

SEARCH STRATEGY

Medline search strategy:

(MH "Precursor Cell Lymphoblastic Leukemia-Lymphoma+")

AB "acute lymph* leuk#emia" OR TI "acute lymph* leuk#emia"

AB (("b cell" N2 ("acute lymphoblastic leuk#emia" OR "all"))) OR TI (("b cell" N2 ("acute lymphoblastic leuk#emia" OR "all")))

AB "precursor b-cell lymphoblastic leuk#emia-lymphoma" OR TI "precursor b-cell lymphoblastic leuk#emia-lymphoma"

AB "precursor cell lymphoblastic leuk#emia lymphoma" OR TI "precursor cell lymphoblastic leuk#emia lymphoma"

AB "b-all" OR TI "b-all"

S1 OR S2 OR S3 OR S4 OR S5 OR S6

(MH "Receptors, Antigen, T-Cell+")

AB (("car" OR "chimeric antigen receptor") N3 ("immunotherap*" OR "therap*" OR "t-cell*"))) OR TI (("car" OR "chimeric antigen receptor") N3 ("immunotherap*" OR "therap*" OR "t-cell*")))

AB "car-t" OR TI "car-t"

AB "cart19" OR TI "cart19"

S8 OR S9 OR S10 OR S11

S7 AND S12

Embase search strategy

acute lymphoblastic leukemia'/de

'acute lymph* leuk*mia':ti,ab

('b cell' NEAR/2 ('acute lymphoblastic leuk*mia' OR 'all')):ti,ab

'precursor b-cell lymphoblastic leuk*mia-lymphoma':ti,ab

'precursor cell lymphoblastic leuk*mia-lymphoma':ti,ab

'b-all':ti,ab

'acute lymphoblastic leukemia'/de OR 'acute lymph* leuk*mia':ti,ab OR ('b cell' NEAR/2 ('acute lymphoblastic leuk*mia' OR 'all')):ti,ab OR 'precursor b-cell lymphoblastic leuk*mia-lymphoma':ti,ab OR 'precursor cell lymphoblastic leuk*mia-lymphoma':ti,ab OR 'b-all':ti,ab

chimeric antigen receptor t-cell immunotherapy'/de

((('car' OR 'chimeric antigen receptor') NEAR/3 ('immunotherap*' OR 'therap*' OR 't-cell*'))):ti,ab

'car-t':ti,ab

'cart19':ti,ab

'chimeric antigen receptor t-cell immunotherapy'/de OR ((('car' OR 'chimeric antigen receptor') NEAR/3 ('immunotherap*' OR 'therap*' OR 't-cell*'))):ti,ab OR 'car-t':ti,ab OR 'cart19':ti,ab

('acute lymphoblastic leukemia'/de OR 'acute lymph* leuk*mia':ti,ab OR ('b cell' NEAR/2 ('acute lymphoblastic leuk*mia' OR 'all')):ti,ab OR 'precursor b-cell lymphoblastic leuk*mia-lymphoma':ti,ab OR 'precursor cell lymphoblastic leuk*mia-lymphoma':ti,ab OR 'b-all':ti,ab) AND ('chimeric antigen receptor t-cell immunotherapy'/de OR ((('car' OR 'chimeric antigen receptor') NEAR/3 ('immunotherap*' OR 'therap*' OR 't-cell*'))):ti,ab OR 'car-t':ti,ab OR 'cart19':ti,ab)

Cochrane search strategy

MeSH descriptor: [Precursor Cell Lymphoblastic Leukemia-Lymphoma] explode all trees

("precursor b-cell lymphoblastic leukemia-lymphoma" OR "acute lymphoblastic leukemia" OR "precursor lymphoblastic leukemia-lymphoma" OR "b-all"):ti,ab,kw (Word variations have been searched)

#1 OR #2

MeSH descriptor: [Receptors, Antigen, T-Cell] explode all trees

("chimeric antigen receptor therapy" OR "chimeric antigen receptor immunotherapy" OR "CAR-T" OR "CART19"):ti,ab,kw (Word variations have been searched)

