Society for Immunotherapy of Cancer

Cancer Immunotherapy GUIDELINES

SITC Clinical Practice Guideline Webinar – Case Studies in Immunotherapy for the Treatment of Multiple Myeloma

June 16, 2021

5:00-6:00 p.m. ET

This webinar is supported, in part, by grants from Amgen and Merck & Co., Inc.

Webinar faculty

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Learning objectives

Upon completion of the webinar, participants will be able to:

- Plan immunotherapy treatment regimens for challenging patient populations
- Identify management strategies for immunotherapy toxicities
- Select appropriate treatment strategies for patients with relapsed/unresponsive disease
- Articulate the potential risks and benefits for proceeding with any other possible interventions specific to multiple myeloma in the context of an immunotherapy treatment plan

Journal for ImmunoTherapy of Cancer

The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of multiple myeloma

Nina Shah,[1] Jack Aiello,[2] David E Avigan,[3] Jesus G Berdeja,[4] Ivan M Borrello,[5] Ajai Chari,[6] Adam D Cohen,[7] Karthik Ganapathi,[8] Lissa Gray,[9] Damian Green,[10] Amrita Krishnan,[11] Yi Lin,[12,13] Elisabet Manasanch,[14] Nikhil C Munshi,[15] Ajay K Nooka,[16] Aaron P Rapoport,[17] Eric L Smith,[18] Ravi Vij,[19] Madhav Dhodapkar[20]

Guideline development

- *The Institute of Medicine's Standards for Developing Trustworthy Practice Guidelines* were used to develop these recommendations
- Panel consisted of 19 participants, including medical oncologists, a nurse practitioner, and a patient advocate
- Recommendations come from literature evidence, supplemented with clinical experience of the panel members where necessary
- Consensus defined as ≥75% agreement

Outline of topics

1. Patient selection for CAR T treatment
2. CAR T cell toxicities
3. Cytopenias

Case presentation

- 68 year-old male
- Diagnosed with stage III oligo-secretory κ multiple myeloma
- Relevant comorbidities include type 2 diabetes
- Biopsy-proven myeloma and PET-CT evidence of osteolytic lesions
- Cytogenetics: t(4:14)

Prior lines of therapy

1. Bortezomib, lenalidomide and dexamethasone (VRd) → autologous stem cell transplant → lenalidomide maintenance
2. 2 years later- biochemical progression treated by ixazomib, lenalidomide and dexamethasone
3. Daratumumab, pomalidomide and dexamethasone
4. Carfilzomib, cyclophosphamide and dexamethasone

