Exploring the Current and Future Role of B-Cell Maturation Antigen-Directed Therapy in the Management of Multiple Myeloma

Monday, February 7, 2022
5:00 PM – 6:00 PM ET

Faculty

Jesús G Berdeja, MD
Noopur Raje, MD

Moderator

Neil Love, MD

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Faculty

Jesús G Berdeja, MD
Director of Multiple Myeloma Research
Sarah Cannon Research Institute
Tennessee Oncology
Sarah Cannon Center for Blood Cancer
Nashville, Tennessee

Noopur Raje, MD
Director, Center for Multiple Myeloma
Massachusetts General Hospital Cancer Center
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Commercial Support

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Dr Love — Disclosures

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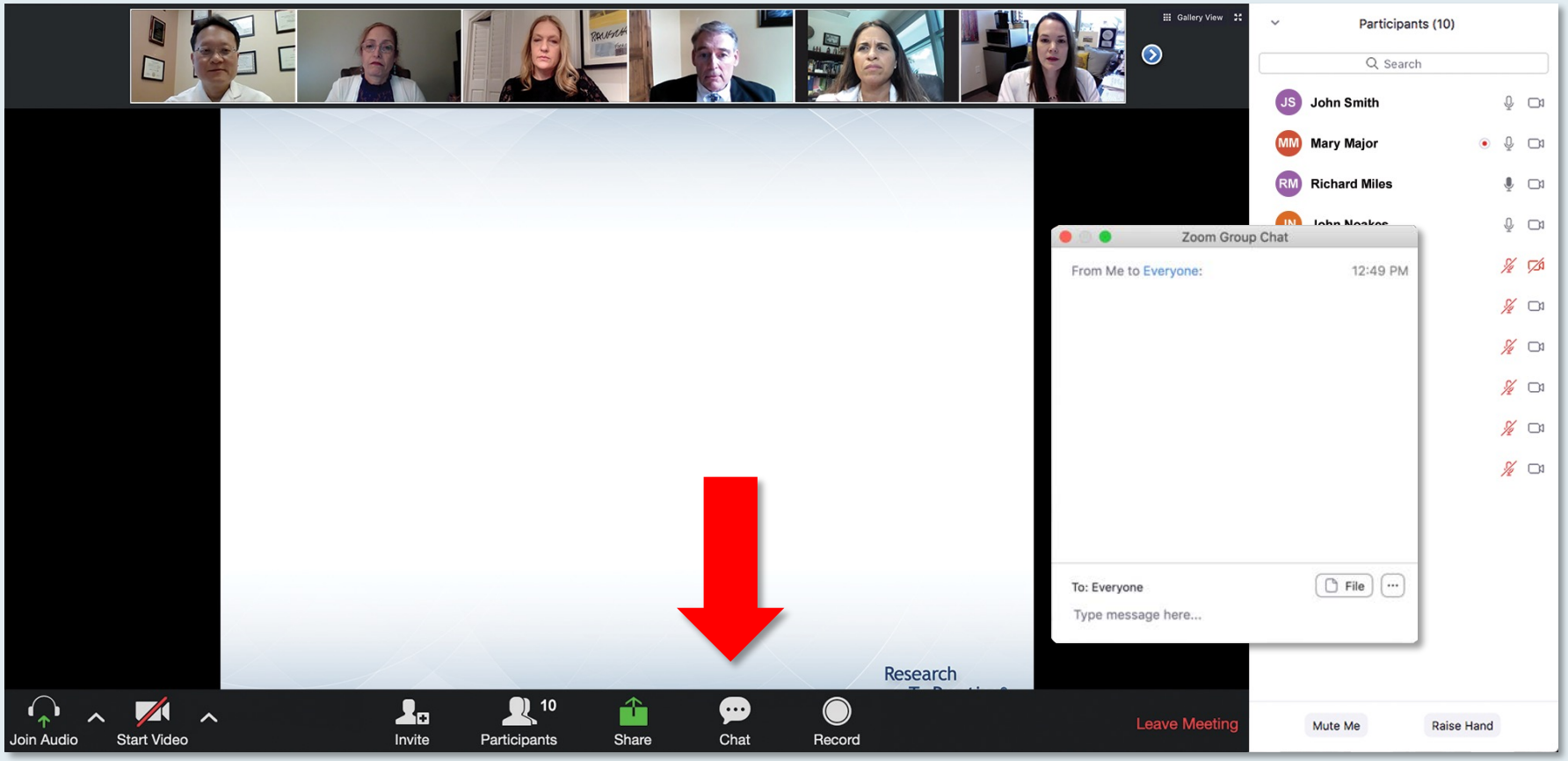
We Encourage Clinicians in Practice to Submit Questions



