Society for Immunotherapy of Cancer

Cancer Immunotherapy GUIDELINES

SITC Clinical Practice Guideline Webinar – Practical Management Pearls for the Treatment of Multiple Myeloma

Friday, April 23, 2021

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

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

Webinar Agenda

5:00-5:05 pm ET Overview: Welcome and Introductions

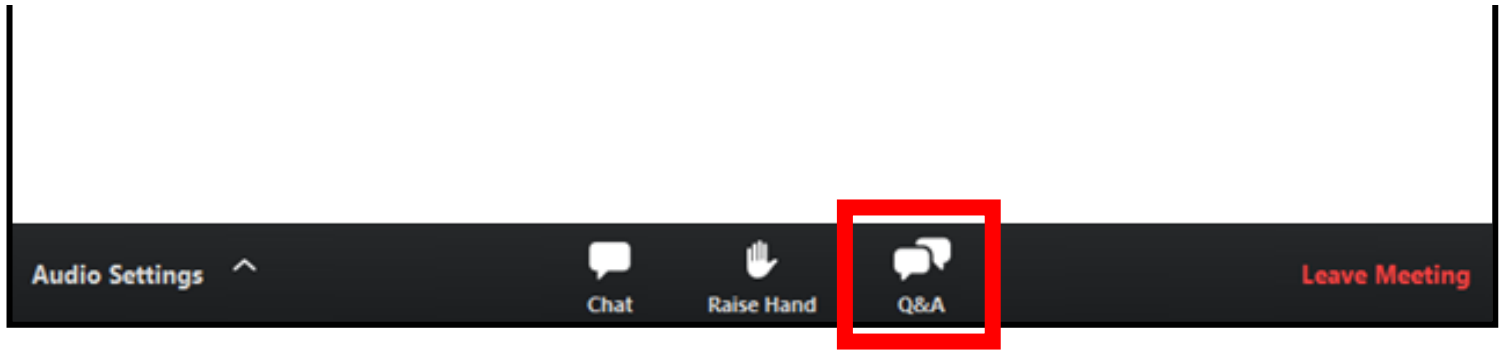
5:05-5:30 pm ET Overview of the multiple myeloma clinical practice guideline
Pearls for:
- Monoclonal antibody therapies
- Antibody-drug conjugates
- CAR T therapies
- T cell engager therapies

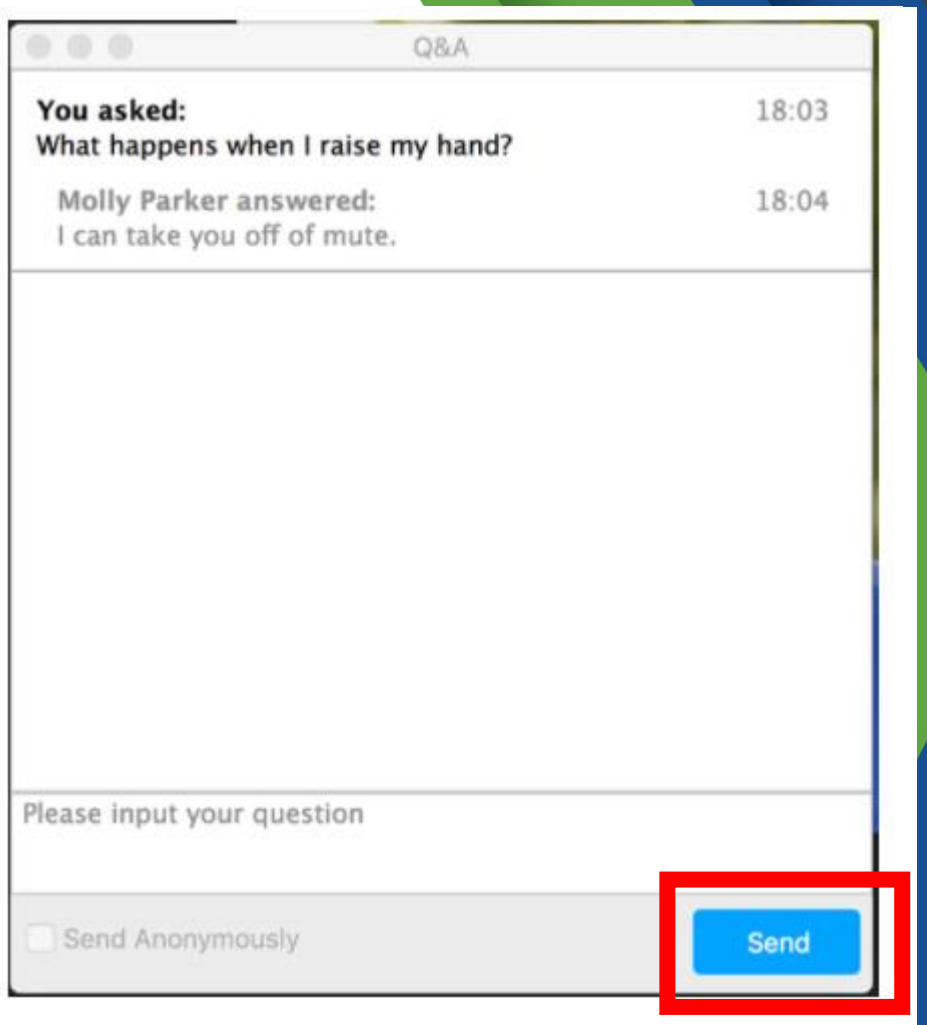
5:30-5:58 pm ET Discussion and Question and Answer Session

