Resources

MM Treatment: Key AEs, Considerations

Drug Class	Name	Key Potential AEs	Nursing Considerations
Proteasome inhibitors	Bortezomib	PN, T, M, F	IV, SC; monitor platelets; safe in renal failure; reduce dose for hepatic disease
	Carfilzomib	C, M, F, DVT, PN	Hydration, cardio/pulmonary; reduce dose for hepatic disease
	Ixazomib	PN, T, GI, R	Reduce dose for hepatic/renal disease
Immunomodulatory agents	Lenalidomide	DVT, M, BD, R, D, rash	ASA if low risk and DOACs and warfarin if high risk for clots; weekly CBC x 8 wks
	Thalidomide	DVT, M, BD, PN, drowsiness	As above
	Pomalidomide	DVT, M, BD, F	As above
Monoclonal antibodies	Daratumumab	IR, M, RD	Infusion reaction risk; pre/post med as directed; interrupt infusion if reaction
	Elotuzumab	IR, M, RD	As above
	Isatuximab	IR, M, RD	As above
	Daratumumab Hyaluronidase	ARR,M, RD	SQ administration over 5 minutes

AE, adverse event; ARR, administration related reaction ; ASA, acetylsalicylic acid; BD, birth defects; C, cardiac; D, diarrhea; DOAC, direct oral anticoagulant; DVT, deep vein thrombosis; F, fatigue; GI, gastrointestinal toxicities; IR, infusion reaction; IV, intravenous; LMWH, low molecular weight heparin; M, myelosuppression; MM, multiple myeloma; N, nausea; PN, peripheral neuropathy; R, renal dose adjustment necessary; RD, response disruption; SQ, subcutaneous; T, thrombocytopenia

US Food and Drug Administration. FDA approved drug products.

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Alkylating agents	Melphalan	M, N, D	CBC diff monthly; renal dose adjustment
	Cyclophosphamide	M, N, D	Monitor CBC platelets and differential, antiemetics
Corticosteroids	Prednisone	H, MS	Monitor blood sugar, insomnia, weight gain
	Dexamethasone	H, MS	As above
Selective inhibitors of nuclear export (SINE)	Selinexor	D, N, T, F	Monitor Na+ and intake Prophylactic use of antiemetics

CBC, complete blood count; D, diarrhea; F, fatigue; H, hyperglycemia; M, myelosuppression; MM, multiple myeloma; MS, metabolic syndrome; N, nausea; T, thrombocytopenia

US Food and Drug Administration. FDA approved drug products.

Options to Consider Regarding 4+ Prior Lines*

	Type of Immunotherapy	Availability/Logistics	Adverse Events
Ide-cel[1]	CAR--T (BCMA)	• Cellular therapy center • Manufacturing slot • Manufacturing time • One-time therapy • REMS and CRS/ICANS management	• CRS/NT (potentially severe) • Infections • Cytopenias (potentially severe)
Cilta-cel[2,3]	CAR-T (BCMA)		
Teclistamab[4,5]	Bispecific (BCMA)	• REMS and CRS/ICANS management • Readily available • Continuous therapy (SQ)	• CRS/NT (unlikely severe) • Infection risk (perhaps higher) • Cytopenias (unlikely severe)
Talquetamab[6] -	Bispecific (GPRC5D)		• CRS/NT • Skin-related events (rash) • Nail-related events • Dysgeusia • Weight loss
Elranatamab[7]	Bispecific (BCMA)		• CRS/NT • Infection risk • Cytopenias

*Ide-cel was recently approved for patients after one or more lines of therapy and cilta-cel after 2 or more lines of therapy.
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; GPRC5D, G protein–coupled receptor class C group 5 member D; ICANS, immune cell-associated neurotoxicity syndrome; NT, neurotoxicity; REMS, Risk Evaluation and Mitigation Strategy; SQ, subcutaneous

1. Munshi NC, et al. *N Engl J Med*. 2021;384:705-716; 2. Berdeja J, et al. *Lancet*. 2021;398:314-324; 3. Lin Y, et al. ASCO 2023, abstract 8009; 4. Moreau P, et al. *N Engl J Med*. 2022;387:495-505; 5. van de Donk N, et al. ASCO 2023, abstract 8011; 6. Chari A, et al. *N Engl J Med*. 2022;387(22):2232-2244; 7. Lesokhin AM, et al. *Nat Med. 2023;*29:2259–2267.