#4 OR #5

#3 AND #6

Table S1: Baseline patient characteristics

FIRST AUTHOR AND YEAR	n	AGE		PRIOR TREATMENTS				DISEASE STATUS PRIOR TO CAR-T				EXTRAMEDULLARY OR CNS DISEASE		Ph+ (n, %)	PMID	
		MEDIAN AGE (RANGE), YEARS	ADULT OR COMBINED	MEDIAN PRIOR LINES OF THERAPY (RANGE)	PRIOR BiTE (n, %)	PRIOR CAR-T (n, %)	PRIOR AlloHSCT (n, %)	MEDIAN RELAPSES (RANGE)	CR OR ≤5% BLASTS (n, %)	MRD NEGATIVE CR (n, %)	RELAPSE OR >5% BLASTS (n, %)	MEDIAN BLAST % (RANGE)	EMD (n, %)			CNS DISEASE (n, %) OR EXCLUDED
DAI, 2020	6	23.5 (17 to 44)	Combined	NA	NA	0	0	2 (1 to 3)	1 (16.7)	0	5 (83.3)	46.9 (3.6 to 89.1)	NA	1 (16.7)	1 (16.7)	32245502
DAI, 2015	9	35 (15 to 65)	Combined	NA	0	0	3 (33.3)	NA	3 (33.3)	0	6 (66.7)	73.4 (<5% to 94.9)	4 (44.4)	2 (22.2)	5 (55.6)	26451310
FREY, 2020	35	34 (21 to 70)	Adult	3 (1 to 7)	11 (31.4)	0	13 (37.1)	NA	2 (5.7)	0	27 (77.1)	NA	NA	Excluded	3 (8.6)	31815579
GU, 2020	20	18 (3 to 52)	Combined	2 (1 to 5)	NA	NA	NA	NA	3 (15)	0	17 (85)	35.5 (3 to 96)	2 (10)	Excluded	2 (10)	32894185
HAY, 2019	53	39 (20 to 76)	Adult	3 (1 to 11)	10 (18.9)	0	23 (43.4)	NA	19 (35.9)	0	34 (64.15)	28 (0-98.5)	18 (34)	5 (9.4)	11 (20.8)	30728140
HUA, 2020	11	28 (12 to 39)	Combined	NA	0	2 (18.2)	11 (100)	2 (1 to 4)	1 (9.1)	0	10 (90.9)	NA	NA	NA	5 (45.5)	32507386
HU, 2017	15	32 (7 to 57)	Combined	NA	0	0	7 (46.7)	2 (1 to 6)	1 (6.7)	1 (6.7)	13 (86.7)	63.50 (3 to 83)	1 (6.7)	Excluded	4 (26.7)	28039267
JIANG, 2019	58	28 (10 to 65)	Combined	3 (1 to 4)	0	0	3 (5.2)	2 (1 to 3)	15 (25.9)	6 (10.3)	37 (63.8)	12.10 (0.01 to 94.9)	NA	NA	7 (12.1)	31321805
LI, 2018	10	33 (18 to 59)	Adult	2 (1 to 3)	0	0	1 (10)	2 (1 to 3)	4 (40)	0	6 (60)	12.75 (0.5 to 58.5)	2 (20)	Excluded	2 (20)	29637550
MA, 2020	9	34.1 (16 to 57)	Combined	NA	NA	0	0	NA	4 (44.4)	0	5 (55.6)	5.20 (1.09 to 63.9)	NA	2 (22.2)	2 (22.2)	32774493
ORTÍZ-MALDONADO, 2020	38	24.5 (3 to 67)	Combined	4 (2 to 10)	9 (23.7)	0	33 (86.8)	NA	NA	0	17 (44.7)	NA	NA	NA	NA	33010231
PARK, 2018	53	44 (23 to 64)	Adult	3 (2 to 4)	13 (24.5)	0	19 (35.9)	NA	15 (28.3)	6 (11.3)	27 (50.9)	63 (5 to 97)	5 (9.4)	NA	16 (30.2)	29385376
SHAH, 2021	55	40 (IQR 28 to 52)	Adult	2 (2 to 3)	25 (45)	0	23 (42)	NA	5 (9)	NA	50 (91)	60 (17 to 90)	6 (11)	0	15 (27.2)	34097852
WANG, BJH, 2020	23	42 (10 to 67)	Combined	2 (2 to 3)	0	0	0	NA	0	0	23 (100)	40.4 (8.2 to 87.5)	0	3 (13.1)	7 (30.4)	32232846
WANG, BLOOD, 2020	51	27 (9 to 62)	Combined	NA	NA	0	9 (17.7)	1 (1 to 3)	13 (25.5)	NA	38 (74.5)	59 (0.5-97.5)	NA	0*	13 (25.5)	31697824
ZHANG, 2020	43	24 (4 to 60)	Combined	NA	NA	0	43 (100)	NA	13 (30.2)	0	30 (69.7)	NA	0	NA	5 (11.6)	33077866

*7 patients with CNS2 disease were excluded, & modified intention to treat dataset