5:58-6:00 pm ET Closing Remarks

How to submit questions

- Click the “Q&A” icon located on at the bottom of your Zoom control panel
- Type your question in the Q&A box, then click “Send”
- Questions will be answered in the Question & Answer session at the end of the webinar (as time permits)





Webinar Faculty

Nina Shah, MD – *University of California San Francisco Medical Center* (Expert Panel Chair)

Jesus G. Berdeja, MD – *Sarah Cannon Research Institute*

Yi Lin, MD, PhD – *Mayo Clinic*

Learning objectives

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

- Appraise and classify multiple myeloma-specific considerations for immunotherapy agents and associated toxicities
- Appropriately manage multiple myeloma-specific toxicities or irAEs associated with immunotherapy
- Determine optimal sequencing of immunotherapies in relapsed/refractory disease
- Consider the integration of immunotherapies into treatment plans for early-stage disease

Outline

- Overview of the multiple myeloma clinical practice guideline
- Pearls for:
  - Monoclonal antibody therapies
  - Antibody-drug conjugates
  - CAR T therapies
  - T cell engager therapies
- Discussion and Q&A

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

Key takeaways from the Multiple Myeloma Guideline

- Monoclonal antibodies targeting CD38 and SLAMF7 are available and recommended for multiple indications in myeloma
- New agents such as antibody-drug conjugates, CAR T cell therapies and bi- and tri-specific T cell engaging antibodies are changing the standard of care

Shah, J Immunother Cancer 2020

Difficult questions in multiple myeloma

- When and how to use anti-CD38 agents in front line
- Managing CD38-refractory disease
- Recognizing and managing unique toxicities from antibody-drug conjugates
- Patient selection for CAR T or T cell engagers
- Managing toxicities and complications from CAR T and T cell engagers

Outline

- Overview of the multiple myeloma clinical practice guideline
- Pearls for:
  - Monoclonal antibody therapies
  - Antibody-drug conjugates
  - CAR T therapies
  - T cell engager therapies
- Discussion and Q&A