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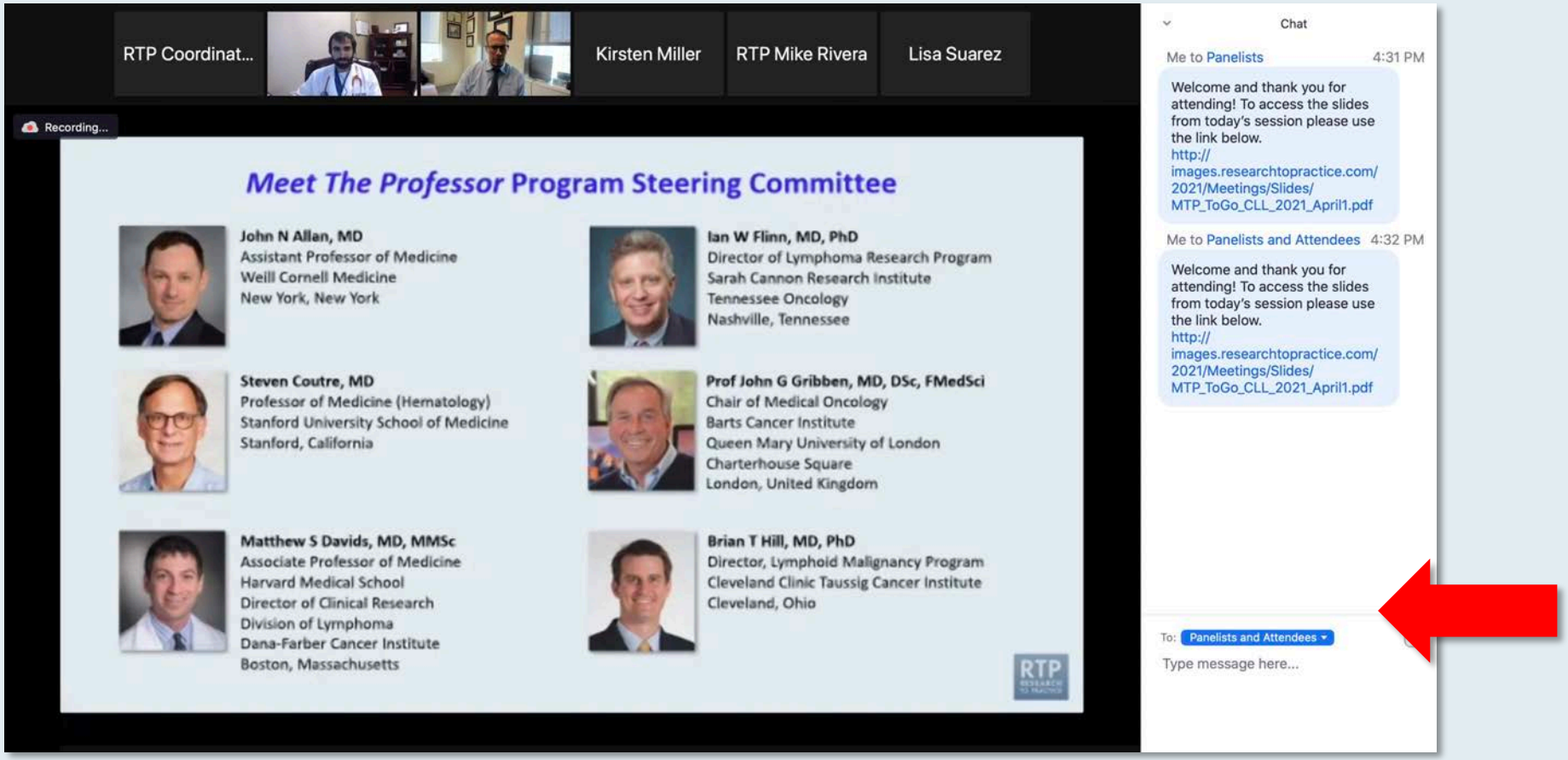
Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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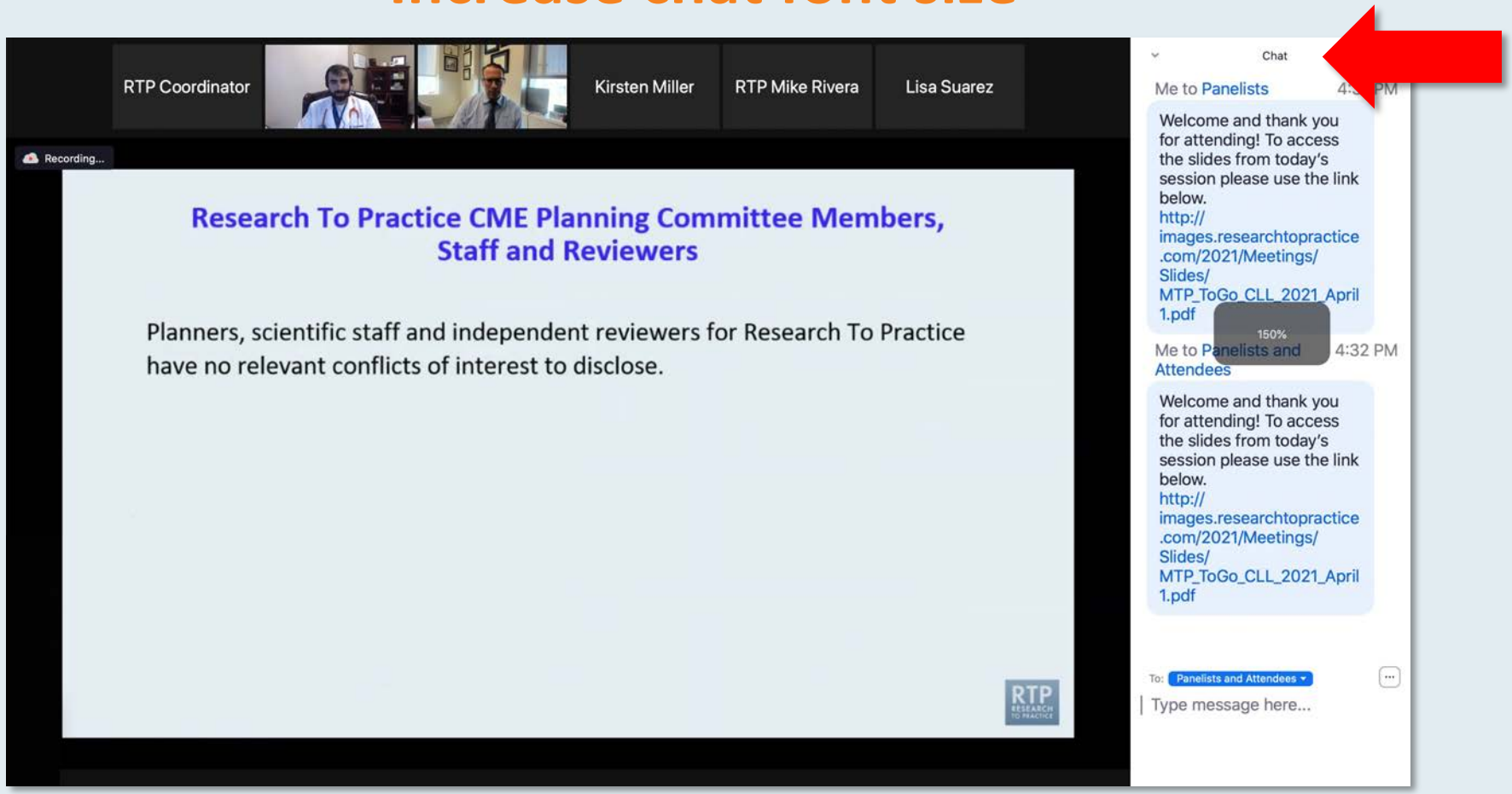
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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WITH DR NEIL LOVE

Managing Transplant-Ineligible Newly Diagnosed Multiple Myeloma

DR SAAD ZAFAR USMANI
MEMORIAL SLOAN KETTERING CANCER CENTER

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Key Considerations in the Optimal Clinical Care of Patients with Small Cell Lung Cancer

Wednesday, February 9, 2022
5:00 PM – 6:00 PM ET

Faculty

Luis Paz-Ares, MD, PhD
Jared Weiss, MD

Moderator

Neil Love, MD

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Recent Advances and Real-World Implications in Medical Oncology: A Daylong Multitumor Educational Symposium in Partnership with the North Carolina Oncology Association and the South Carolina Oncology Society

Saturday, February 12, 2022
8:30 AM – 4:00 PM ET

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Recent Advances and Real-World Implications in Medical Oncology: Agenda

Module 1	**Chronic Lymphocytic Leukemia and Lymphomas** 8:35 AM – 9:40 AM
Module 2	**Multiple Myeloma** 9:40 AM – 10:45 AM
Module 3	**Genitourinary Cancers** 10:45 AM – 11:50 AM
Module 4	**Breast Cancer** 12:30 PM – 1:35 PM
Module 5	**Gastrointestinal Cancers** 1:35 PM – 2:40 PM
Module 6	**Lung Cancer** 2:40 PM – 3:45 PM

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Meet The Professor

Current and Future Role of Immunotherapy in the Management of Lung Cancer

Tuesday, February 15, 2022
5:00 PM – 6:00 PM ET

Faculty

Charu Aggarwal, MD

Moderator

Neil Love, MD

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Prostate Cancer (Part 1 of a 2-Part Series)

Thursday, February 17, 2022

7:00 PM – 9:00 PM PT

Faculty

Neeraj Agarwal, MD
Himisha Beltran, MD
Fred Saad, MD
A Oliver Sartor, MD

Moderator

Alan H Bryce, MD

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Bladder Cancer (Part 2 of a 2-Part Series)

Friday, February 18, 2022

6:30 PM – 8:00 PM PT

Faculty

Shilpa Gupta, MD
Daniel P Petrylak, MD
Guru Sonpavde, MD

Moderator

Sumanta Kumar Pal, MD

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TO PRACTICE

Meet The Professor

Optimizing the Management of Acute Myeloid Leukemia

Thursday, February 24, 2022
5:00 PM – 6:00 PM ET

Faculty
Amir Fathi, MD

Moderator
Neil Love, MD

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Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Tuesday, March 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Michael E Williams, MD, ScM