Table S2: CAR-T characteristics

FIRST AUTHOR AND YEAR	n	CAR-T CONSTRUCT (n, %)	T-CELL ORIGIN	ANTIGEN TARGET	CD19 SCFV CLONE	DOSE		LYMPHODEPLETION REGIMEN (n, %)			
						MEDIAN DOSE	RANGE	FLU/CY COMBINATIONS	SINGLE AGENT CY	OTHER	NONE
DAI, 2020	6	41BB	Autologous	Bispecific C19/22	FMC63	2 X 10 ⁶ /kg	1.7 to 3X10 ⁶ /kg	6 (100)	0	0	0
DAI, 2015	9	41BB	Autologous: 7 (77.8) Allogenic: 2 (22.2)	CD19	FMC63	4.5 X 10 ⁶ /kg	3X10 ⁶ to 1X10 ⁷ /kg	0	0	2 (22.2)	7 (77.8)
FREY, 2020	35	41BB	Autologous	CD19	Murine	Total dose: 5 X 10 ⁸	Total dose: 5X10 ⁷ to 5X10 ⁸	5 (14.3)	25 (71.4)	3 (8.6)	2 (5.7)
GU, 2020	20	41BB	Autologous	CD19	HI19α	5 X 10 ⁶ /kg	5X10 ⁶ /kg	20 (100)	0	0	0
HAY, 2019	53	41BB	Autologous	CD19	FMC63	2 X 10 ⁵ /kg	2X10 ⁵ to 2X10 ⁶ /kg	42 (79.2)	9 (17)	2 (3.8)	0
HUA, 2020	11	41BB	Allogenic	CD19	FMC63	5 X 10 ⁶ /kg	1.5 to 10X10 ⁶ /kg	11 (100)	0	0	0
HU, 2017	15	41BB	Autologous	CD19	FMC63	3.7 X 10 ⁶ /kg	1.1 to 9.8 X10 ⁶ /kg	15 (100)	0	0	0
JIANG, 2019	58	41BB	Autologous	CD19	NA	1.66 X 10 ⁶ /kg	0.89 to 4X10 ⁶ /kg	58 (100)	0	0	0
LI, 2018	10	41BB: 5 (50) CD28: 5 (50)	Autologous	CD19	FMC63	0.62 x 10 ⁶ /kg	0.1 to 9.79 x 10 ⁶ /kg	9 (90)	0	0	1 (10)
MA, 2020	9	41BB	Autologous	CD19	Murine	1 x 10 ⁶ /kg	1 x 10 ⁶ /kg	9 (100)	0	0	0
ORTÍZ-MALDONADO, 2020	38	41BB	Autologous	CD19	A3B1 hybridoma	NA	0.4 to 5 x 10 ⁶ /kg	38 (100)	0	0	0
PARK, 2018	53	CD28	Autologous	CD19	Murine	3 X 10 ⁶ /kg	1 to 3 x 10 ⁶ /kg	10 (18.9)	43 (81.1)	0	0
SHAH, 2021	55	CD28	Autologous	CD19	Murine	1 X 10 ⁶ /kg	1 X 10 ⁶ /kg	55 (100)	0	0	0
WANG, BJH, 2020	23	41BB	Autologous	CD19	Humanized	1.0 x 10 ⁶ /kg	1 x 10 ⁶ /kg	0	0	23	0
WANG, BLOOD, 2020	51	Third generation	Autologous	Sequential CD19 followed by CD22	Murine	CAR19: 2.6x 10 ⁶ /kg; CAR22: 2.7x 10 ⁶ /kg	CAR19: 1.1 to 4.1X 10 ⁶ /kg; CAR22: 1.5 to 3.9 x 10 ⁶ /kg	51 (100)	0	0	0
ZHANG, 2020	43	41BB: 25 (58.1) CD28: 18 (41.9)	Allogenic	CD19	NA	1.76 x 10 ⁶ /kg	0.4 to 12 x 10 ⁶ /kg	39 (90.7)	4 (9.3)	0	0