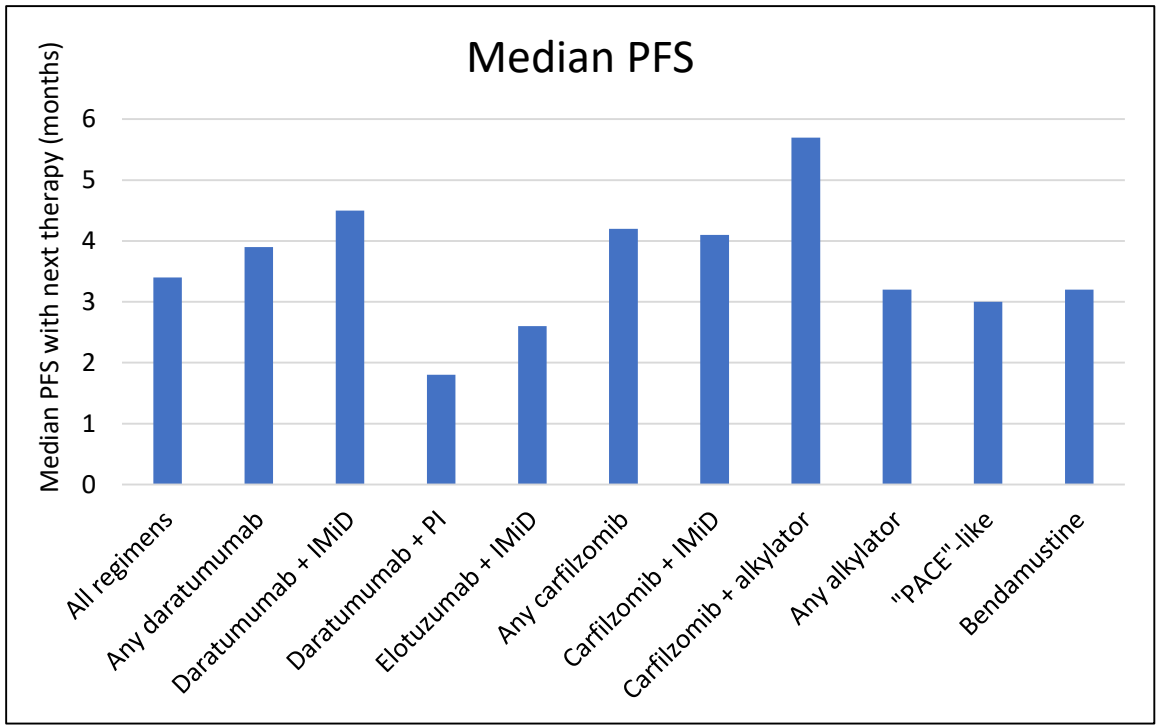
Question #1

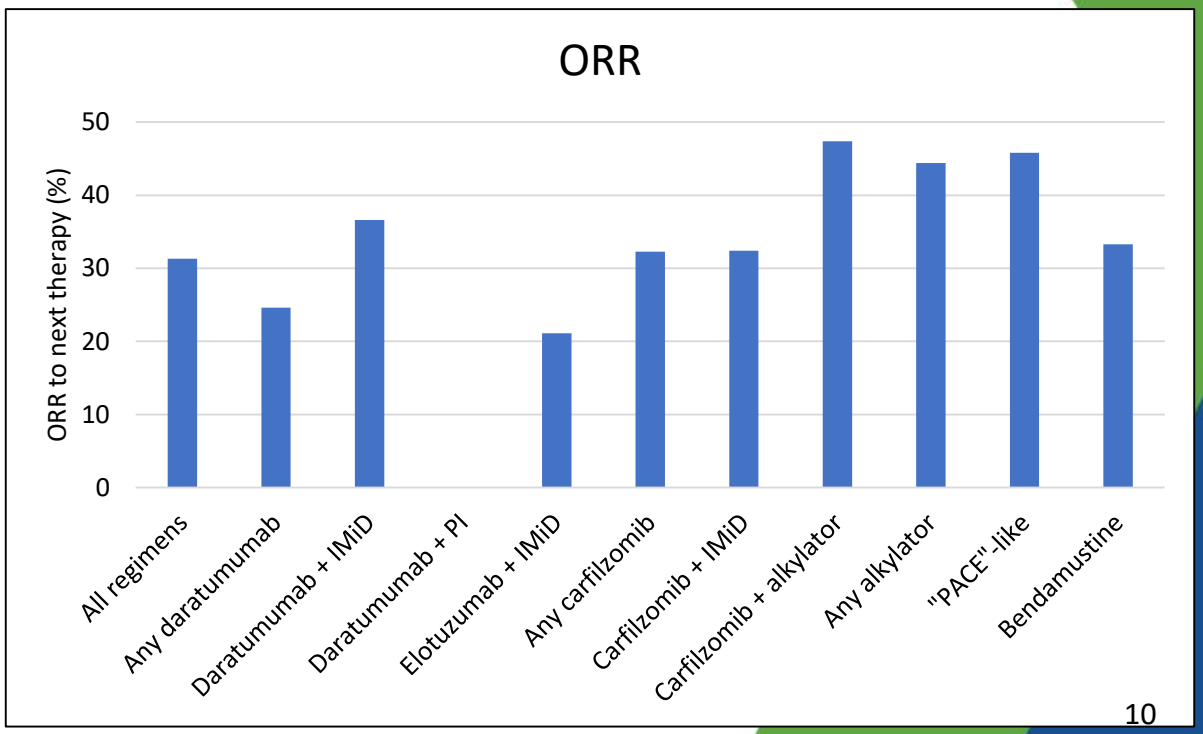
Of the following therapies, which would likely provide the longest PFS at this point in the patient's treatment?

A. Belantamab mafadotin
B. Idecabtagene vicleucel
C. Selinexor + dexamethasone
D. Melphalan flufenamide

Management of CD38-refractory disease

- The MAMMOTH study investigated patient outcomes after becoming CD38-refractory
- Median OS for patients after becoming CD38-refractory was 8.6 months, regardless of next line of therapy





Gandhi, Leukemia 2019

DREAMM-2: belantamab mafodotin

A phase 2, open-label, randomized 2-dose study in RRMM after an anti-CD38 therapy.
A primary analysis of DREAMM-2 was completed at a median follow-up time of 6.3 and 6.9 months for the 2.5 mg/kg and 3.4 mg/kg cohorts, respectively. An additional analysis was completed at 13 months of follow-up.

POPULATION

- Measurable disease
- ECOG PS 0-2
- **3 or more prior lines** of antimyeloma therapy
- **Refractory to a proteasome inhibitor and an IMiD and failed an anti-CD38 antibody**
- Prior anti-BCMA therapy excluded
- Prior auto-SCT allowed; allo-SCT excluded

RANDOMIZE 1:1*

Treatment until disease progression or unacceptable toxicity

Belantamab mafodotin 2.5 mg/kg
IV, every 3 weeks
(n=97)

Belantamab mafodotin 3.4 mg/kg
IV, every 3 weeks
(n=99)

Primary Outcome

ORR:
% of patients with ≥PR†

Key Secondary Outcomes

- DOR (time from ≥PR until PD or death due to PD)
- Other efficacy: CBR, PFS, OS, TTBR, TTR
- Safety, including keratopathy (MECs)

*Patients stratified based on number of previous lines of therapy (≤4 vs >4) and presence or absence of high-risk cytogenetic features.
†According to International Myeloma Working Group (IMWG) 2016 criteria.

1. Lonial S, et al. Lancet Oncol. 2020;21(2):207-221. doi:10.1016/S1470-2045(19)30788-0. 2. Lonial S, et al. ASCO 2020 (virtual). Poster 436.

DREAMM-2: 13-month follow-up

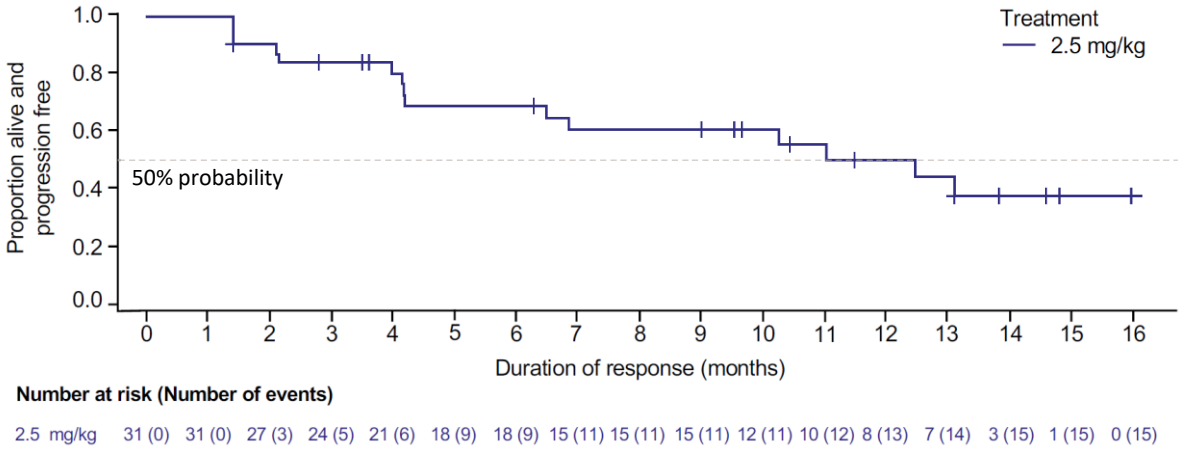
Duration of Response

	Belantamab mafodotin 2.5 mg/kg group (n=31)
Median DOR, months (95% CI)	**11.0** (4.2–NR)