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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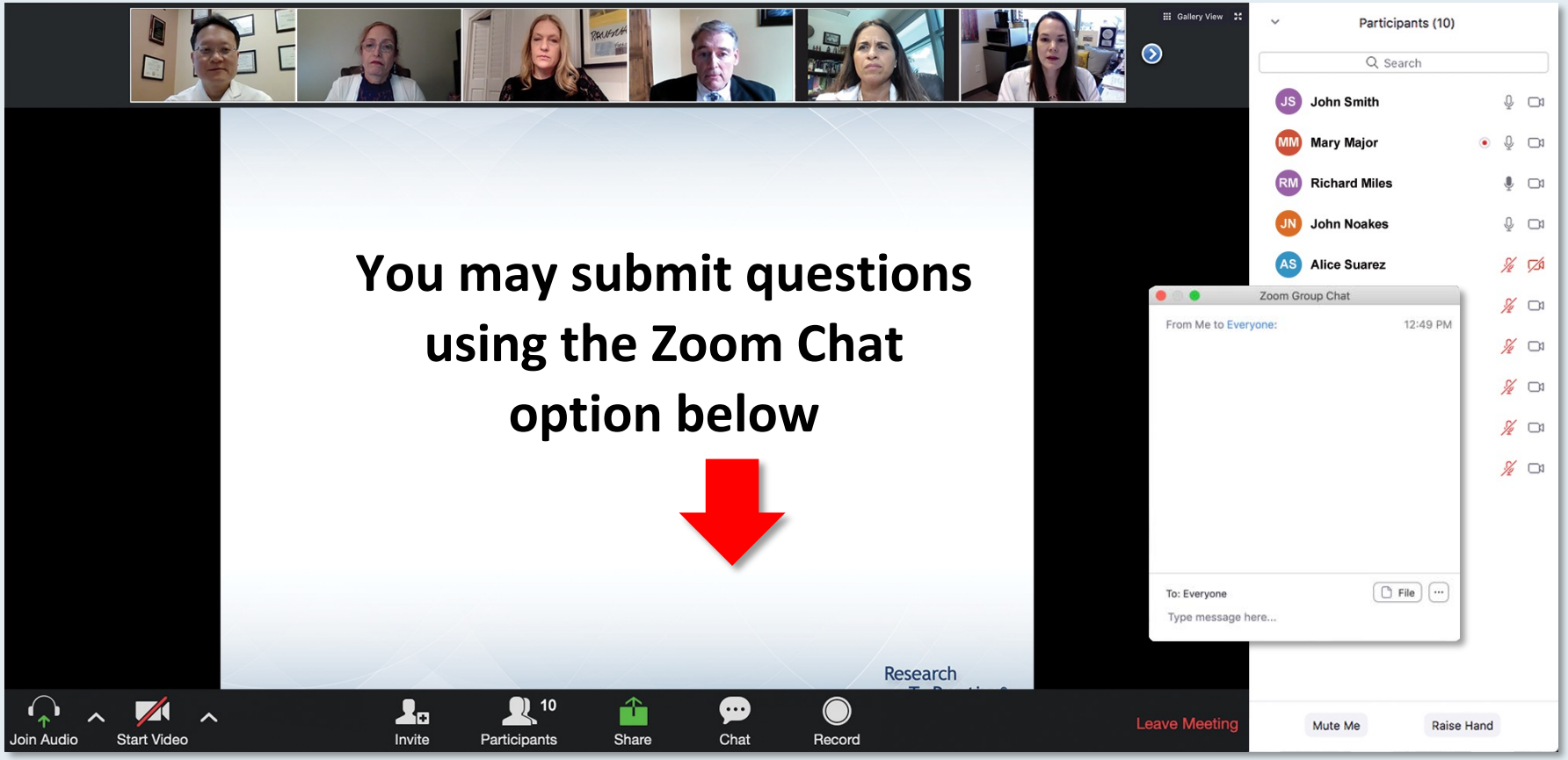

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Optimal Integration of Currently Available Anti-BCMA Strategies into the Management of RR Multiple Myeloma

Jesús G. Berdeja, M.D.
Director of Myeloma Research
Sarah Cannon Research Institute
Nashville, TN, USA

SARAH CANNON
Research Institute

Investigational Bispecific Antibodies Targeting BCMA in MM

Noopur Raje, MD
Center for Multiple Myeloma
MGH Cancer Center

Professor of Medicine
Harvard Medical School

MASSACHUSETTS GENERAL HOSPITAL

MASSACHUSETTS GENERAL HOSPITAL
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Agenda

Introduction: Monday Night with Research To Practice

MODULE 1: Targeting BCMA

MODULE 2: CAR T-Cell Therapy

MODULE 3: Bispecific Antibodies

MODULE 4: Belantamab Mafodotin

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What were you doing in 2010?

1. High school or earlier
2. College
3. Medical school
4. Fellowship/residency
5. In practice less than 10 years
6. In practice 10-25 years
7. In practice for more than 25 years
8. Retired

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TO PRACTICE

Exploring the Current and Changing Paradigm for the Management of Newly Diagnosed Diffuse Large B-Cell Lymphoma

Wednesday, February 2, 2022
5:00 PM – 6:15 PM ET

Faculty

Christopher R Flowers, MD, MS
Neha Mehta-Shah, MD, MSCI
Grzegorz Nowakowski, MD

Moderator

Neil Love, MD

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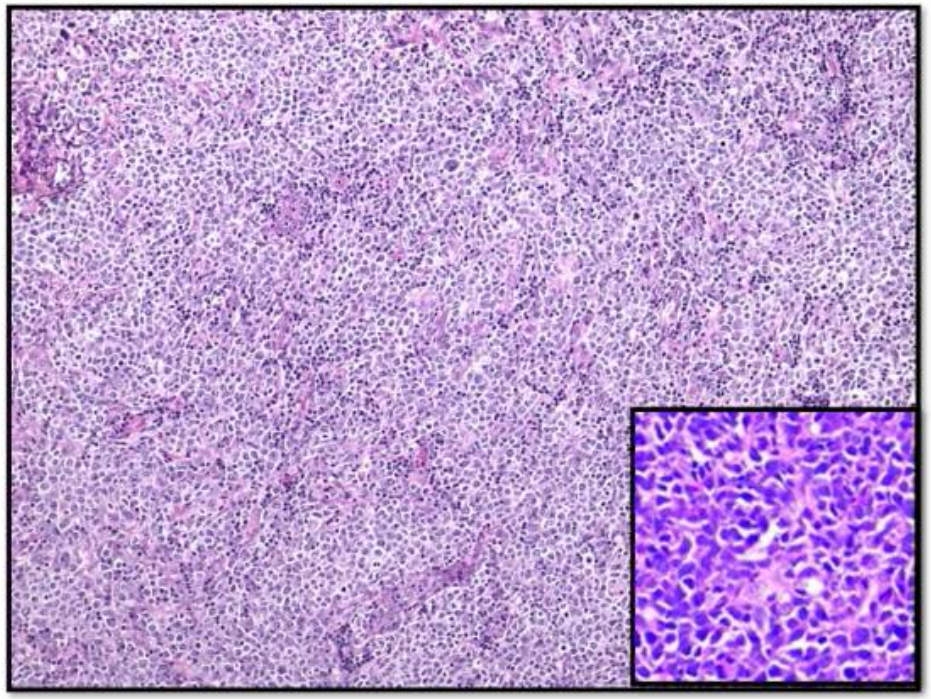
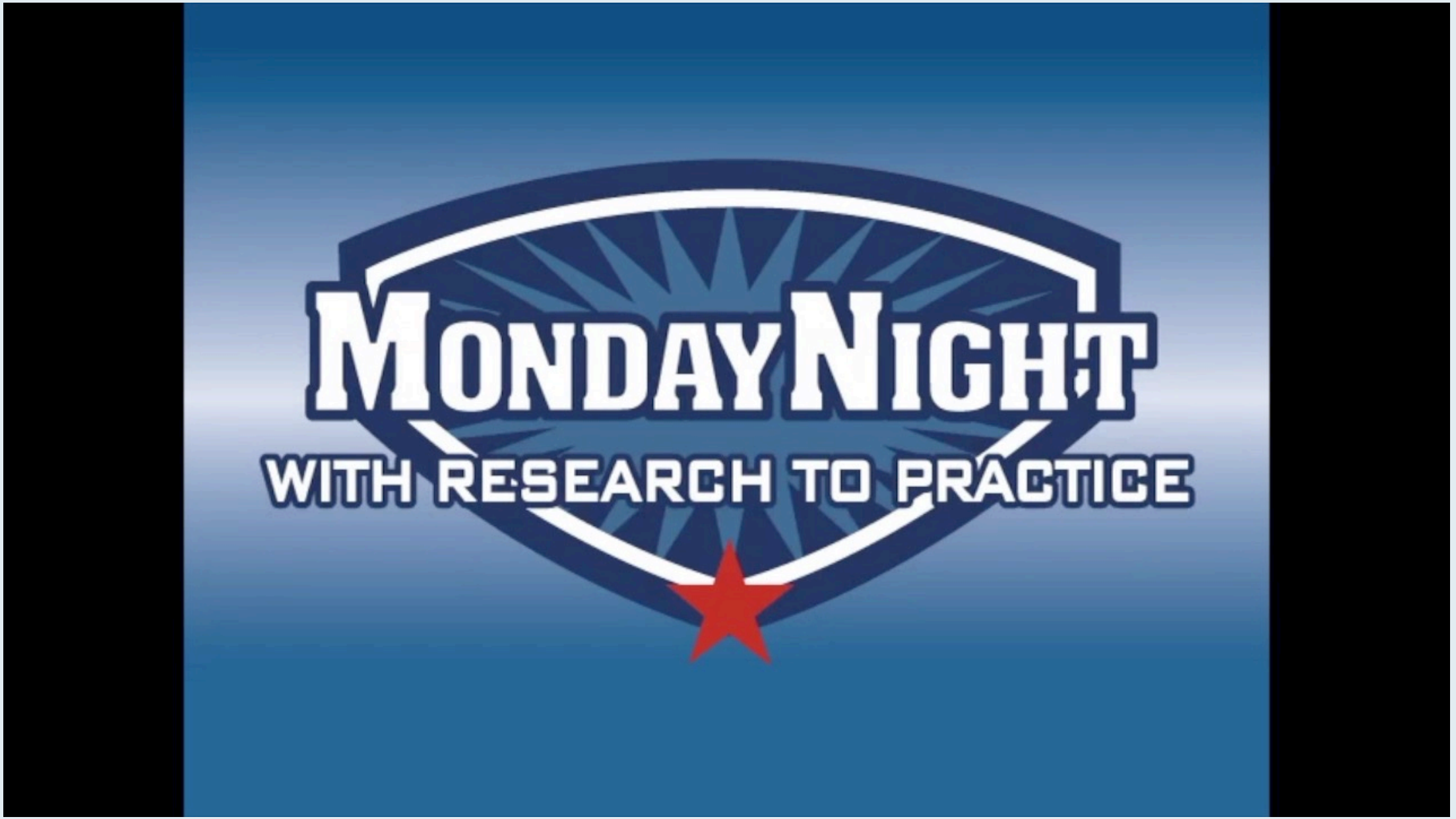
DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)

