al	2016	35	Adult CLL (≥18 eligible)	Per discreti- on of treating	Lentivirus	CD19/ FMC63	4-1BB	Stage 1:5x10e7 vs. 5x10e8	Stage 1: High dose:

Centre	Authors	Year	N	Disease (median age/age range)	Cond. Reg.	Gene trans- fer	Target/ scFV	Costim. Domain	Cell dose	Response
					physician				Stage 2: 5x10e8	ORR: 6/11 (55%), CR: 4/11 (36%) Low dose: ORR: 4/13 (31%) CR: 1/13 (8%) Stage 2: ORR: 9/17 (53%), CR: 6/17 (35%) ORR: 5/7 (71%), CR: 4/7 (57%), 3 patients with on- going CR 12mo+
Multi-centre (ZUMA-1) [78]	Locke et al.	2017	7	Adult DLBCL (59/ 29-69)	Flu/Cy	Gamma Retrovirus	CD19/ FMC63	CD28	2x10E6/kg	ORR: 59% CR: 43% PR: 16% ORR: 80% CR: 60%
Multi-Centre (JULIET) [79]	Schuster et al.	2017	141	Adult DLBCL (56/ 24-75)	Flu/Cy or Benda	Lentivirus	CD19 /FMC63	4-IBB	0.1-6x10E8	
Multi-Centre (TRANSCEND NHL 001) [34]	Abramson et al.	2017	28	Adult B-NHL (63/ 37-79)	Flu/Cy	Lentivirus	CD19/ FMC63	4-IBB	5x10E7	
Myeloma PLA [80]	Guo et al.	2016	5	Adult R/R MM (57/ 48-68)	Per discreti- on of treating physician	Lentivirus	CD138/NK-92	4-1BB	0.756x10E6/kg	SD: 4/5 (80%) 12wks-8mo
BCM [47]	Ramos et al.	2016	16	Adult R/R B- NHL, CLL and MM B-NHL+CLL: (69/ 53-75) MM: (57/ 53-69)	Cy	Gamma Retrovirus	K light chain/ CRL-1758	CD28	1.7x10E7-1.9x10E8	B-NHL/CLL: ORR: 4/9 (44%) CR: 2/9 (22%), PR: 1/9 (11%) SD: 1/9 (11%) MM: SD: 4/7 (57%) at 2-17 mo CR: 1/12 (8%, 17 wks VGPR: 2/12 (17%, 8-26+ wks) PR: 1/12 (8%, 2 wks) SD: 8/12 (67%, 2-16 wks) Followup>6 mo: sCR: 6/7 (86%) Followup <6mo: near CR criteria, progressive decrease in M-protein, ex- pected to meet CR criteria later in the follow up ORR: 6/6 (100%) CR: 2/6 (33%)
NCI [81]	Ali et al.	2016	12	Adult R/R MM (≥18 eligible)	Flu/Cy	Gamma Retrovirus	BCMA/ 11D5-3	CD28	0.3-9x10E6/kg	
XJU [37]	Fan et al.	2017	19	Adult R/R MM (not reported)	Not reported	Not re- ported	BCMA/ Non-scFv ba- sed	Not re- ported	0.6-7x10E6/kg	
SCRI [36]	Berdeja et al.	2017	11	Adult R/R MM (≥18 eligible)	Flu/Cy	Lentivirus	BCMA/ not reported	4-1BB	5-12x10E7	
Allogeneic CAR-T-cell DLIs MDACC [48]	Kebriaei et al.	2015	21	R/R adult B-NHL and B-ALL after all HSCT (36/ 21-62)	None	SB Transposon	CD19/ FMC63	CD28	1x10E7-1x10E8/m ²	Allo CAR-T CR: 10/21 (48%) at 5.2 mo
NCI	Brudno et al	2016	20	R/R adult B-cell	none	Gamma	CD19/	CD28	1-10x10E6/kg	Allo CAR-T

Centre	Authors	Year	N	Disease (median age/age range)	Cond. Reg.	Gene trans- fer	Target/ scFV	Costim. Domain	Cell dose	Response
[49]				mal. After allo HSCT (48.5/ 20-68)		Retrovirus	FMC63			ORR: 8/20 (40%) CR: 6/20 (30%) PR: 2/20 (10%) MRD- CR: 4/5 (ALL only)

MKSCC: Memorial Sloan Kettering Cancer Center, New York; FHCRC: Fred Hutchinson Cancer Research Centre, Seattle; SRI: Seattle Children's Research Institute; CHOP: Children's Hospital of Philadelphia; UPenn: University of Pennsylvania, Philadelphia; NCI: National Cancer Institute, Bethesda; PLA: People's Liberation Army General Hospital, Beijing; BCM: Baylor College of Medicine, Houston; MDACC: MD Anderson Cancer Centre, Houston; XJU: Xi'an Jiaotong University, Xi'an. SCRI: Sarah Cannon Research Institute, Nashville.