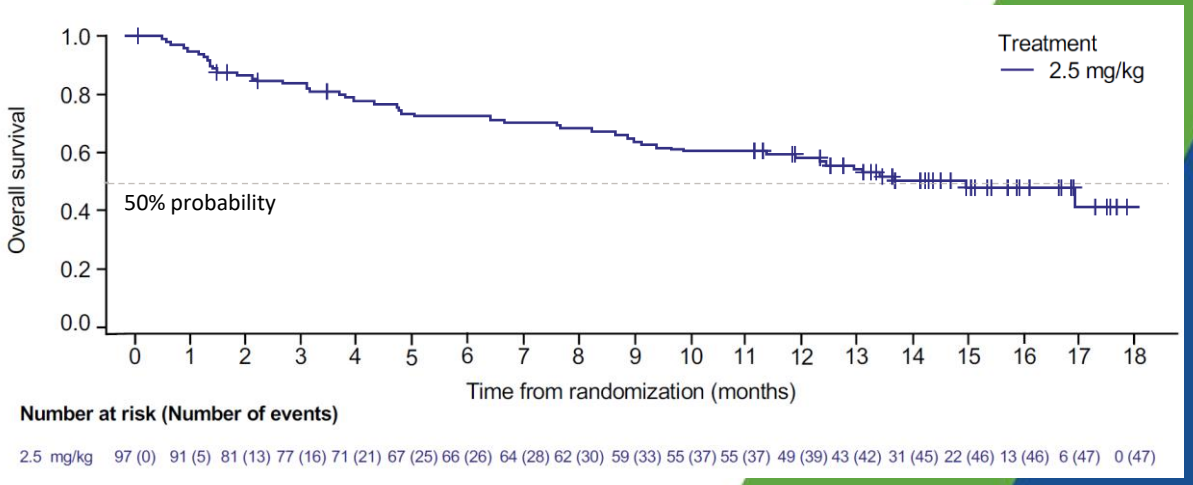
PFS and OS

	Belantamab mafodotin 2.5 mg/kg group (N=97)
Median PFS, months (95% CI)	**2.8** (1.6–3.6)
Median OS, months (95% CI)	**13.7** months (9.9–NR)

Duration of Response



Overall Survival



*As discussed in the MM Practical Management Pearls webinar, **ocular toxicities** are common with belantamab mafodotin.*

Lonial S, et al. Presented at: ASCO. 2020 (Abstr 8536).

Phase 2b STORM study of selinexor + dex (Sd) for patients with RRMM

Key inclusion criteria
- Prior tx with bor, cfz, len, pom, dara, glucocorticoids, alkylating agent
- Refractory to ≥1 IMiD, 1 PI, dara, glucocorticoids, and most recent tx
- ECOG PS 0-2

Key exclusion criteria
- Systemic AL amyloidosis
- Active CNS involvement
- Grade ≥3 peripheral neuropathy or grade ≥2 painful neuropathy

28d cycle

Selinexor
80 mg po d1 and 3 qw

Dexamethasone
20 mg po d1 and 3 qw

Primary Endpoint: ORR (≥PR)
Secondary Endpoints: DOR, minimal response (≥25% to 50% reduction in serum myeloma protein) or better, PFS, OS

Baseline characteristic	N=122
Median age, y (range)	65.2 (40-86)
ECOG PS 2, n (%)	11 (9)
Any high-risk chromosomal abnormality: del(17p)/p53, t(4;14), t(4;16), gain(1q), n (%)	65 (53)
Median prior tx, n (range)	7 (3-18)
Refractory to, n (%)	
Cfz, pom, dara	117 (96)
Cfz, len, pom, dara	101 (83)
Bor, cfz, pom, dara	94 (77)
Bor, cfz, len, pom, dara	83 (68)

Efficacy	N=122
Median duration of tx, weeks (range)	9.0 (1-60)
ORR, n (% [95% CI])	32 (26 [19-35])
sCR	2 (2)
VGPR	6 (5)
PR	24 (20)
Minimal response, n (%)	16 (13)
Median DOR, mo [95% CI]	4.4 [3.7-10.8]
Median PFS, mo [95% CI]	3.7 [3.0-5.3]
Median OS, mo [95% CI]	8.6 [6.2-11.3]

Safety	N=123
Most common (≥10%) grade ≥3 AEs, n (%)	
Thrombocytopenia	72 (59)
Anemia	54 (44)
Fatigue	31 (25)
Hyponatremia	27 (22)
Neutropenia	26 (21)
Leukopenia	17 (14)
Lymphopenia	14 (11)
Nausea	12 (10)
D/c due to tx-related AE, n (%)	22 (18)
Dose modification or interruption due to AE, n (%)	Not reported (80)
Serious AE, n (%)	78 (63)
Tx-related	39 (32)
Grade 5 AEs, n (%)	12 (10)

Chari A et al. *N Engl J Med*. 2019;381(8):727-738.