- Most common aggressive type of non-Hodgkin lymphoma
  - 30-40% of all non-Hodgkin lymphoma
  - Affects 7/100,000 people per year in US
- Heterogeneous entity
  - DLBCL, not otherwise specified
    - Germinal Center phenotype
    - Non-Germinal Center phenotype
  - T-cell/histiocyte-rich large B-cell lymphoma
  - Primary Cutaneous DLBCL, leg type
  - EBV+ DLBCL of the elderly
  - Primary CNS lymphoma
  - Primary Mediastinal DLBCL
  - CD5+ DLBCL
  - High grade B-cell lymphoma, not otherwise specified



Courtesy of Neha Mehta-Shah, MD, MSCI



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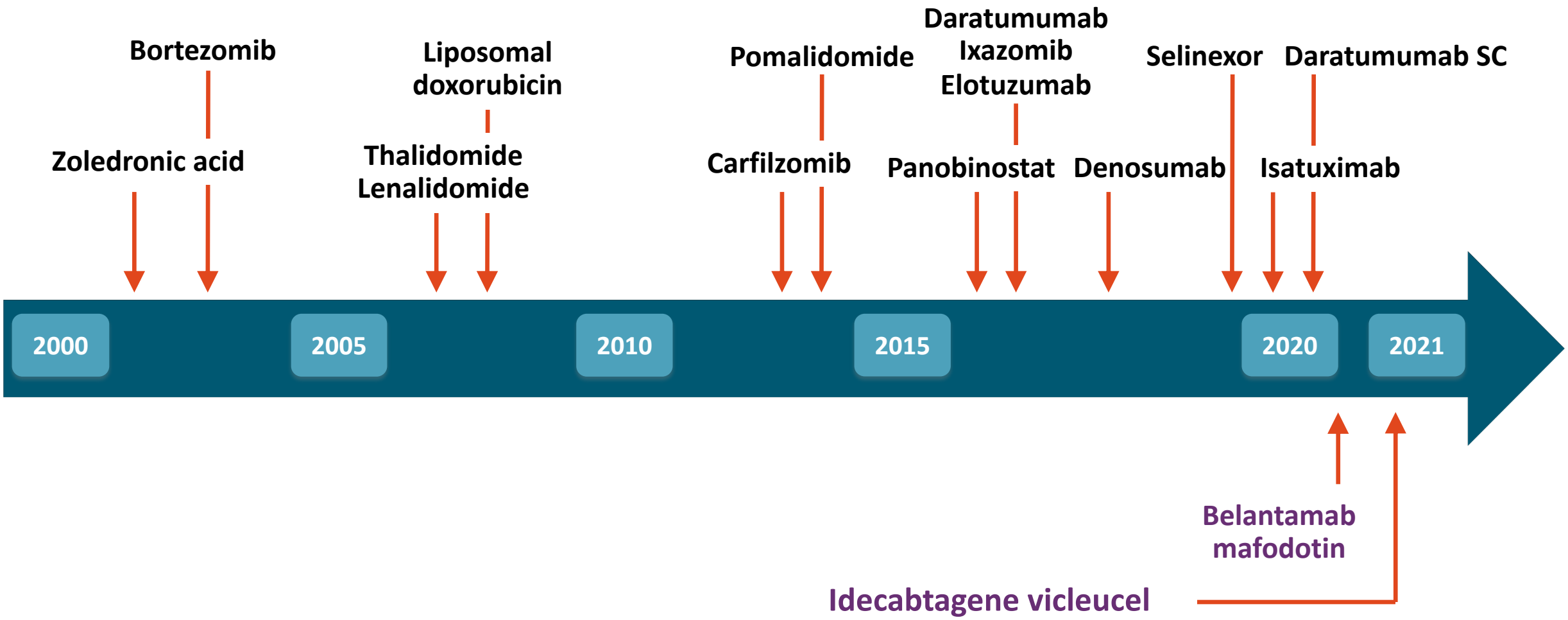
Myeloma Drugs Approved Since 2000



Courtesy of Jesús G Berdeja, MD

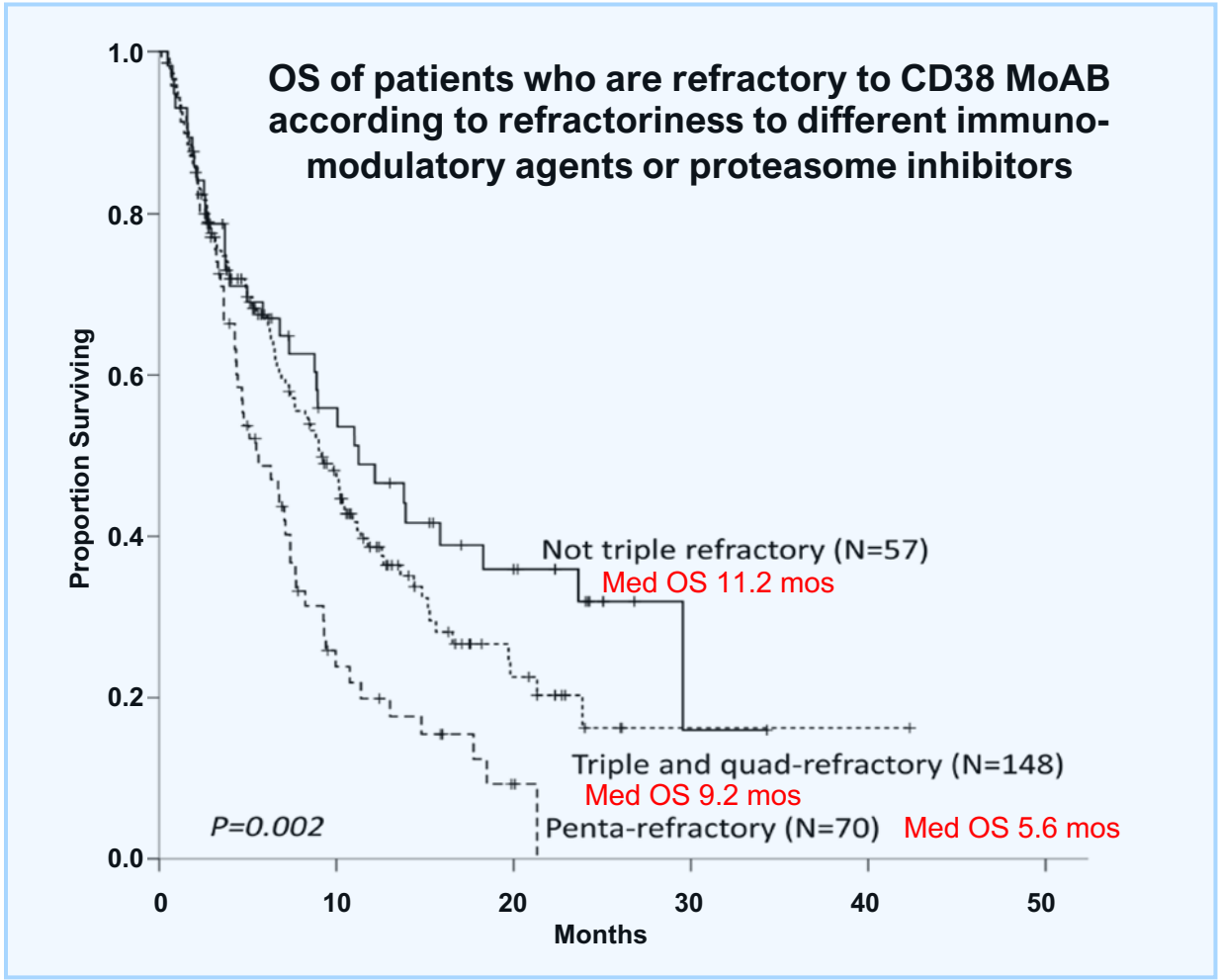
Despite Progress in MM There Remains Need for New Tx