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Drug Class	Name	Key Potential AEs	Nursing Considerations
CAR T	Ide Cel Cilta Cel	C, N, M, I	• REMS • CRS and neurotoxicity • Hospitalize for close monitoring, near facility for one month • Monitor for cytopenias and infections • IVIG may be needed
Bispecifics	Teclistamab Talquetamab Elranatamab	C, N, I	• REMS • CRS and neurotoxicity • Monitor in hospital recommended • Monitor for cytopenias and infection on going • IVIG may be needed • Skin and nail and taste changes (talquetamab)

C, cardiac; I, immune-related AEs; M, myelosuppression; N, neurotoxicity

CRS Grading: ASTCT Grading Scale[1]

CRS parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever	Temp ≥38°C	Temp ≥38°C	Temp ≥38°C	Temp ≥38°C
		With		
Hypotension	None	Not requiring vasopressors	Requiring vasopressor with or without vasopressin	Requiring multiple vasopressors
		And/Or		
Hypoxia	None	Requiring low-flow nasal cannula or blow-by	Requiring high-flow cannula, face mask, nonrebreather mask or Venturi mask	Requiring positive pressure (eg, CPAP, BiPAP, intubation, and mechanical ventilation)

ASTCT, American Society for Transplantation and Cellular Therapy; BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure

1. Lee DW, et al. *Biol Blood Marrow Transplant.* 2019;25:625-638.

Management of CRS[1,2]

ASTCT CRS Grade	Management
Grade 1	• Antipyretics and IV hydration • Diagnostic work-up to rule out infection • Antibiotics if neutropenic
Grade 2	• Supportive care as in grade 1 • IV fluid boluses and/or supplemental oxygen • Tocilizumab +/- dexamethasone or its equivalent of methylprednisolone
Grade 3	• Supportive care as in grade 1 • Consider monitoring in ICU • Vasopressor support and/or supplemental oxygen • Tocilizumab + dexamethasone 10 mg to 20 mg IV every 6 hours or its equivalent of methylprednisolone
Grade 4	• Supportive care as in grade 1 • Monitoring in ICU • Vasopressor support and/or supplemental oxygen via positive pressure ventilation • Tocilizumab + methylprednisolone 1,000 mg/day • Refractory CRS: anakinra, siltuximab, dasatinib, ruxolitinib, etanercept

ICU, intensive care unit; IV, intravenous

1. Neelapu SS, et al. *Nat Rev Clin Oncol.* 2018;15:47-62; 2. Neelapu SS. *Hematol Oncol*. 2019;37:48-52.

Treatment of CRS: Tocilizumab

Description	Humanized anti-IL-6 receptor $IgG1_K$ monoclonal antibody
Mechanism of action	Inhibits IL-6 mediated signaling by binding to both soluble and membrane-bound human IL-6 receptors
FDA Expanded Approval 8/30/17	For the treatment of CAR T cell-induced severe or life-threatening CRS in patients 2 years of age and older
Dose	• Adults: 8 mg/kg once (max dose of 800 mg) • As frequent as every 8 hours, max of 4 doses total
Administration	Intravenous over 1 hour
Required doses	Ensure that 2 doses of tocilizumab are available prior to infusion of CAR T cells
Monitor	• For 7 days at the certified healthcare facility following infusion for signs and symptoms of CRS • Monitor patients for signs or symptoms of CRS for 4 weeks after infusion and seek immediate medicate attention

CAR, chimeric antigen receptor

Neelapu SS, et al. *Nat Rev Clin Oncol.* 2018;15:47-62. Neelapu SS, et al. *Nat Rev Clin Oncol*. 2018;15:218.

ICANS Assessment: What is Your ICE Score?

Orientation	Orientation to year, month, city, hospital: 4 points
Following commands	Ability to follow simple commands: 1 point
Naming	Ability to name 3 objects: 3 points
Writing	Ability to write a standard sentence: 1 point
Attention	Ability to count backwards from 100 by 10: 1 point

Grade 1: 7-9 points; Grade 2: 3-6; Grade 3: 0-2; Grade 4: unarousable, unable to complete assessment [1]

ICE, immune effector cell-associated encephalopathy

1. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-638.