Table S3: Outcomes and toxicities

FIRST AUTHOR, JOURNAL AND YEAR	n	RESPONSE RATE				1-YEAR SURVIVAL (%)		MEDIAN FOLLOW UP months, (range)	ALLO-HSCT POST CAR-T (n, %)	RELAPSE (n, %)			CYTOKINE RELEASE SYNDROME (n, %)		NEUROTOXICITY (n, %)		CRS GRADING CRITERIA	NEURO-TOXICITY GRADING CRITERIA
		CR/CRi		MRD NEGATIVE CR		PFS (95% CI)	OS (95% CI)			TOTAL	CD19 AND/OR CD22+	CD19-	ALL GRADE	≥ GRADE 3	ALL GRADE	≥ GRADE 3		
		n/total	% (95% CI)	n/total	% (95% CI)													
DAI, 2020	6	6/6	100 (54-100)	6/6	100 (54-100)	5 (0 -21)	NA	NA	1 (16.6)	3 (50)	2 (33.3)	1(16.7)	6 (100)	0	0	0	Lee ¹	ASTCT ²
DAI, 2015	9	3/9	33 (7-70)	2/9	22 (3-60)	45 (8-77)	29 (5-59)	NA	0	6 (66.7)	NA	NA	NA	3 (33.3)	2 (22.22)	0	CTCAE ³	CTCAE
FREY, 2020	35	24/35	69 (51-83)	19/19	100 (82-100)	56 (38-70)	69 (53-80)	13 (0.2-52.7)	9 (25.7)	NA	NA	NA	33 (94.3)	22 (62.9)	14 (40)	2 (5.7)	Penn ⁴	CTCAE
GU, 2020	20	18/20	90 (68 -99)	18/20	90 (68-99)	30 (11-52)	56 (35-73)	10 (0.5-24)	14 (70)	8 (40)	5 (25)	3 (15)	19 (95)	9 (45)	13 (65)	8 (40)	Lee	CTCAE
HAY, 2019	53	45/53	85 (72-93)	45/53	85 (72-93)	47 (36-58)	64 (53-73)	30.9	18 (34)	22 (41.5)	14 (26.4)	6 (11.3)	40 (75.5)	10 (18.9)	NA	12 (22.6)	Lee	CTCAE
HUA, 2020	11	8/11	73 (39-94)	7/11	64 (31-89)	57 (23-81)	80 (40-94)	NA	0	1 (9.1)	NA	NA	6 (54.5)	2 (18.2)	0	0	Lee	NA
HU, 2017	15	12/15	80 (52-96)	12/15	80 (52-96)	6 (0-21)	32 (8-60)	4.7 (1- 9.4)	4 (26.7)	6 (40)	2 (13.3)	2 (13.3)	10 (66.7)	6 (40)	5 (33.3)	NA	Lee	CTCAE
JIANG, 2019	58	51/58	88 (77- 95)	47/58	81 (69-90)	48(35-60)	61 (48-72)	7.7 (0.7-33.9)	21 (36.2)	22 (37.9)	12 (20.7)	10 (17.2)	NA	22 (37.9)	NA	NA	Lee	CTCAE
LI, 2018	10	6/10	60 (26-88)	5/10	50 (19-81)	14(1-41)	NA	NA	0	5 (50)	5 (50)	0	8 (80)	0	NA	NA	CTCAE	NA
MA, 2020	9	9/9	100 (66-100)	9/9	100 (66-100)	NA	NA	11.3 (4.1-12.2)	5 (55.6)	2 (22.2)	NA	1 (11.1)	8 (88.9)	2 (22.2)	NA	NA	NA	NA
ORTÍZ-MALDONADO, 2020*	38	23/27	85 (66 -96)	23/27	85 (66-96)	34 (12-57)	64(29-86)	5.5 (1.9 -23.6)	0	15 (39.5)	13 (34.2)	2 (5.3)	21 (55.3)	5 (13.2)	NA	1 (2.6)	Lee	CTCAE
PARK, 2018	53	44/53	83 (70-92)	32/48	67 (52-80)	26 (13-41)	52 (35-67)	29 (1 -65)	17 (32.1)	25 (47.2)	9 (17)	4 (7.5)	45 (84.9)	14 (26.4)	23 (43.4)	22	MSKCC ⁵	CTCAE
SHAH, 2021	55	39/55	71 (57-82)	42/55	76 (63 - 87)	49 (18-74)	71 (56-82)	16.4 (IQR 13.8-19.6)	10 (18)	12 (31)	6 of 9 (66)	3 of 9 (33)	49 (89)	13 (24)	33 (60)	14 (25)	Lee	CTCAE
WANG, BJH, 2020	23	19/23	83 (61-95)	18/23	78 (56-93)	57 (33 – 76)	47 (27-65)	NA	5 (21.8)	7 (30.4)	5 (21.7)	2 (8.7)	23 (100)	5 (21.7)	3 (13)	1 (4.3)	CTCAE	CTCAE
WANG, BLOOD, 2020	51	48/51	94 (84-99)	48/50	96 (86-100)	53 (38-65)	63(48-74)	16.7 (1-33.3)	12 (23.5)	24 (47.1)	23 (45.1)	1 (2)	NA	11 (21.6)	7 (13.7)	1 (2)	Lee	CTCAE
ZHANG, 2020	43	34/43	79 (64-90)	NA		43 (24-61)	43(24-61)	7 (6-47)	NA	25 (58.1)	NA	NA	38 (88.4)	7 (16.3)	9 (20.9)	0	ASTCT	CTCAE

*CR, MRD negative CR, PFS, OS reported for patients >18 years

Table S4: Meta-regression

Variable	OS		PFS		CR		MRD negative remission	
	coefficients	p-value	coefficients	p-value	coefficients	p-value	coefficients	p-value
Age	-0.002 [-0.0292, 0.0253]	0.888	-0.0133 [-0.0502, 0.0235]	0.478	-0.0079 [-0.0181, 0.0023]	0.129	-0.0050 [-0.0123, 0.0023]	0.181
Prior allotransplant	0.0419 [-0.7437, 0.8275]	0.917	-0.2521 [-1.157, 0.6529]	0.585	-0.1350 [-0.4266, 0.1567]	0.364	-0.1245 [-0.2998, 0.0509]	0.164
Median blast percentage prior to transplant	0.6220 [-0.5708, 1.8149]	0.307	0.3615 [-1.3829, 2.1058]	0.685	-0.2851 [-0.7196, 0.1493]	0.198	-0.2370 [-0.5625, 0.0884]	0.154
T-cell construct (% 41BB)	0.1396 [-0.3380, 0.6172]	0.567	0.1881 [-0.4907, 0.867]	0.587	0.0457 [-0.1489, 0.2402]	0.645	-0.0085 [-0.1481, 0.1311]	0.905
T-cell origin (% autologous)	-0.3050 [-0.9541 to 0.3441]	0.357	0.3736 [-0.4694, 1.2166]	0.385	-0.0206 [-0.2556, 0.2143]	0.863	0.0941 [-0.0887, 0.2770]	0.313