Phase 2 HORIZON study of melflufen + dex

Key eligibility criteria (N=157)

- RRMM refractory to pom or anti-CD38 mAb or both
- ≥2 prior lines of therapy, including an IMiD and a PI
- ECOG PS ≤2

Melflufen 40 mg + dex 40 mg[a] (until PD or unacceptable toxicity)	28-Day Cycle			
	D1	D8	D15	D22
Melflufen (IV)	✓			
Dex (oral)	✓	✓	✓	✓

- **Primary endpoint:** ORR
- **Secondary endpoints:** DOR, PFS, OS, CBR, best response, TTR, TTP, TTNT, safety

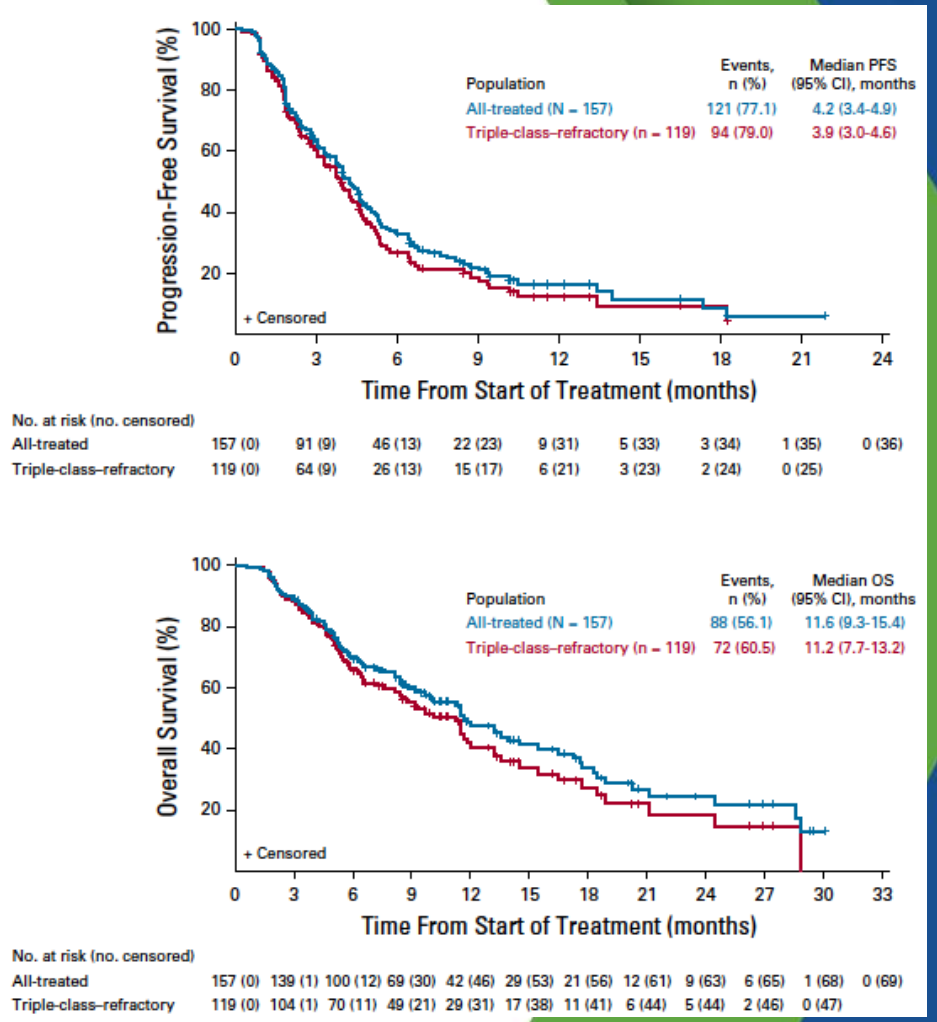
TEAEs (In ≥15% of Patients) in the All-Treated Population, n (%)	(N=157)		
	Any Grade	Grade 3	Grade 4
Any AE	157 (100)	40 (25)	100 (64)
Hematologic			
Neutropenia	129 (82)	50 (32)	74 (47)
Thrombocytopenia	128 (82)	40 (25)	80 (51)
Anemia	111 (71)	66 (42)	1 (<1)
Nonhematologic			
Nausea	50 (32)	1 (<1)	0
Fatigue	46 (29)	4 (3)	0
Asthenia	42 (27)	5 (3)	1 (<1)
Diarrhea	42 (27)	0	0
Pyrexia	38 (24)	3 (2)	0
Cough	26 (17)	0	0
URTI	25 (16)	3 (2)	0
Constipation	23 (15)	1 (<1)	0

[a] Patients aged ≥75 years received dex 20 mg. [b]High-risk cytogenetics at study entry was based on FISH defined as t(4; 14), del(17/17p), and t(14; 16); 31 patients (20%) had unknown cytogenetics.

Richardson PG, et al. *J Clin Oncol*. 2021;39(7):757-767.

Phase 2 HORIZON study of melflufen + dex: Efficacy

Response		All Treated (N=157)	Triple-Class Refractory (n=119)
ORR, n (%) [95% CI]		46 (29) [22, 37]	31 (26) [18, 35]
INV-Assessed Best Overall Response, n (%)	sCR	1 (1)	0
	CR	0	0
	VGPR	17 (11)	13 (11)
	PR	28 (18)	18 (15)
	Minimal response	25 (16)	16 (13)
CBR, n (%) [95% CI]		71 (45) [37, 53]	47 (39) [31, 49]



Richardson PG, et al. *J Clin Oncol*. 2021;39(7):757-767.