The MAMMOTH study

- Retrospective study of 275 patients from 14 academic centers in the US who had MM refractory to anti-CD38 monoclonal antibodies (MoAB)
- Median number of prior therapies = 4 (range 1–16)
- Prior autologous stem cell transplantation = 72%

Efficacy

- mOS from T_0 for the entire cohort: 8.6 months (95% CI 7.5–9.9)
- At least one subsequent treatment regimen was given post T_0 in 249 (90%) patients
  - ORR to first regimen after T_0 = 31%
  - mPFS = 3.4 months
  - mOS = 9.3 months

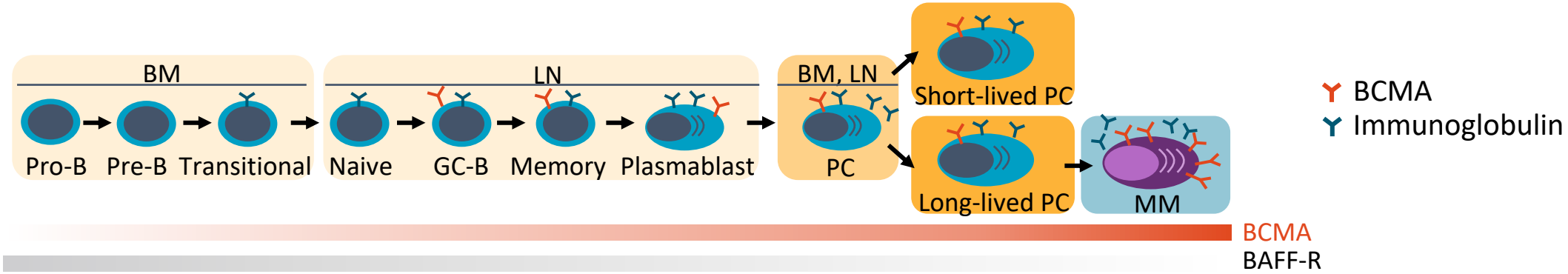


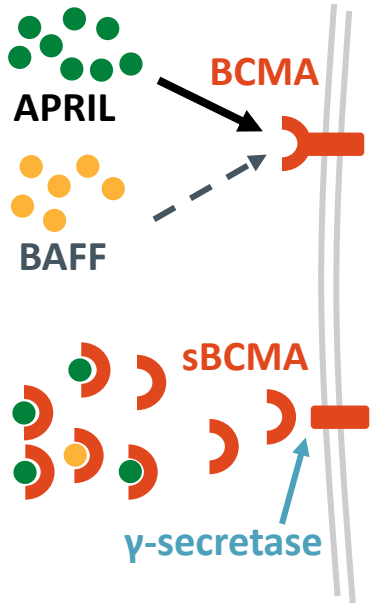
Gandhi UH, et al. *Leukemia*. 2019;33(9):2266–2275.

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

BCMA as a Target in Myeloma Treatment





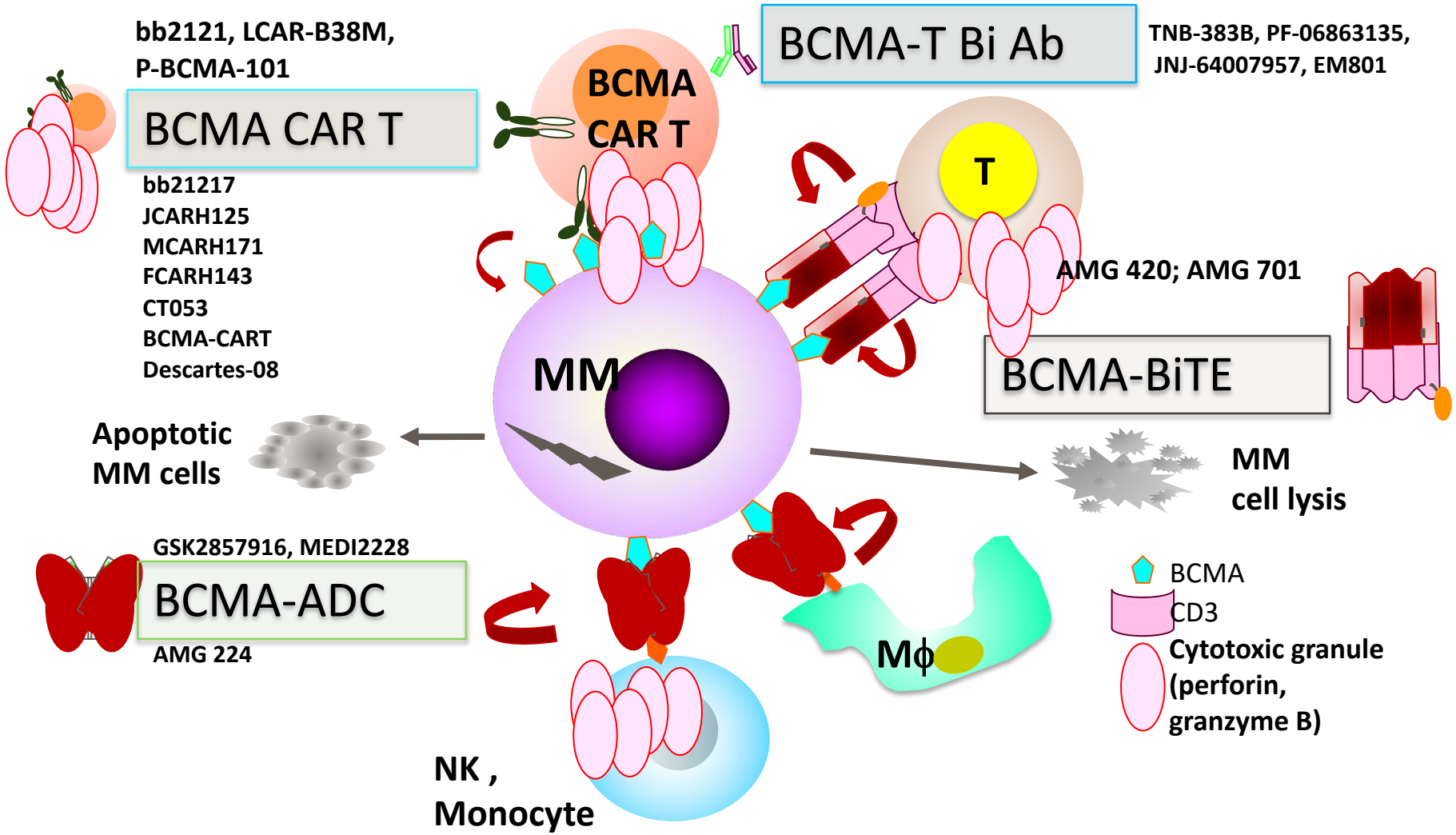
- BCMA: antigen expressed specifically on PCs and myeloma cells
- Higher expression on myeloma cells than normal PCs
- Not expressed in other tissues

- Cell-surface receptor in TNF superfamily
- Receptor for APRIL and BAFF
- Key role in B-cell maturation and differentiation
- Promotes myeloma cell growth, chemotherapy resistance, immunosuppression in bone marrow microenvironment

Cho. Front Immunol. 2018;9:1821. Moreaux. Blood. 2004;103:3148. Sanchez. Br J Haematol. 2012;158:727.

