

Immune effector cell-associated hematotoxicity: mechanisms, clinical manifestations, and management strategies

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Table S1. Cytopenia Rates in the Pivotal CAR T-cell Therapy Studies

Study	Disease	Product	Number of patients	CRS grade ≥ 3	Any grade ≥ 3 neutropenia	Any grade ≥ 3 thrombocytopenia	Any grade ≥ 3 anemia	Grade ≥ 3 neutropenia present 1 month	Grade ≥ 3 thrombocytopenia present 1 month
ZUMA-1^{1,2}	LBCL	Axi-cel	108	13%	78%	38%	43%	26%	24%
ZUMA-7^{3,4}	LBCL	Axi-cel	170	6%	69%	15%	30%	13%	4%
ZUMA-12⁵	LBCL	Axi-cel	40	8%	13%	15%	30%	N/A	N/A
JULIET⁶	LBCL	Tisa-cel	11	22	20%	12%	39%	24%	41%
BELINDA⁷	LBCL	Tisa-cel	155	5%	40%	32%	33%	N/A	N/A
TRANSCEND LBCL⁸	LBCL	Liso-cel	269	42%	60%	27%	37%	N/A	N/A
PILOT⁹	LBCL	Liso-cel	61	1%	47%	20%	11%	25%	23%
TRANSFORM¹⁰	LBCL	Liso-cel	90	1%	80%	49%	49%	37%	37%
ZUMA-5¹¹	FL & MZL	Axi-cel	148	7%	33%	9%	25%	N/A	N/A
ELARA Tisa-cel¹²	FL	Tisa-cel	97	49%	32%	9%	13%	N/A	N/A
TRANSCEND FL¹³	FL	Liso-cel	130	1%	58%	10%	10%	15%	15%

ZUMA-2¹⁴	MCL	Brex-cel	68	15%	85%	51%	50%	N/A	N/A
TRANSCEND MCL¹⁵	MCL	Liso-cel	88	1%	56%	25%	38%	24%	32%
ZUMA-3¹⁶	B-ALL	Brex-cel	55	24%	49%	43%	49%	26%	18%
KarMMa-1¹⁷	MM	Ide-cel	128	5%	89%	52%	60%	40%	48%
KarMMa-3¹⁸	MM	Ide-cel	225	5%	76%	42%	51%	N/A	N/A
CARTITUDE- 1¹⁹	MM	Cilta-cel	97	4%	95%	60%	68%	N/A	N/A
CARTITUDE- 4²⁰	MM	Cilta-cel	176	1%	90%	41%	36^	26%	26%

LBCL: Large B-cell Lymphoma, Axi-cel: Axicabtagene Ciloleucel, Tisa-cel: Tisagenlecleucel, Liso-cel: Lisocabtagene Maraleucel, Brex-cel: Brexucabtagene Autoleucel, FL: Follicular Lymphoma, MZL: Marginal Zone Lymphoma, MCL: Mantle Cell Lymphoma, B-ALL: B-cell Acute Lymphoblastic Leukemia, MM: Multiple Myeloma, CRS: Cytokine Release Syndrome, N/A: Not Available

Table S2. Key Studies Analyzing Stem Cell Boost Administration

References	Single /multi center	CAR-T product	Disease	Patient number	Cell source	Number of infused cells/kg (median)	Time from CAR-T to stem cell infusion (median), days	Duration of neutropenia before cell boost, days	Response / engraftment	Median time to response, days (range)	Toxicity
Gagelmann et al²¹	Multi	Axi-cel: 20 Tisa-cel: 7 allo CAR-T cells: 3 Brex-cel: 1	LBCL B-ALL MCL	31	Auto: 30 Allo: 1	3.6×10^6 (1.1-11.5)	43	38 (7-151)	Neut: 26/31 (84%)	9 (7-14)	No
Mullanfiroze et al²²	Single	CAR-T cells investigational: 6 Tisa-cel: 1	B-ALL	7	Allo	6.75×10^6 (2.5-11.2)	79 (57-502)	Not reported	Neut: 4/5 evaluable	Neut: 42 (11-192) Plt: 33 (7-73)	No aGVHD or cGVHD Grade 2 CRS 10 days after SCB
Rejeski et al²³	Multi	Axi-cel: 9 Tisa-cel: 2 Brex-cel: 1	LBCL B-ALL MCL	12	Auto: 9 Allo: 3	3.1×10^6 (1.7-7.5)	69 (35-617)	42	Neut: 11/11 (100%) Plt: 7/9 (78%)	Neut: 15 (6-124) Plt: 21 (12-34)	No GVHD
Davis et al²⁴	Multi	BCMA directed CAR-T	RRMM	19	Auto	2.75×10^6 (1.76-7.38)	53 (24-126)	Not reported	18/19 (95%) patients successfully recovered hematopoiesis	Neut: 14 (9-39) Plt: 17 (12-39) Hgb: 23 (6-34)	No infusion reactions
Mohan et al²⁵	Multi	BCMA directed CAR-T (ide-cel) or (cilta-cel) or investigational	RRMM	16	Auto	3.84×10^6 (1.05–9.04)	116 (29–270)	Not reported	Neut: 16/16 (100%)	Not reported	No side effects reported

Axi-cel: Axicabtagene Ciloleucel, Tisa-cel: Tisagenlecleucel, Liso-cel: Lisocabtagene Maraleucel, Brex-cel: Brexucabtagene Autoleucel, BCMA: B-cell Maturation Antigen, Ide-cel: Idecabtagene Vicleucel, Cilta-cel: Ciltacabtagene Autoleucel, LBCL: Large B-cell Lymphoma, B-ALL: B-cell Acute Lymphoblastic Leukemia, MCL: Mantle Cell Lymphoma, RRMM: Relapse/Refractory Multiple Myeloma, Auto: Autologous, Allo: Allogeneic, aGVHD: Acute Graft-Versus-Host Disease, cGVHD: Chronic Graft-Versus-Host Disease, CRS: Cytokine Release Syndrome, SCB: Stem Cell Boost, Neut: Neutrophils, Plt: Platelet, Hgb: Hemoglobin

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