Phase 2 KarMMa: Idecabtagene vicleucel

Ide-cel is a CAR T-cell therapy targeting BCMA

Key eligibility criteria

- ≥3 prior regimens with ≥2 consecutive cycles each (or best response of PD)
- RRMM after ≥3 prior tx, including PI, IMiD, and anti-CD38 mAb

Screening

Apheresis

Bridging therapy

Cy (300 mg/m^2) + Flu (30 mg/m^2), Day -5 to -3

Ide-cel (BCMA-targeted CAR T-cell) infusion, Day 1
150 x 10^6 CAR T-cells
300 x 10^6 CAR T-cells
450 x 10^6 CAR T-cells

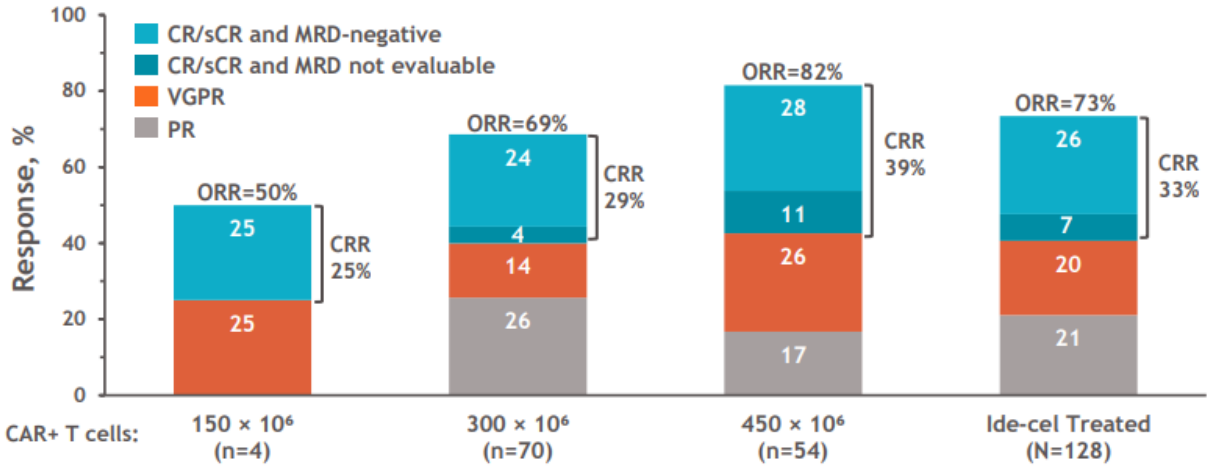
Follow-up

AEs in ≥25% (N=128)		Any Grade	Grade 3/4
Hematologic, n (%)	Neutropenia	117 (91)	114 (89)
	Anemia	89 (70)	77 (60)
	Thrombocytopenia	81 (63)	67 (52)
	Leukopenia	54 (42)	50 (39)
	Lymphopenia	35 (27)	34 (27)
GI, n (%)	Diarrhea	45 (35)	2 (2)
	Nausea	37 (29)	0
Other, n (%)	Hypokalemia	45 (35)	3 (2)
	Fatigue	43 (34)	2 (2)
	Hypophosphatemia	38 (30)	20 (16)
	Hypocalcemia	34 (27)	10 (8)
	Pyrexia	32 (25)	3 (2)
	CRS	**107 (84)**	**7 (6)**
	Neurotoxicity	**23 (18)**	**4 (3)**

Primary endpoint: ORR
Secondary endpoints: CRR (key), safety, DoR, PFS, OS, PK, MRD, QoL, HEOR
Exploratory endpoints: immunogenicity, BCMA expression/loss, cytokines, T-cell immunophenotype, GEP in BM

Munshi NC, et al. ASCO 2020. Abstract 8503.

Phase 2 KarMMa: efficacy



	150x10⁶ (n=4)	300x10⁶ (n=70)	450x10⁶ (n=54)	150-450x10⁶ (N=128)
Median DOR, mo [95% CI]	NR [2.8-NE]	9.9 [5.4-11.0]	11.3 [10.3-11.4]	10.7 [9.0-11.3]
Median PFS, mo [95% CI]	2.8 [1.0-NE]	5.8 [4.2-8.9]	12.1 [8.8-12.3]	8.8 [5.6-11.6]
Median OS, mo [95% CI]	Not reported	Not reported	Not reported	19.4 [18.2-NE]

- Primary (ORR >50%) endpoint was met: 73% (95% CI, 65.8-81.1; *P*<0.0001)
- Key secondary endpoint (CRR >10%) was met: 33% (95% CI, 24.7-40.9; *P*<0.0001)
- Median time to first response of 1.0 months (range, 0.5-8.8)
- Median time to CR of 2.8 months (range, 1.0-11.8)
- Median follow-up of 13.3 months across target dose levels
- 78% of all Ide–cel-treated patients were event-free at 12 months

•Munshi NC, et al. ASCO 2020. Abstract 8503.

•CI, confidence interval; CR, complete response; CRR, complete response ratio; DOR, duration of response; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; sCR, stringent complete response.

Factors that may impact selection of CAR T cell therapy

- Prior treatments
- Performance status
- Comorbidities
- Ability to withstand potential toxicity

Case continued: CAR T treatment

- Patient decides to proceed with anti-BCMA CAR T therapy
- Successful lymphodepletion (Flu-Cy), CAR T cell manufacturing and infusion

Question #2

How long does the lead-up to CAR T treatment take on average, from deciding to treat to administering CAR T cells to the patient?