Courtesy of Jesús G Berdeja, MD

BCMA-Targeted Immunotherapy in MM

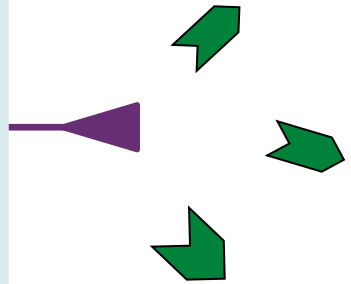


Courtesy of Noopur Raje, MD

BCMA-Targeted Therapies for Multiple Myeloma

Myeloma cell

BCMA



Antibody–Drug Conjugates

*Belantamab mafodotin**

MEDI2228

CC-99712

Bispecific Antibody Therapies

AMG 701

CC-93269

REGN5458

JNJ-64007957 (Teclistamab)

PF-06863135 (Elranatamab)

TNB-383B

CAR T-Cell Therapies

*Idecabtagene vicleucel**

Ciltacabtagene autoleucel

P-BCMA-101

bb21217

ALLO-715

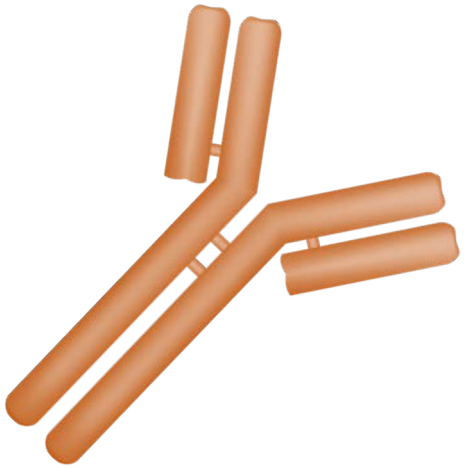
*Now approved for adults with R/R multiple myeloma after ≥4 prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal Ab (August 2020)

*Now approved for adults with R/R multiple myeloma after ≥4 prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal Ab (March 2021)

Courtesy of Jesús G Berdeja, MD

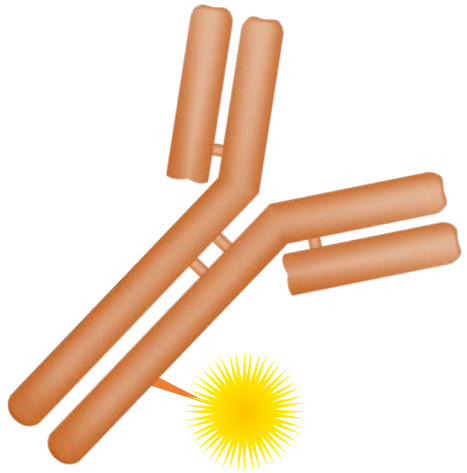
Types of Antibodies

Naked



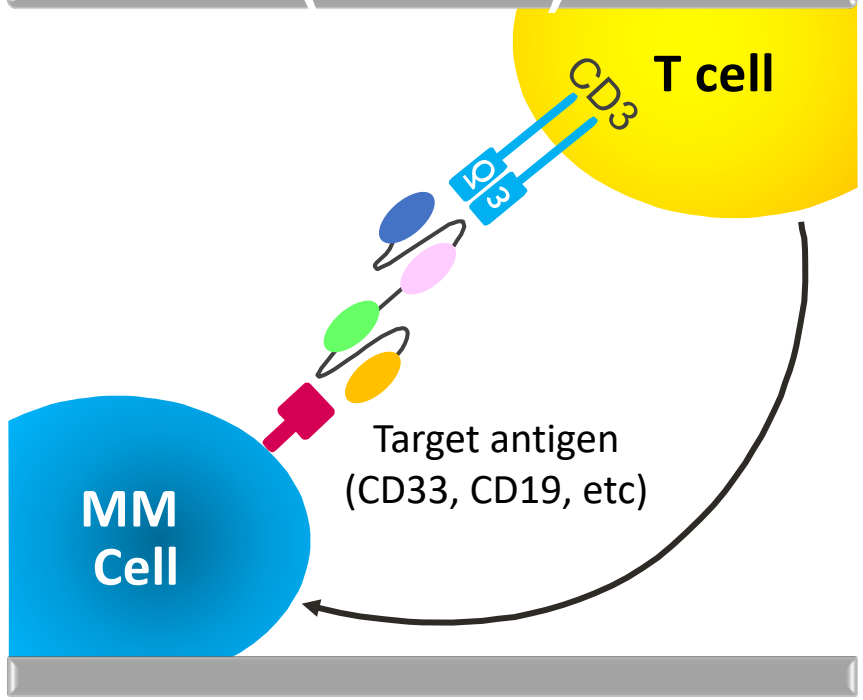
Nothing is attached

Antibody Drug Conjugates (ADC)



A toxin or radioactive isotope is attached

Bispecific Antibodies (BsAbs)



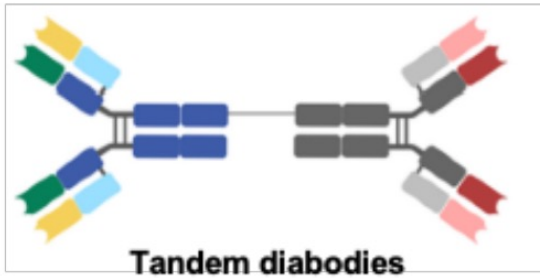
Engineered so that one end binds to MM cell, the other end binds to T cell

Courtesy of Noopur Raje, MD

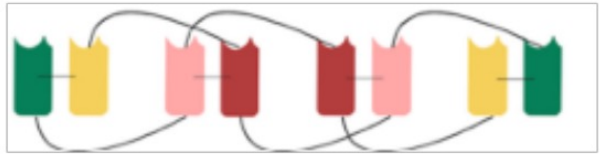
BsAbs – Many Different Platforms

Bispecific T-cell Engager or BiTE

Dual Affinity Re-Targeting or DART

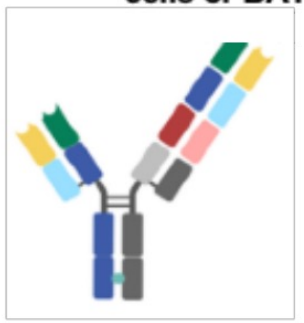


Tandem diabodies or TandAb

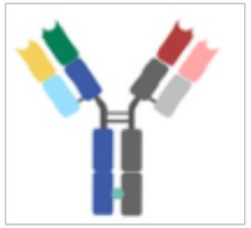


BsAb armed activated T-cells or BAT

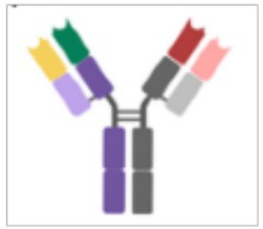
T-cell dependent BsAb Xmab



CrossMAb



Duobody



Trifunctional Antibody or TriFAb

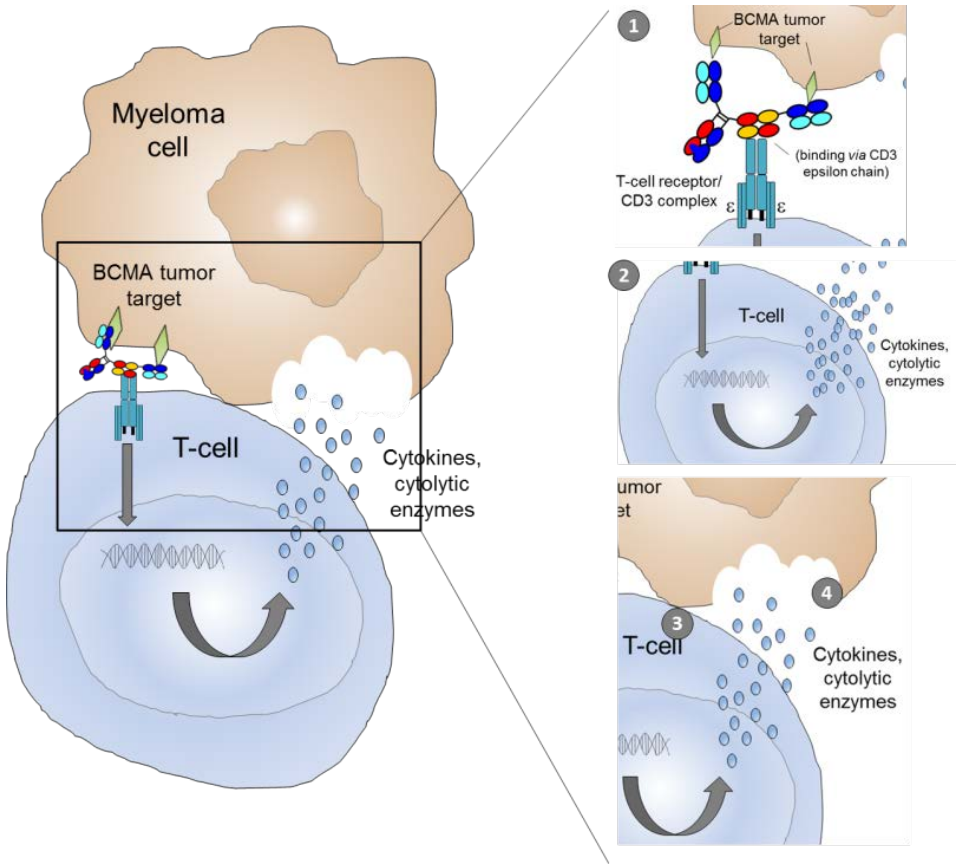
Courtesy of Noopur Raje, MD

Adapted from Lejeune M et al. Front Immunol 2020 11:762.