Table S5: Summary of log-transformate hazard rate of OS and information sources for individual studies

Study	N	OS			Individual Patient Data	log(Rate) (SE) per month
		P(T>12)	P(T>24)	Median OS (month)		
Ortiz	27	64.5% (40-89)%				-3.309 (0.526)
Wang	51	62.8% (48-74.4)%				-3.250 (0.232)
Zhang	43	43.0% (25-62)%				-2.654 (0.272)
Jiang	58	61.1% (45-70)%				-3.193 (0.206)
Frey	35		47% (28-63)%			-3.459 (0.259)
Park	53			12.9 (8.7-23.4)		-2.924 (0.252)
Gu	20				Data based on KM curve	-3.041 (0.302)
Shah	55	71%[57-82]%				-3.556 (0.266)
Wang BJH	23				Data based on KM curve	-2.776 (0.289)
Dai (2015)	9				Reported Data	-2.258 (0.447)
Hua	11				Reported Data	-3.970 (0.707)
Hu	15				Reported Data	-2.349 (0.408)
Hay	53				Data based on KM curve	-3.290 (0.180)

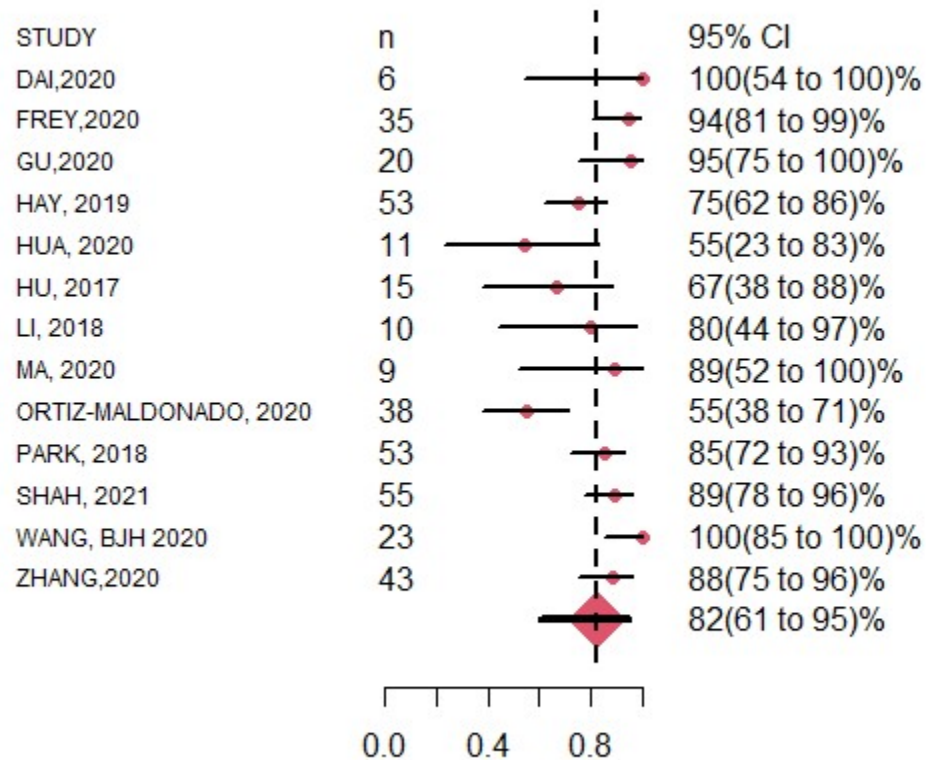
Table S6: Summary of log-transformate hazard rate of PFS and information sources for individual studies

Study	N	PFS			Individual Patient Data	log(Rate) (SE) per month
		P(T>12)	P(T>24)	Median PFS (month)		
Ortiz	27	34.0% (12-57)%				-2.409 (0.339)
Wang	51	52.9% (38.5-65.5)%				-2.936 (0.208)
Zhang	43	43.0% (25-62)%				-2.655 (0.272)
Frey	35		31% (15-49)%			-3.020(0.250)
Park	53			6.10 (5.10-11.5)		-2.175 (0.212)
Gu	20			6.93(3.13-10.73)		-2.302 (0.314)
Dai (2015)	9				Reported Data	-2.708 (0.577)
Dai (2020)	6				Reported Data	-1.357 (0.354)
Hua	11				Reported Data	-3.390 (0.577)
Hu	15				Reported Data	-1.430 (0.316)
Hay	53				Data based on KM curve	-2.772 (0.164)
Jiang	58				Reported Data	-2.793 (0.183)
Li	10				Reported Data	-1.792 (0.408)
Shah	55			11.6 (2.7-15.5)		-2.818 (0.446]
Wang BJH	23				Data based on KM curve	-3.076 (0.354)