A. 3-5 days
B. 1-2 weeks
C. 3-5 weeks
D. 2-3 months

Administration of CAR T therapy

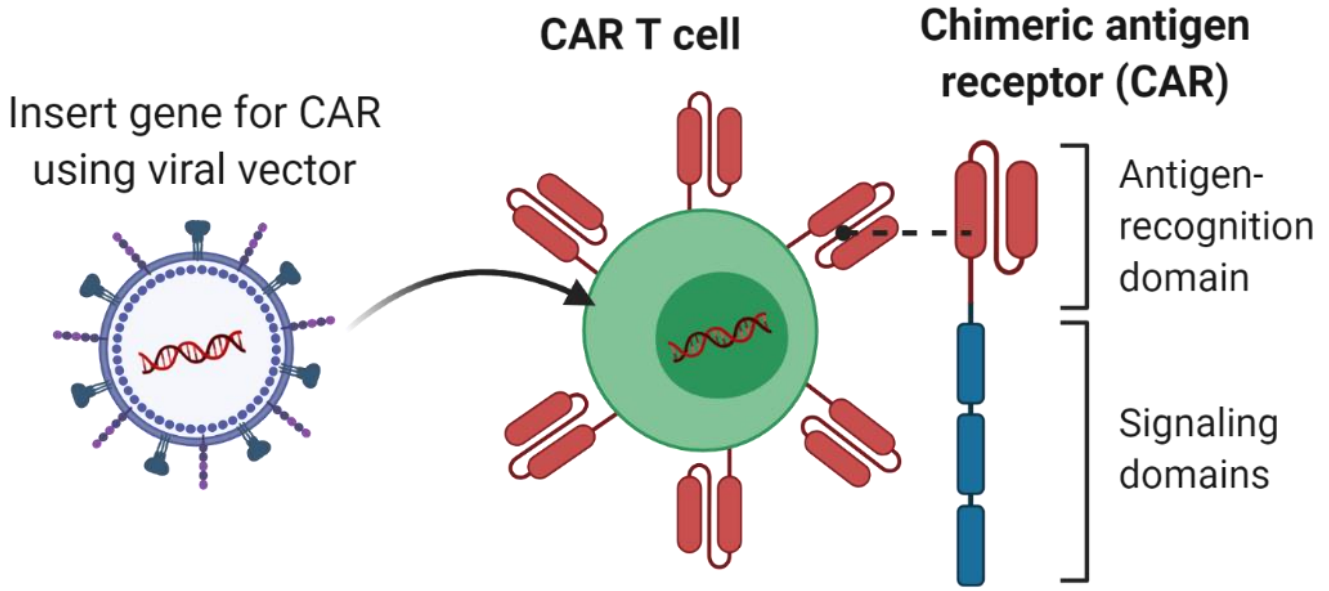
1 Consultation and workup

2 Leukapheresis

3 Bridging therapy (if needed)

Beaupierre, Clin J Oncol Nursing 2019

CAR manufacturing

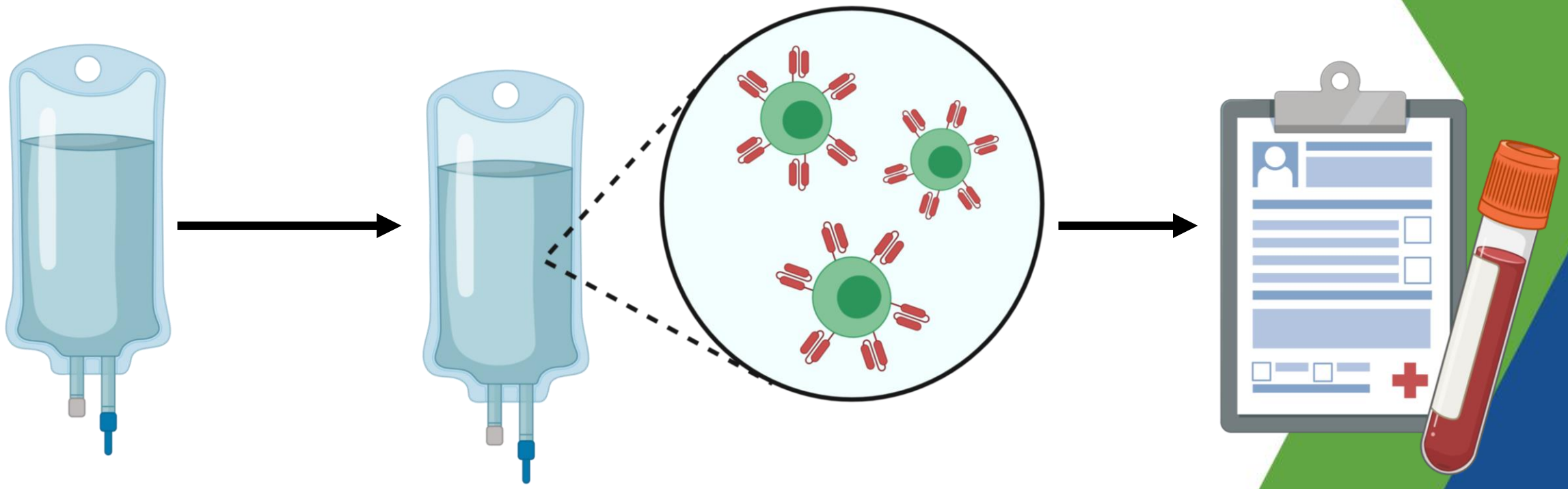


Administration of CAR T therapy

4 **Lymphodepleting chemotherapy**

5 **CAR T infusion and monitoring**

6 **Long-term follow-up**



Beaupierre, Clin J Oncol Nursing 2019

Question #3

Two days after CAR T infusion, the patient develops a fever of 101°F, heart rate of 110 bpm with low blood pressure, and requires 2L O2 by nasal cannula.

How should this patient be managed?

A. Blood cultures and antibiotics
B. Steroids
C. Tocilizumab
D. A & C

ASTCT CRS grading

CRS parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever	≥ 38°C	≥ 38°C	≥ 38°C	≥ 38°C
with				
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
and/or				
Hypoxia	None	Requiring low-flow nasal cannula or blow-by	Requiring high-flow nasal cannula, face mask, non-rebreather mask or venturi mask	Requiring positive pressure (e.g. CPAP, BiPAP, intubation and mechanical ventilation)

**Note that many early clinical trials used different CRS grading systems, but the ASTCT system is now standard.*

Lee, Santomasso, Biol Blood Marrow Transpl 2018

Question #4

Patient does not require a vasopressor to manage hypotension, and needs low-flow nasal cannula oxygen for hypoxia.

What grade of CRS would this patient have by ASTCT grading?