Supplementary table 2. Adverse events in trials using CAR-T-cell therapy in B-cell malignancy

Centre	Authors	Year	CRS incidence and severity	CRS management	Neurological toxicity	Non-relapse mortality
B-ALL						
MKSCC [24, 53, 55]	Park et al.	2015	11/46 (24%) with sever CRS (requiring vasopressors and mechanical ventilation) No fatalities	Not reported	13/46 (28%) with >= grade 3 neurological toxicity, requiring intubation in 3 patients All reversible (100%)	None reported
FHCRC [46]	Turtle et al.	2016	25/30(83%) with CRS, 7/30 (23%) with severe CRS (requiring ICU care) fatal in 2	CS alone (n=3) or CS+ Toci (n=7)	15/30 (50%) with >= grade 3 neurological toxicity Reversible in 14/15 (93%)	2/30 (7%)
Multi centre (ZUMA-3) [74]	Shah et al.	2017	CRS grade >=3 (in 20%, fatal in 1	Not reported	>= grade 3 neurological toxicity in 40% Reversible in 5/6 (83%)	1/10 (10%)
CHOP/UPenn [43, 52]	Grupp et al.	2015	48/53 (90%) with CRS, requiring respiratory or hemodynamic support in 28% No fatalities	Toci +/- CS (n=9), reversed in all patients	Initial cohort: 13/25 (52%) aphasia,delirium, seizures,hallucination; All reversible (100%)	None reported
NCI [31]	Lee et al.	2015	15/20 (75%) with CRS (NCI grade 3: n=3, grade 4: n=3), 1 patient with cardiac arrest No fatalities	Toci alone (n=2) or Toci+CS (n=2)	4/20 (20%), ≥ grade 3 neurological toxicity in 1/20 (5%) All reversible (100%)	None reported
B-NHL and CLL						
NCI [75]	Kochenderfer et al.	2015	Fever: 12/15, hypotension 4/15 1 death due to cardiac arrythmia, likely not CRS related	Toci (n=2)	6/15 (40%), confusion, aphasia, obtundation All reversible	1 death due to cardiac arrhythmia in patient with pre-existing reduction in LVEF in absence of CRS symptoms, likely unrelated to treatment
FHCRC [35]	Turtle et al.	2015	0/12 with severe CRS (Cy cohort) 2/16 With severe CRS (Flu/Cy cohort) No fatalities	Not reported	Not reported	1/28 (4%) due to refractory pulmonary aspergillus infection
UPenn [76]	Schuster et al.	2015	16/24 (67%) with CRS (UPenn grade 2: n=14, grade 3: n=1, grade 4: n=1) No fatalities	Not reported	3/24 (13%), delirium: n=2, encephalitis: n=1 Reversible in 2/3 (67%)	1/24 (4%)
MKSCC [77]	Sauter et al.	2015	50% with CRS No fatalities	Toci +/- Cs, reversed in all patients	Not reported	1/8 (12.5%) due to Mucormycosis
UPenn [21, 33]	Porter et al.	2016	19/35 (54%) with CRS (UPenn grade 3-4: n=7) No fatalities	Toci (n=4), reversed in all patients	Not reported	None reported
Multi-Centre (ZUMA-1) [78]	Locke et al.	2017	6/7 (86%) with CRS 1/7 (14%) with severe CRS (NCI Grade >=3 Fatal in 1	Toci alone (6/7) or + CS (4/7), 6/7 responded, 1/7 improved initially but later died due to sepsis	4/7 (57%) with >= grade 3 neurotoxicity All reversible (100%)	1/7 (14%) due to sepsis
Multi-Centre (JULIET) [79]	Schuster et al.	2017	57% with CRS 17% with grade 3 (UPenn) 9% with grade 4 (UPenn) No fatalities	Toci in 16%	≥ grade 3 neuological toxicity in 13%	None reported
Multi-Centre (TRANSCEND NHL 001) [34]	Abramson et al.	2017	10/28 (36%) with grade 1-2 CRS, no severe CRS	Toci in 1/10 (10%)	Neurotoxicity in 5/28 (18%), 4/28 (14%) with ≥ grade 3 neurotoxicity All reversible (100%)	None reported

Myeloma

Centre	Authors	Year	CRS incidence and severity	CRS management	Neurological toxicity	Non-relapse mortality
PLA [80]	Guo et al.	2016	Fevers consistent with CRS in 4/5 patients No fatalities	Not reported	Not reported	None reported
BCM [47]	Ramos et al.	2016	None reported	Not reported	None	None reported
NCI [81]	Ali et al.	2016	3/12 with CRS, 1/12 with severe CRS No fatalities	Not reported	Not reported	None reported
XJU [37]	Fan et al.	2017	14/19 (74%) with CRS No fatalities	Not reported	Not reported	None reported
SCRI [36]	Berdeja et al.	2017	Grade 1-2 CRS (NCI) in 8/11 (73%), no higher grade CRS No fatalities	Not reported	No grade ≥ 2 neurotoxicity reported	None reported
Allogeneic CAR-T-cell DLIs						
MDACC [48]	Kebriaei et al.	2015	None reported	Not reported	None	Not reported
NCI [49]	Brudno et al.	2016	Grade ≥ 3 Fevers, tachycardia, hypoten- sion consistent with CRS in 12/20	Not reported	Not reported	Not reported

MKSCC: Memorial Sloan Kettering Cancer Center, New York; FHCRC: Fred Hutchinson Cancer Research Centre, Seattle; SCRI: Seattle Children's Research Institute; CHOP: Children's Hospital of Philadelphia; UPenn: University of Pennsylvania, Philadelphia; NCI: National Cancer Institute, Bethesda; PLA: People's Liberation Army General Hospital, Beijing; BCM: Baylor College of Medicine, Houston; MDACC: MD Anderson Cancer Centre, Houston; XJU: Xi'an Jiaotong University, Xi'an. SCRI: Sarah Cannon Research Institute, Nashville. CS: Corticosteroid; Toci: Tocilizumab.