Monoclonal antibody therapies for R/R multiple myeloma

Regimen	FDA-approved indication
Daratumumab + bortezomib + dexamethasone	R/R MM after ≥1 prior therapy
Daratumumab + lenalidomide + dexamethasone	R/R MM after ≥1 prior therapy
Daratumumab + pomalidomide + dexamethasone	R/R MM after ≥2 prior therapies, including lenalidomide and proteasome inhibitor
Daratumumab + carfilzomib + dexamethasone	R/R MM after 1-3 prior therapies
Daratumumab	R/R MM after ≥3 prior therapies
Isatuximab + pomalidomide + dexamethasone	R/R MM after ≥2 prior therapies
Isatuximab + carfilzomib + dexamethasone*	R/R MM after 1-3 prior therapies
Elotuzumab + lenalidomide + dexamethasone	R/R MM after 1-3 prior therapies
Elotuzumab + pomalidomide + dexamethasone	R/R MM after ≥2 prior therapies, including lenalidomide and proteasome inhibitor

**FDA-approved after Guideline published*

Front-line use of daratumumab

Trial	Population	Treatment arms	N	Landmark PFS	MRD negativity
GRIFFIN	Transplant-eligible	D-VRd vs VRD	207	24-month: 95.8% vs 89.8%	51.0 % vs 20.4%
CASSIOPEIA	Transplant-eligible	D-VTd vs VTd	1085	18-month: 93% vs 85%	64% vs 44%
MAIA	Transplant-ineligible	D-Rd vs Rd	737	30-month: 70.6% vs 55.6%	28.8% vs 9.2%
ALCYONE	Transplant-ineligible	D-VMP vs VMP	706	Median: 36.4 mo vs 19.3 mo	28.3% vs 7%

Shah, J Immunother Cancer 2020; San-Miguel, ASH 2020

Infusion reactions with antibody therapies

Therapies require premedication:

- **Daratumumab**: antihistamines, antipyretics and corticosteroids
- **Isatuximab**: dexamethasone, acetaminophen, H2 antagonists and diphenhydramine
- **Elotuzumab**: dexamethasone, diphenhydramine, ranitidine and acetaminophen

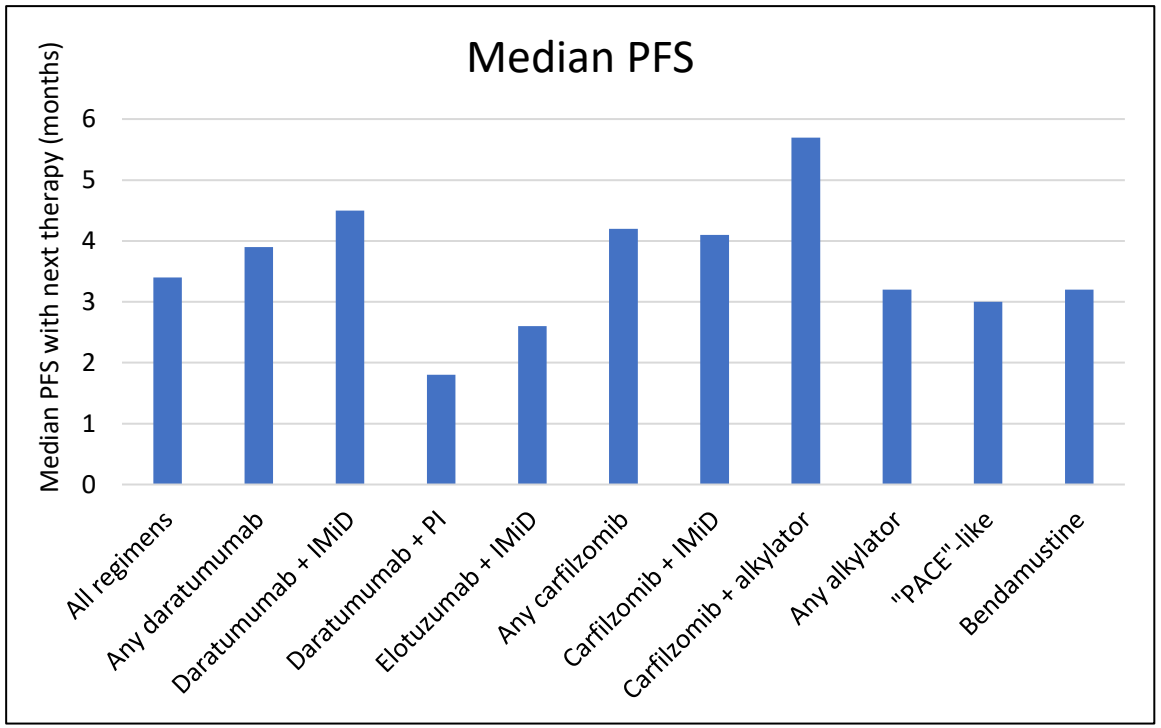
Study	Grade 1-2	Grade 3-4
Daratumumab		
CASTOR (n=251)	45.3%	8.6%
POLLUX (n=286)	47.7%	5.3%
ALCYONE (n=346)	28%	4%
Isatuximab		
NCT01749969 (n=57)	47%	8.7%
NCT01084252 (n=97)	49.5%	2.1%
Elotuzumab		
Zonder (n=34)	58.8%	3%
ELOQUENT-2 (n=318)	9%	1%