A. Grade 1
B. Grade 2
C. Grade 3
D. Grade 4

Ide-cel CRS guidance

CRS grade*	Tocilizumab	Corticosteroids
Grade 1 Symptoms require symptomatic treatment only	If onset 72 hours or more after infusion, treat symptomatically. If onset less than 72 hours after infusion, consider tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).	Consider dexamethasone 10 mg IV every 24 hours.
Grade 2 Symptoms require and respond to moderate intervention	Administer tocilizumab 8 mg/kg over 1 hour. Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen.	Consider dexamethasone 10 mg IV every 12-24 hours.
	If no improvement within 24 hours or rapid progression, repeat tocilizumab and escalate dose and frequency of dexamethasone. If no improvement within 24 hours or continued rapid progression, switch to methylprednisolone 2 mg/kg followed by 2 mg/kg divided 4 times per day. After 2 doses of tocilizumab, consider alternative anti-cytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.	
Grade 3 Symptoms require and respond to aggressive intervention	Per Grade 2	Administer dexamethasone 10 mg IV every 12 hours.
	If no improvement within 24 hours or rapid progression, repeat tocilizumab and escalate dose and frequency of dexamethasone. If no improvement within 24 hours or continued rapid progression, switch to methylprednisolone 2 mg/kg followed by 2 mg/kg divided 4 times per day. After 2 doses of tocilizumab, consider alternative anti-cytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.	
Grade 4 Life-threatening symptoms	Per Grade 2	Administer dexamethasone 20 mg IV every 6 hours.
	After 2 doses of tocilizumab, consider alternative anti-cytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total. If no improvement within 24 hours, consider methylprednisolone (1-2 g, repeat every 24 hours if needed; taper as clinically indicated) or other anti-T cell therapies.	

**Note that the ide-cel prescribing information uses the Lee grading criteria, not ASTCT.*

Case continued: Outcomes after CRS

- After administration of one dose of tocilizumab, fever reduced and hypotension improved
- Headache persisted, despite other CRS symptoms improving
- At 5 days post-CAR T infusion, patient developed a stutter, anomia and minor handwriting changes
- Symptoms progressed, until patient had an ICE score of 3 and would only awaken to tactile stimuli

Question #5

What criteria is most appropriate to grade this patient's neurotoxicity?

A. CTCAE
B. CARTOX
C. Lee
D. ASTCT

Immune effector cell-associated encephalopathy (ICE) score

- **Orientation**: Orientation to year, month, city, hospital: 4 points (1 point each)
- **Naming**: Name 3 objects (e.g., clock, pen, button): 3 points (1 point each)
- **Following commands**: (e.g., Show me 2 fingers or close your eyes and stick out your tongue): 1 point
- **Writing**: Ability to write a standard sentence (e.g., Our national bird is the bald eagle): 1 point
- **Attention**: Count backwards from 100 by 10: 1 point
- **Total scale**: 0-10

ASTCT ICANS grading - adults

Neurotoxicity domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score	7–9	3–6	0–2	0 (patient is unarousable)
Depressed level of consciousness	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse; stupor or coma
Seizure	N/A	N/A	Any clinical seizure focal or generalized that resolves rapidly or non-convulsive seizures on EEG that resolve with intervention	Life-threatening prolonged seizure (>5 min), 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 ICP/cerebral edema	N/A	N/A	Focal/local edema on neuroimaging	Diffuse cerebral edema on neuroimaging, decerebrate or decorticate posturing, cranial nerve VI palsy, papilledema, or Cushing's triad

Lee, Santomasso, Biol Blood Marrow Transpl 2018

Ide-cel ICANS guidance

Neurologic toxicity grade*	Corticosteroids and anti-seizure medications
Grade 1	Start non-sedating anti-seizure medicines (e.g. levetiracetam) for seizure prophylaxis. If 72 hours or more after infusion, observe patient. If less than 72 hours after infusion, consider dexamethasone 10 mg IV every 12-24 hours for 2-3 days.
Grade 2	Start non-sedating anti-seizure medicines (e.g. levetiracetam) for seizure prophylaxis. Start dexamethasone 10 mg IV every 12 hours for 2-3 days, or longer for persistent symptoms. Consider taper for a total corticosteroid exposure of greater than 3 days. Corticosteroids are not recommended for isolated Grade 2 headaches. If no improvement after 24 hours, or worsening of neurologic toxicity, increase the dose and/or frequency of dexamethasone up to a maximum of 20 mg IV every 6 hours.
Grade 3	Start non-sedating anti-seizure medicines (e.g. levetiracetam) for seizure prophylaxis. Start dexamethasone 10-20 mg IV every 6-12 hours. Corticosteroids are not recommended for isolated Grade 3 headaches. If no improvement after 24 hours or worsening of neurologic toxicity, escalate to methylprednisolone (2 mg/kg loading dose, followed by 2 mg/kg divided into 4 times per day; taper within 7 days). If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylprednisolone (1-2 g, repeat every 24 hours if needed; taper as clinically indicated) and cyclophosphamide 1.5 g/m^2.
Grade 4	Start non-sedating anti-seizure medicines (e.g. levetiracetam) for seizure prophylaxis. Start dexamethasone 20 mg IV every 6 hours. If no improvement after 24 hours or worsening of neurologic toxicity, escalate to high-dose methylprednisolone (1-2 g, repeated every 24 hours if needed; taper as clinically indicated). If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylprednisolone (1-2 g, repeat every 24 hours if needed; taper as clinically indicated) and cyclophosphamide 1.5 g/m^2.