Figure S1: Risk of bias summary

Author	Was the hypothesis/ aim/ objective of the study stated?	Was the study conducted prospectively?	Were patients from more than one centre?	Were patients recruited consecutively?	Were the eligibility criteria clearly stated?	Were the characteristics of the patients included in the study described?	Did patients enter the study at a similar point in the disease?	Was the intervention of interest described?	Were additional interventions clearly described?	Were relevant outcome measures established a priori in the introduction or methods section?	Were outcome assessors blinded to the intervention that patients received?	Were the relevant outcomes measured using appropriate objective or subjective methods?	Were the relevant outcome measures made before and after the intervention?	The study does not perform selective outcome reporting?	Were details of the statistical tests reported?	Was follow-up period reported?	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Were the adverse events reported?	Were both competing interests and sources of support for the study reported?
Dai_2015,	?	?	-	?	?	+	+	+	?	+	+	+	+	?	+	+	?	?	+
Dai_2020,	+	+	-	?	+	+	+	+	?	+	+	+	+	+	+	+	?	+	+
Frey,	+	+	-	?	+	+	+	+	?	+	+	+	+	+	+	+	?	+	+
Ou,	+	+	-	?	+	+	+	+	?	+	+	+	+	+	+	+	?	+	+
Hay,	+	+	-	?	+	+	+	+	+	+	+	+	+	+	+	+	?	+	+
Hu,	+	+	-	?	+	+	+	+	?	+	+	+	+	+	+	+	?	?	+
Hua,	+	+	-	?	+	+	+	+	?	+	+	+	+	+	+	+	?	?	+
Jiang,	+	+	-	?	+	+	+	+	+	+	+	+	+	+	+	+	?	?	+
Li,	+	+	-	?	?	+	+	+	?	+	+	?	+	+	+	+	?	?	+
Ma,	+	+	-	?	+	+	+	+	?	+	+	?	+	+	+	+	?	?	+
Ortiz-Maldonado,	+	+	+	?	+	+	+	+	-	+	+	+	+	+	+	+	?	?	+
Park,	+	+	-	?	+	+	+	+	?	+	+	+	+	+	+	+	?	?	+
Shah,	+	+	+	?	+	+	+	+	?	+	+	+	+	+	+	+	?	?	+
Wang_BJH,	+	+	-	?	+	+	+	+	?	+	+	+	+	+	+	+	?	?	+
Wang_Blood,	+	+	-	?	+	+	+	+	?	+	+	+	+	+	+	+	?	?	+
Zhang,	+	+	-	?	?	+	+	+	?	+	+	+	+	+	+	+	?	?	+

Figure S2 : Cytokine Release Syndrome (All Grade): 82% [61-95%]



Cytokine release syndrome (all grade)

Figure S3: Cytokine Release Syndrome (Grade 3 or higher): 27% [18-36%]

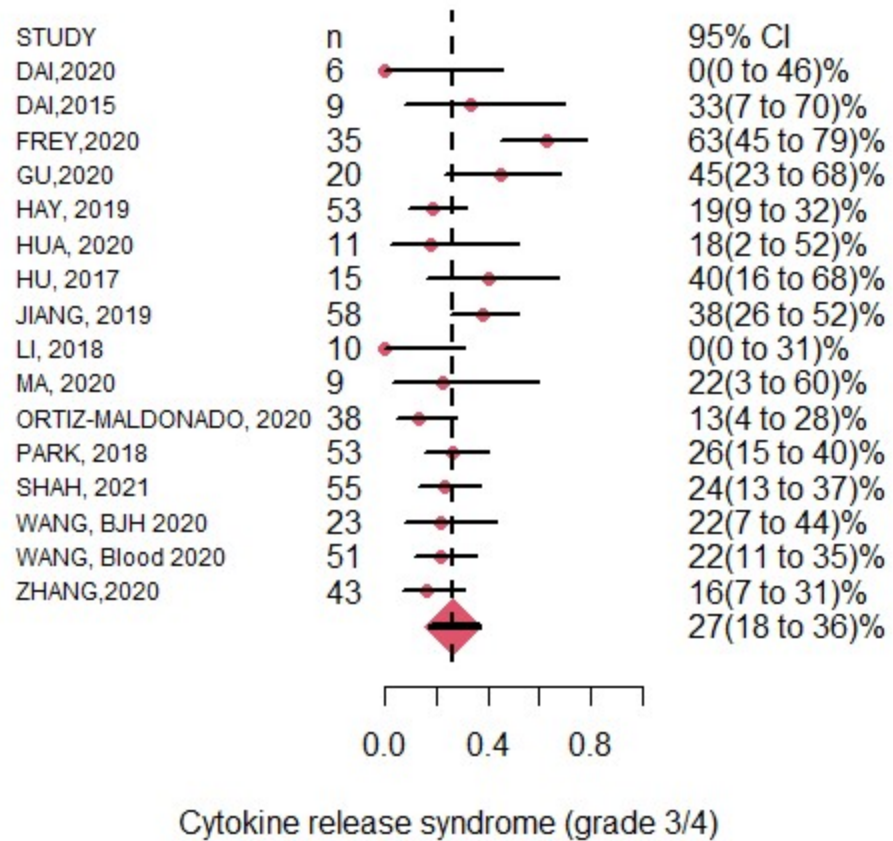


Figure S4: Neurotoxicity (All Grade): 34% [24-47%]