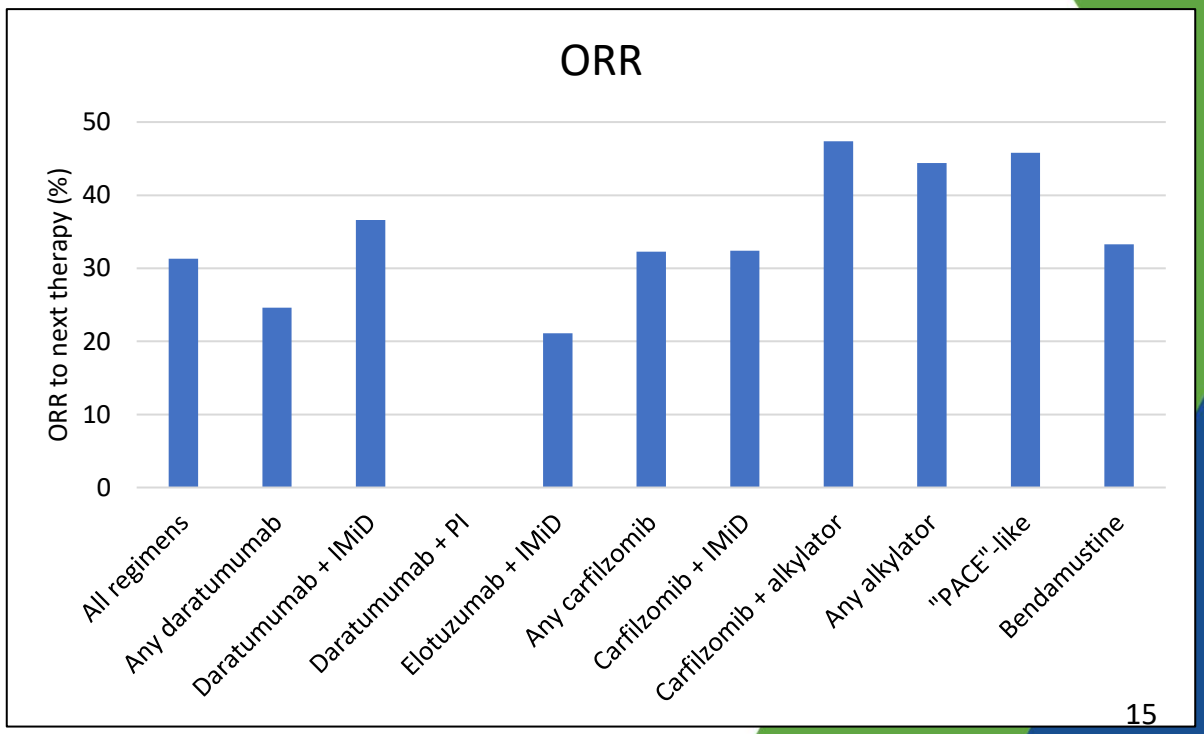
Daratumumab may be administered either intravenously or subcutaneously

Martin, Blood 2017; Nooka, JCO Oncol Pract 2018; Mikhael, Leukemia 2020.