BCMA bispecific antibodies in myeloma

- **Potential to overcome the limitations of immunosuppressive tumor microenvironment by redirecting T cells to kill tumor target cells**
- BCMA (B-cell maturation antigen, CD269)
- **IgG-like bispecific antibody** (long serum half-life, retain Fc function):[1–3]
  - Anti-BCMAxCD3[4]
  - Ab-957[1]
  - CC-93269[2,3]
  - Bi-Fab[5]
- **Non-IgG** like BiTE® (better tissue penetrance, access to epitopes):
  - BI 836909[6]

Mechanism of action of CC-93269 BCMA-TCB



α-BCMA: bivalent high affinity binding
α-CD3ε chain: monovalent low affinity binding

BCMA, B cell maturation antigen; CTL, cytotoxic T cell; Ig, immunoglobulin; TCB, T-cell bispecific.

1.Pillarisetti K, *et al.* Abstract 2116; Presented at ASH 2016; San Diego, California; 2. Seckinger A, *et al. Cancer Cell* 2017;**31**:396–410; 3. Cho S-F, *et al. Front Immunol* 2018;**9**:1821; 4 Panowski SH, *et al.* Abstract 383; Presented at ASH 2016; San Diego, California; 5. Ramadoss NS, *et al. J Am Chem Soc* 2015;**137**:5288–91; 6. Hipp S, *et al. Leukemia* 2017;**31**:1743–51.

Courtesy of Noopur Raje, MD

Agenda

Introduction: Monday Night with Research To Practice

MODULE 1: Targeting BCMA

MODULE 2: CAR T-Cell Therapy

MODULE 3: Bispecific Antibodies

MODULE 4: Belantamab Mafodotin

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Case Presentation – Dr Raje: A 74-year-old man with multiregimen-relapsed MM who receives CAR T-cell therapy

A 74-year-old male who presented with kappa light chain MM.
Received RVD followed by ASCT.
Relapsed and was treated with Dara PD — developed rapidly progressive disease with EMD.
Received 3 cycles of DCEP and came for further evaluation.
Was offered CAR T cells against BCMA on clinical trial.
Was treated in the interim with Dara KPd.
Received CAR T cells-BB 21217.

Remains in remission with MRD-negative disease for 22 months.

Case Presentation – Dr Berdeja: A 67-year-old man with multiregimen-relapsed MM who receives CAR T-cell therapy

- 67-yr-old man diagnosed with R-ISS II IgGK multiple myeloma with standard-risk cytogenetics
- Initial treatment: RVd therapy; achieved a VGPR and subsequently received HDM and autograft
- After 24 mos of maintenance therapy, his M spike increased consistent with PD
- Treated with daratumumab, bortezomib, dex; achieved a VGPR, lasting 12 mos
- Treated with elotuzumab, pomalidomide, dex; achieved a PR, lasting 10 mos

Case Presentation – Dr Berdeja: A 67-year-old man with multiregimen-relapsed MM who receives CAR T-cell therapy (continued)

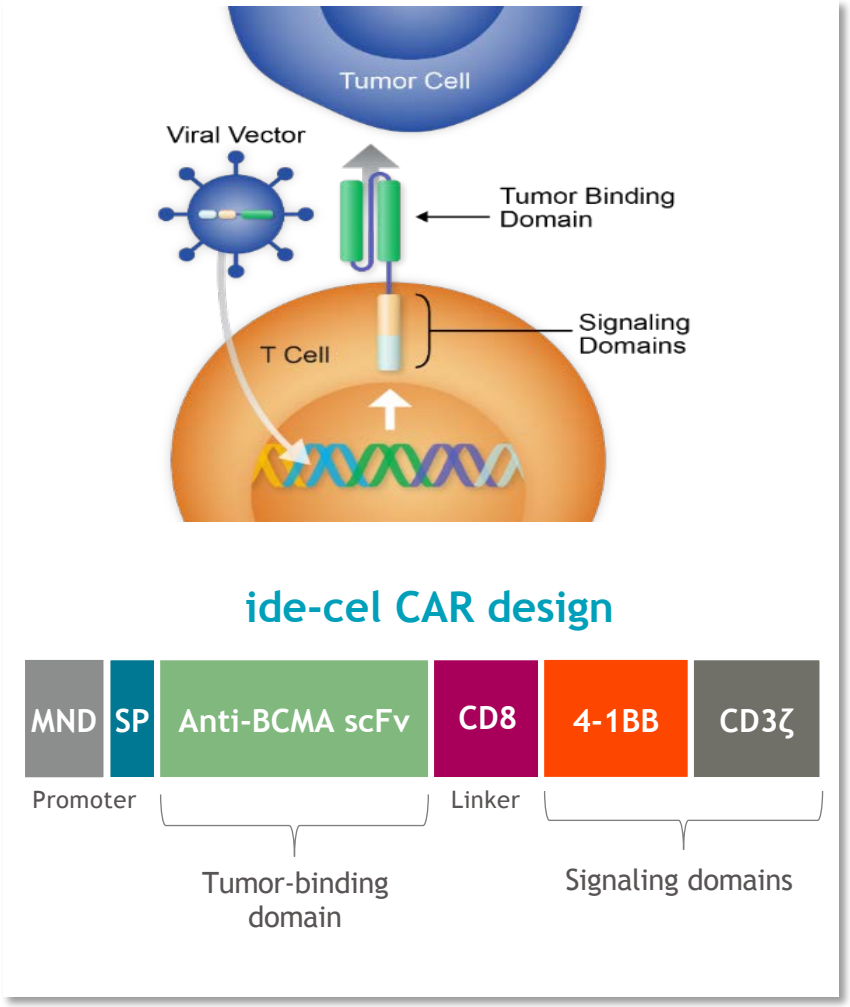
- Treated with carfilzomib, pomalidomide, dex; achieved a PR
- 6 mos later, patient presents with increasing back pain and found to have a new pathological fracture with an increase in M protein to 1 g/dL HPI
- He was referred for CAR T-cell trial with ide-cel
- Baseline bone marrow with 70% plasmacytosis, FISH+ for Dup(1q) and t(4;14)
- He underwent leukapheresis for T-cell collection successfully
- During CAR T manufacturing he underwent an abbreviated cycle of dara/btz/dex with SD
- He received fludarabine and cyclophosphamide LP chemo

Case Presentation – Dr Berdeja: A 67-year-old man with multiregimen-relapsed MM who receives CAR T-cell therapy (continued)

- He was admitted to the hospital and received ide-cel
- On D +1 he developed fever and hypotension responsive to fluids. He was felt to have Grade 2 CRS and given tocilizumab x 1 with prompt resolution. He did well thereafter and was discharged home
- Main issue post CART was persistent cytopenias requiring intermittent transfusions and GCSF prn but eventually resolved
- D30 response assessment was VGPR, MRD- 10^{-6} by 6 mos
- Response lasted 20 months

SARAH CANNON

Phase II KarMMa: Idecabtagene Vicleucel (Ide-cel) in RRMM



- RRMM
- ≥3 prior regimens with ≥2 consecutive cycles each (or best response of PD)
- Previously exposed to:
  - IMiD agent
  - Proteasome inhibitor
  - Anti-CD38 antibody
- Refractory to last prior therapy per IMWG*