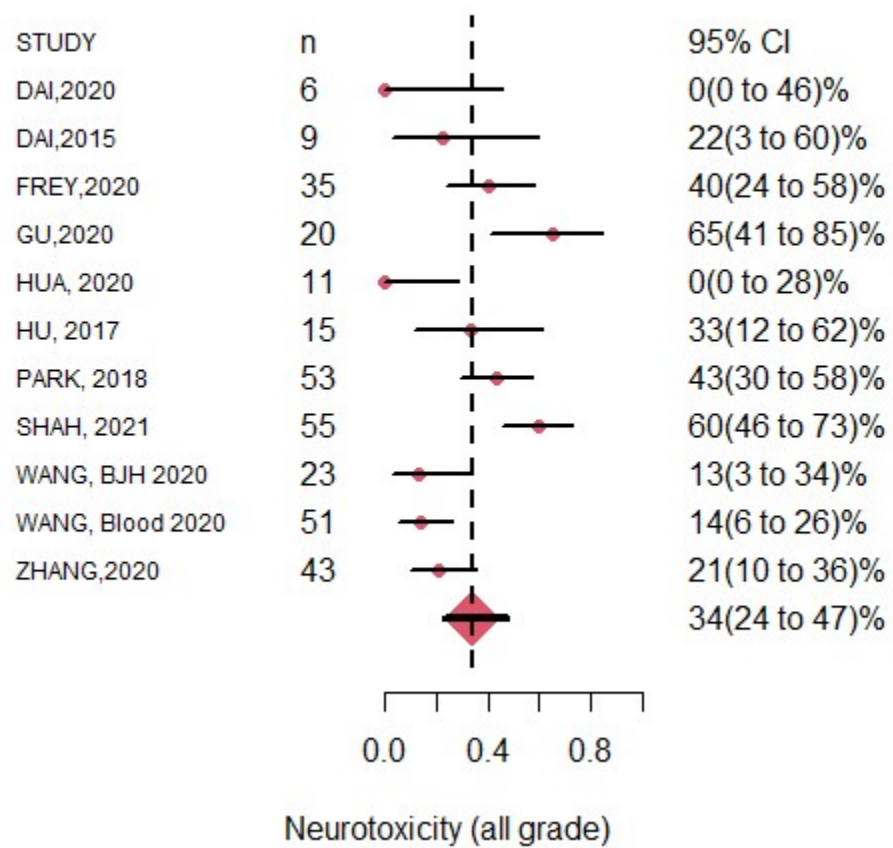


Figure S5: Neurotoxicity Grade 3 or higher: 14% [1-25%]

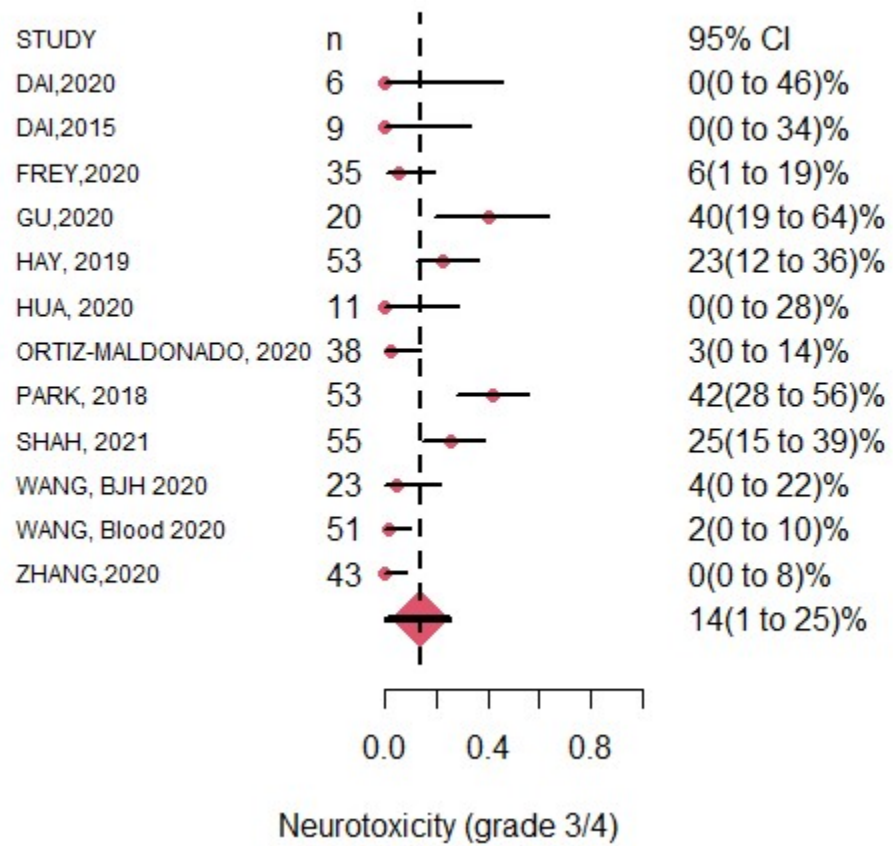


Figure S6: Progression free survival at 12-months for adult-only studies: 39% [18%-60%]