Management of CD38-refractory disease

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



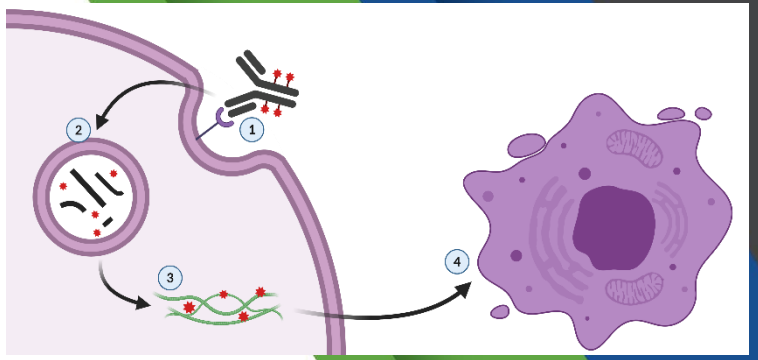


Gandhi, Leukemia 2019

Outline

- Overview of the multiple myeloma clinical practice guideline
- Pearls for:
  - Monoclonal antibody therapies
  - Antibody-drug conjugates
  - CAR T therapies
  - T cell engager therapies
- Discussion and Q&A

Belantamab mafodotin



- FDA-approved August 2020 (this guideline published July 2020, so not included) for R/R MM after ≥4 prior therapies, including anti-CD38, PI, and IMiD
- Anti-BCMA humanized antibody conjugated to MMAF

Trial	Phase	Patient population	N	Treatment arm(s)	ORR	Median PFS
DREAMM-1	1	R/R MM after ASCT, alkylators, PI, and IMiD	35	3.4 mg/kg belantamab mafodotin Q3W	60%	12 months
DREAMM-2	2	R/R MM after IMiD, PI, and anti-CD38	196	2.5 mg/kg belantamab mafodotin Q3W	31%	2.9 months
				3.4 mg/kg belantamab mafodotin Q3W	34%	4.9 months

Trudel, Blood Cancer J 2019; Lonial, Lancet Oncol 2019.

Ocular toxicities of belantamab mafodotin

- Patients should receive pre-treatment eye exam
- Symptoms may include dry eyes, blurred vision, changes in vision, and exam findings
- 72% of patients on trials had keratopathy on exam
- Around 50% of patients on clinical trials reported significantly worsening vision symptoms
- Management approaches:
  - Belantamab mafodotin dose reductions
  - Supportive care, like lubricating eye drops

Popat, ASH 2020 #2278; Lonial, ASH 2020 #3224

Outline

- Overview of the multiple myeloma clinical practice guideline
- Pearls for:
  - Monoclonal antibody therapies
  - Antibody-drug conjugates
  - CAR T therapies
  - T cell engager therapies
- Discussion and Q&A

Comparing CAR T and T cell engagers

	CAR T cells	T cell engagers
Structure	Synthetic gene construct encoding an scFv against tumor antigen linked to activation/costimulatory motifs	Recombinant protein with two specificities: one for tumor antigen and one for T cell antigen (usually CD3)
Effector cell types	Engineered CD8+ and CD4+ T cells	Endogenous CD8+ and CD4+ T cells
Trafficking	Active	Passive
Clinical applications	Pre-treatment lymphodepletion followed by a single infusion	No lymphodepletion; repeat administration and continuous infusions
Specificity	Manufactured for each patient	“Off-the-shelf”
Availability	Limited to REMS program facilities	Most cancer centers
Typical CRS incidence	80-90+% of patients; median onset 1-7 days	30-40% of patients; occurs during infusion
Response kinetics	TTR: 1-2 months; DoR: 10+ months	TTR: 1 month; DoR: 8 months
Secondary immunosuppression	Yes – due to lymphodepletion and targeting immune cell antigens	Yes – due to targeting immune cell antigens