ICANS Assessment[1]

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score	7-9	3-6	0-2	0 (unable to perform)
Depressed level of consciousness	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Unarousable, requires vigorous or repetitive stimuli to arouse. Stupor or coma.
Seizure	N/A	N/A	Any clinical seizure that resolves rapidly or nonconvulsive seizures on EEG that resolve without intervention	Life-threatening prolonged seizure; or repetitive clinical or electrical seizures without return to baseline in between
Motor findings	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
Elevated intracranial pressure/cerebral edema	N/A	N/A	Focal/local edema on neuroimaging	Diffuse cerebral edema on neuroimaging, papilledema

EEG, electroencephalogram

1. Lee DW, et al. *Biol Blood Marrow Transplant.* 2019;25:625-38.

ICANS Management

ASTCT ICANS Grade	Management
Grade 1	• Aspiration precautions and IV hydration • Seizure prophylaxis and levetiracetam • EEG • Image of brain • Consider tocilizumab
Grade 2	• Supportive care as in grade 1 • Consider dexamethasone or its equivalent of methylprednisolone
Grade 3	• Supportive care as in grade 1 • Dexamethasone 10 mg to 20 mg IV every 6 h or its equivalent of methylprednisolone • Control seizures with benzodiazepines (for short-term control) and levetiracetam +/- phenobarbital and/or lacosamide • High-dose methylprednisolone 1000 mg/day for focal/local edema
Grade 4	• Supportive care as in grade 1 • High-dose methylprednisolone 1000 mg/day • Control seizures with benzodiazepines (for short-term control) and levetiracetam +/- phenobarbital and/or lacosamide • Imaging of spine for focal motor weakness • For diffuse cerebral edema, lower ICP by hyperventilation, hyperosmolar therapy with mannitol/hypertonic saline, and/or neurosurgery consultation for ventriculoperitoneal shunt

ICP, intracranial pressure

Neelapu SS, et al. *Nat Rev Clin Oncol.* 2018;15:47-62. Neelapu SS. *Hematol Oncol*. 2019;37:48-52.

Medications Can Reduce Infection Risk

Type of Infection Risk	Medication Recommendation(s) for Healthcare Team Consideration[1]
Viral: HSV/VZV	Acyclovir prophylaxis
Bacterial: blood, pneumonia, and urinary tract infection	Consider prophylaxis with levofloxacin
PJP (P. jirovecii pneumonia)	Consider prophylaxis with trimethoprim-sulfamethoxazole
Fungal infections	Consider prophylaxis with fluconazole
COVID-19 and Influenza	Antiviral therapy if exposed or positive for covid per institution recommendations
IgG < 400 mg/dL (general infection risk)	Consider IVIg
ANC < 1000 cells/µL (general infection risk)	Consider GCSF 2 or 3 times/wk (or as frequently as needed) to maintain ANC > 1000 cells/µL and maintain treatment dose intensity

Some people receiving BCMA-targeting therapies have experienced infections that are less common like CMV, PJP, EBV and fungal infections

ANC, absolute neutrophil count; CMV, cytomegalovirus; EBV, Epstein-Barr virus; GCSF, granulocyte colony-stimulating factor; HSV, herpes simplex virus; VZV, varicella zoster virus.

1. Raje NS, et al. *Lancet Haematol*.2022;9(2):143–161.

Comparison of Immunotherapy Approaches

	MoABs	CARs	BiTEs
Off-the-shelf	YES	No	Yes
Ease of administration	+++	+	+ to ++
Repeated dosing required	Yes	No	Yes
Dependent on patient T cell “fitness”	No	Yes	Yes
Adverse events	IRR	CRS, neuro	CRS, neuro
Adverse event duration	NA	~14-21 days	Ongoing
Durable clinical activity seen	Yes	Yes	Yes
Requires LD chemotherapy	N0	Yes	No

LD, lymphodepleting; IRR, infusion-related reaction; MoAB, monoclonal antibody

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