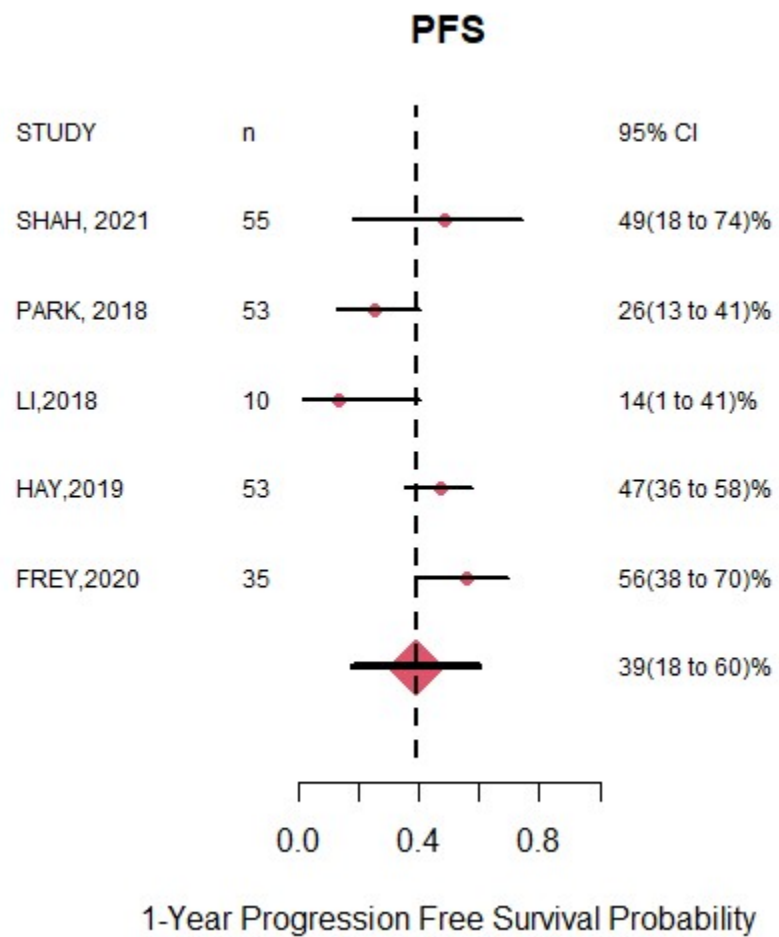
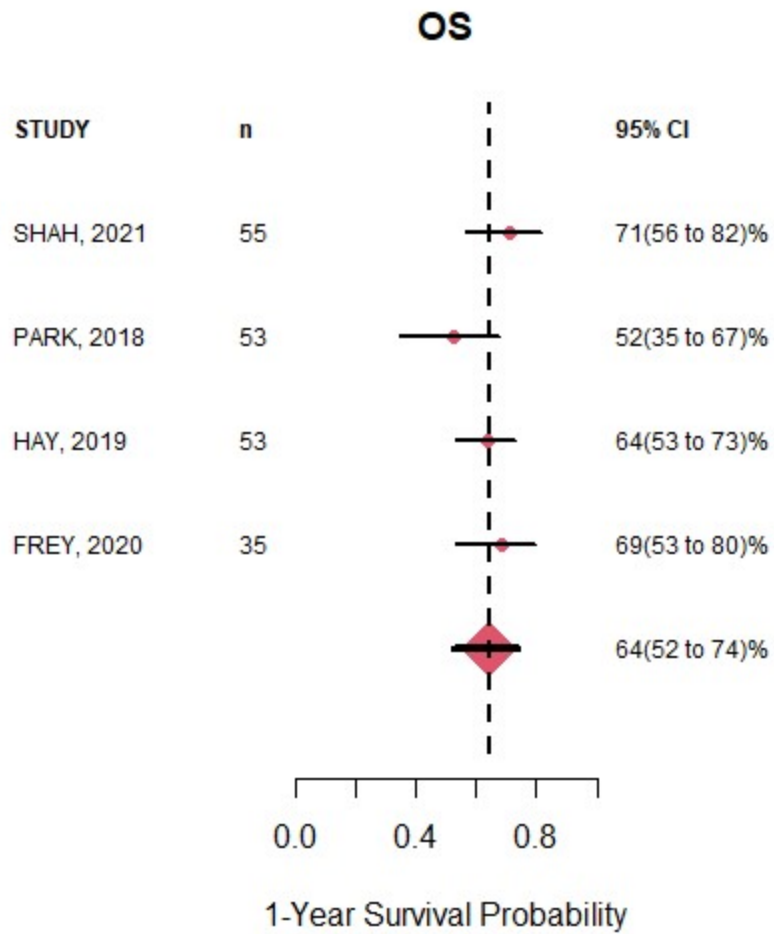


Figure S7: Overall survival at 12 months for adult only studies: 64% [52%-74%]



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