Topp, ASCO 2019; Slaney, Cancer Disc 2018

BCMA CAR T cells

Trial	Phase	Product	ORR	CRS %	ICANS %	Survival data
KARMMA-1	2	Idecabtagene vicleucel (bb2121)*	73%	84%	18%	mPFS: 8.8 mo; 12.1 mo @ high dose
CARTITUDE-1	1b/2	JNJ-4528	97%	92%	16.5%	12-month: 77% progression-free
LUMMICAR-2	1b/2	CT053	94%	77-83%	15-17%	NR
PRIME	1/2	P-BCMA-101	67% with nanoplasmid; 44-75% with original	17%	3.8%	NR
CRB-402	1	Bb21217	68%	70%	16%	mDOR: 17 months
UNIVERSAL	1	Allo-715	60-67%	45%	0%	NR

*Ide-cel was FDA-approved in March 2021 for R/R MM after 4+ prior therapies, after the Guideline published

Early T cell engager studies

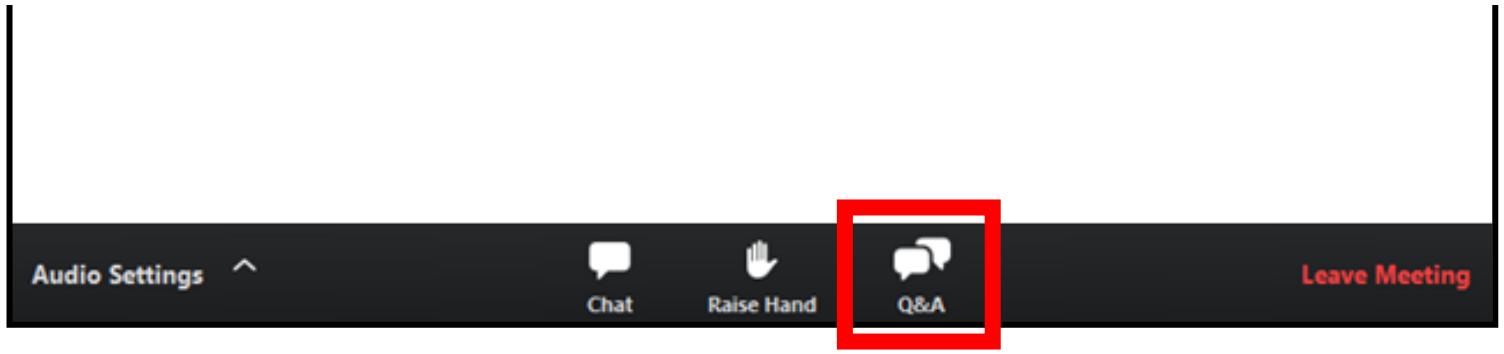
Drug	Target	N	Dosing	ORR	CRS %	ICANS %
Teclistamab	BCMA	68	SC weekly for RP2D	69%	55%	5%
TNB-383B	BCMA	58	Q3W	80% at higher doses	45%	0%
REGN-5458	BCMA	49	Q2W	63% at highest doses	39%	12%
AMG-701	BCMA	85	Weekly	83% at highest dose	64%	3.8%
Talquetamab	GPRC5D	157	Weekly or Q2W, IV or SC	66% at higher doses	54%	46%
Cevostamab	FcRH5	53	Q3W	53% at higher doses	76%	28%