**Note that the ide-cel PI uses CTCAE for grading of ICANS, not the ASTCT criteria.*

Question #6

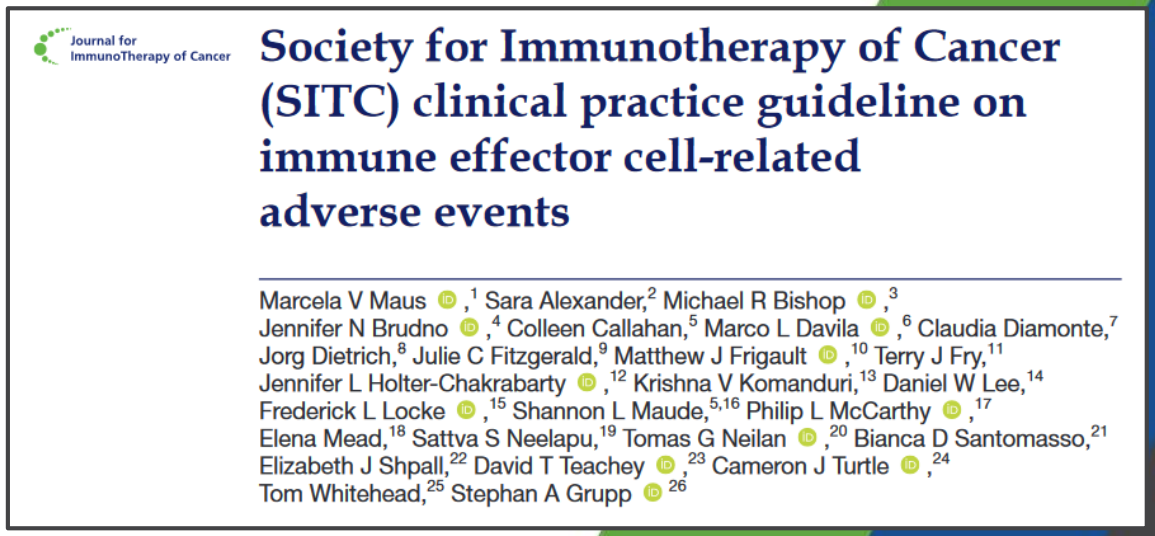
The patient was diagnosed with grade 3 ICANS.

What management technique should be employed for this patient?

A. Another dose of tocilizumab
B. Levetiracetam
C. Supportive care alone
D. High-dose corticosteroids
E. B & D

CAR T toxicities conclusions

- CAR T therapies are associated with significant risk for toxicities
- Providers should be able to quickly recognize and manage potential CRS or ICANS
- See the recently-published SITC Clinical Practice Guideline for additional details



Case continued: Patient discharged

- Recall prior toxicities:
  - Developed grade 2 CRS, which was managed and resolved
  - Grade 3 ICANS managed and resolved
- At 1 month follow-up, patient exhibits grade 3 B cell aplasia and neutropenia
  - ANC: 500 cells/µL
  - IgG: 400 mg/dL

Question #7

What infection prevention approach(es) would you prescribe for a patient about to receive CAR T therapy, given the risk of immunosuppression? (select all that apply)

A. Viral prophylaxis
B. PJP prophylaxis
C. Antifungal prophylaxis
D. Antibacterial prophylaxis

Question #8

What management approach(es) would you consider to address this patient's neutropenia?

A. G-CSF
B. GM-CSF
C. RBC and platelet transfusion
D. Watch and wait

Case continued: COVID risk in cancer patients

- The patient's cytopenia improved, but not completely resolved, by April 2020 after treatment with growth factors
- With the growing COVID-19 pandemic, your patient expresses their concern to you and asks for advice

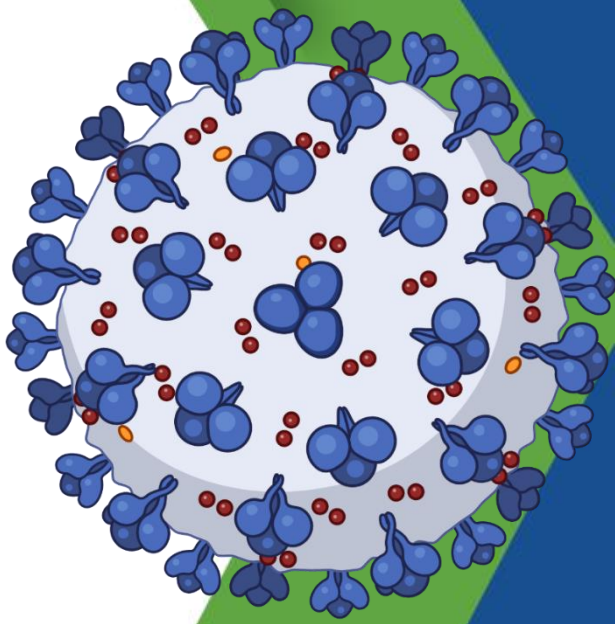
COVID viral shedding in cancer patients with immunosuppression

- Patients with immunosuppression may shed viable SARS-CoV-2 for at least two months after infection
- Viral DNA has been detected up to 78 days after symptom onset
- Patients with prolonged viable virus shedding may also remain seronegative for antibodies
- Guidelines for COVID-19 isolation precautions may need to be adjusted for immunosuppressed patients
- Delay of vaccination recommended until 3 months post-CAR T cell infusion

Aydillo, N Engl J Med 2020

Considerations during the COVID-19 pandemic

- Myeloma Guideline was written before the pandemic and thus does not discuss COVID-19
- SITC's Clinical Practice Guideline on immune effector cell-associated adverse events provides some guidance
- Treatment plans for cancer patients must take into account potential limitations in hospital resources
- Delaying CAR T may not be an option in some cases
- Make sure tocilizumab is readily available
- Ensure adequate staffing and supportive care



Maus, J Immunother Cancer 2020; Bachanova, Biol Blood Marrow Transpl 2020.

Cytopenia conclusions

- Cytopenias are a common occurrence after CAR T and other myeloma treatments
- Infectious prophylaxis is important throughout multiple myeloma treatment, but may need adjusted during CAR T treatment
- The COVID-19 pandemic has impacted cancer care, and patients may require additional guidance

Key messages

- Treatment decisions are highly patient-specific, and should consider any co-morbidities
- Sequencing of therapies is still an ongoing area of investigation
- Emerging therapies like CAR T and ADCs have unique, significant toxicities
- Patients may require supportive care and prophylaxis throughout their treatment course

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This webinar is supported, in part, by grants from Amgen and Merck & Co., Inc.