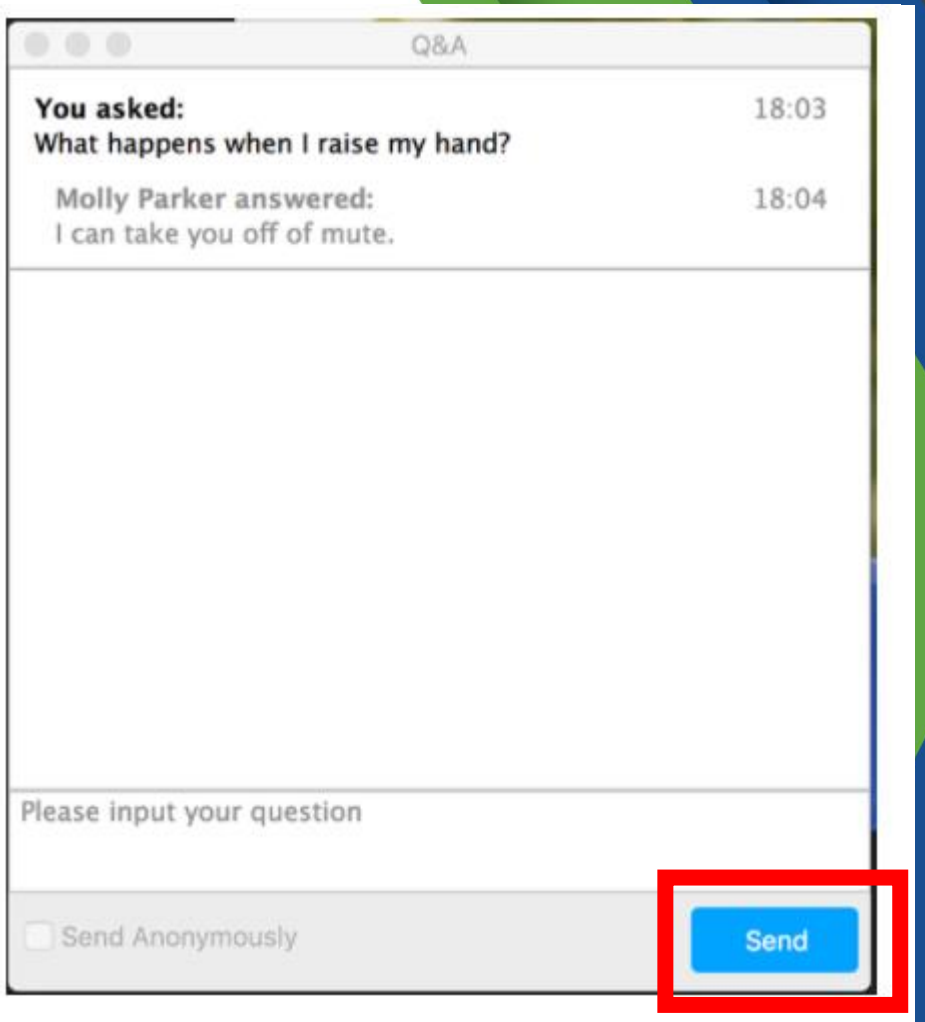
Outline

- Overview of the multiple myeloma clinical practice guideline
- Pearls for:
  - Monoclonal antibody therapies
  - Antibody-drug conjugates
  - CAR T therapies
  - T cell engager therapies
- Discussion and Q&A

How to submit questions

- Click the “Q&A” icon located on at the bottom of your Zoom control panel
- Type your question in the Q&A box, then click “Send”
- Questions will be answered in the Question & Answer session at the end of the webinar (as time permits)





Society for Immunotherapy of Cancer

Cancer Immunotherapy GUIDELINES

Case Studies in Immunotherapy for the Treatment of Multiple Myeloma

June 16, 2021, 5:00-6:00 pm ET

Learn more and register:
https://www.sitcancer.org/research/cancer-immunotherapy-guidelines/myeloma

Journal for ImmunoTherapy of Cancer

Earn CME Credit as a *JITC* Reviewer

JITC also cooperates with reviewer recognition services (such as Publons) to confirm participation without compromising reviewer anonymity or journal peer review processes, giving reviewers the ability to safely share their involvement in the journal.

Learn how to become a reviewer at sitcancer.org/jitc

Targets for Cancer Immunotherapy: A Deep Dive Seminar Series

Eight online seminars will address key questions in the field of cancer immunotherapy **drug development**

SEMINAR 1 – TGF-BETA: A DEEP DIVE IN CANCER IMMUNOTHERAPY TARGETS – May 26, 2021, 2–4 p.m. EDT

SEMINAR 2 – THE TIGIT PATHWAY: A DEEP DIVE IN CANCER IMMUNOTHERAPY TARGETS – June 29, 2021, 2-4 p.m. EDT

Learn more and register at:

https://www.sitcancer.org/education/deepdive