Endpoints

- **Primary:** ORR (null hypothesis ≤50%)
- **Secondary:** CRR (key secondary; null hypothesis ≤10%), Safety, DOR, PFS, OS, PK, MRD‡, QOL, HEOR
- **Exploratory:** Immunogenicity, BCMA expression/loss, cytokines, T cell immunophenotype, GEP in BM

Screened N=158

↓

Leukapheresed N=140

↓

Treated N=128
(Target Dose CAR+ T cells)

150×10^6	n=4
300×10^6	n=70
450×10^6	n=54

↓

Median Follow-up (mo)

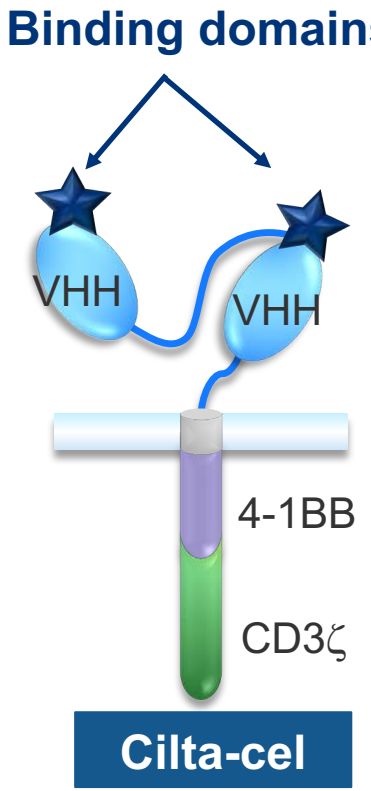
150×10^6	18.0
300×10^6	15.8
450×10^6	12.4
Total	24.8

Munshi et al. NEJM 2021;384:705-16.

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

CARTITUDE-1: A phase 1b/2 study of cilta-cel in RRMM

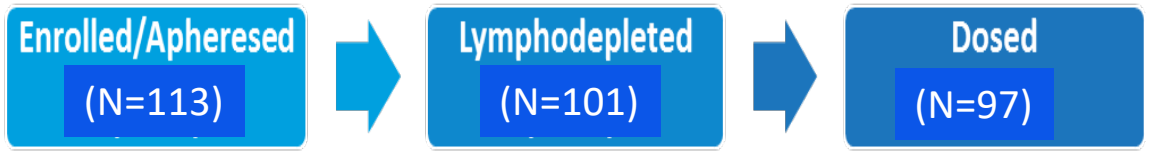


Key Eligibility Criteria

- Progressive MM per IMWG criteria
- Received ≥3 prior therapies or double refractory
- Prior PI, IMiD, anti-CD38 therapy

Primary Objectives

- **Phase 1b**: Characterize safety and confirm recommended phase 2 dose
- **Phase 2**: Evaluate efficacy of cilta-cel



- Target JNJ-4528 Infusion: 0.75x106 (0.5 – 1.0x106) CAR+ viable T cells/kg
- Median administered dose = $0.71x10^6$ ($0.51 – 0.95x10^6$) CAR+ viable T cells/kg

Special Features

- Ciltacabtagene autoleucel (cilta-cel; JNJ-68284528) contains 2 BCMA-targeting single chain antibodies designed to confer avidity
- Identical to the CAR construct used in the LEGEND-2 study

Berdeja et al. Lancet 2021; 398(10297):314-324.

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

CAR T-Associated Toxicities

Acute phase (D0-30)

- Cytokine Release Syndrome (CRS)
- Immune effector cell–associated neurotoxicity syndrome (ICANS)
- Cytopenias
  - MAS or HLH is a very rare and severe form
  - DIC
- B-cell aplasia and hypogammaglobulinemia
- Life threatening if not managed by expert multidisciplinary team
- Tumor lysis is rare and likely varies by disease and disease burden

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Courtesy of Jesús G Berdeja, MD

CAR T-Associated Toxicities

Late phase (D30+)

- Persistent cytopenias
- B-cell aplasia and hypogammaglobulinemia
  - ?IVIG replacement
- T-cell deficiency
  - PJP and VZV prophylaxis, other?
- Infection prophylaxis
- Residual effects of acute toxicity
- Delayed CRS and neurotoxicity are rare but can occur
- Impairment to QOL – fatigue, memory issues, not yet well described

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

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RESEARCH
TO PRACTICE

Case Presentation – Dr Raje: A 62-year-old woman with multiregimen-relapsed MM who receives a bispecific antibody

A 62-year-old African American who was diagnosed with IgA kappa multiple myeloma approximately 4 years back when she presented with an acetabular fracture.

Had a RT THR.
Was treated with RVD followed by rev maintenance—had stem cells collected but refused a transplant.
Relapsed after 18 months. Was treated with dara pom dex. Achieved a PR and then had progressive disease.
Was treated with carfilzomib and cyclophosphamide. Progressed after 6 months. Was offered anti BCMA (Elranatamab) with lenalidomide on trial.

Has been on therapy for >1 year.
Is in MRD-negative disease state.

Courtesy of Noopur Raje, MD

BCMA x CD3 Bispecific Antibodies: Summary

Therapy	Characteristics	N	Population	Safety	Response	DOR/PFS
Teclistamab[1]	▪ Bispecific ▪ IV/SC (RP2D: 1500µg/kg SC) ▪ Weekly and every other week in f/u	157	▪ At SC cohorts: ▪ Median of 5PL ▪ 79% triple refractory ▪ 38% penta refractory	▪ At RP2D: ▪ CRS 70% G1-2 ▪ Neurotox 1% (G1) ▪ Infections 50%	At RP2D, ORR: 65% with 40% sCR/CR	No mature data
AMG701[2]	▪ BiTE modified ▪ IV ▪ Weekly	82	▪ Median of 6PL ▪ 62% triple refractory	▪ CRS 55%, G3-4: 9% ▪ No ICANS ▪ 20% cytopenias	83% ORR at the top dose level and 50% VGPR	No mature data
REGN5458[3]	▪ Bispecific ▪ IV ▪ Weekly and every other week C4->	49	▪ Median of 5PL ▪ 100% triple refractory ▪ 57% penta refractory	▪ CRS 39%, no G3-4 ▪ ICANS 12% ▪ cytopenias 47% and infections 18%	62.5% at 96 mg and 95% of responders were VGPR. Some CR in lower dose levels	Preliminary median DOR: 6m
TNB-383B[4]	▪ Triple chain anti-BCMA bispecific ▪ IV fixed doses ▪ Every 3 weeks	58	▪ Median of 6PL ▪ 64% triple refractory ▪ 34% penta refractory	▪ CRS 45% and no G3-4 ▪ No ICANS ▪ Cytopenias 21% and infections 14%	80% (13% CR) at the dose levels 40-60 mg	No mature data
Elranatamab (PF-3135[5])	▪ Bispecific ▪ SC and weekly ▪ RP2D: 1000 µg/kg	30	▪ Median of 8PL ▪ 87% triple refractory ▪ 23% prior BCMA-based therapy	▪ CRS 73% and no G3-4 ▪ ICANS 20% ▪ ISR 50%	83% ORR at RP2D	No mature data

1. Usmani SZ et al. Lancet 2021. 2. Harrison SJ, et al. Presented at ASH 2020. Abstract 181. 3. Madduri D, et al. Presented at ASH 2020. Abstract 291. 4. Rodriguez C, et al. Presented at ASH 2020. Abstract 293.5. Bahlis NJ, et al. Presented at ASCO 2021. Abstract 8006.

Courtesy of Noopur Raje, MD

Novel Non-BCMA Bispecific Antibodies

Therapy	Characteristics	N	Population	Safety	Response	DOR/PFS
Talquetamab[1]	▪ G protein-coupled receptor family C group 5 member D (GPRC5D) x CD3 bispecific antibody ▪ IV or SC admin	184, 30 at RP2D (405 µg/kg))	▪ Median of 6PL (6PL at RP2D) ▪ 76% triple refractory ▪ 28% penta refractory	▪ Infections in 37% of SC and RP2D patients; G3-4 3% at RP2D ▪ Neurotoxicity in 4 SC patients; 2 (7%) at RP2D ▪ CRS 73%, G3-4 2% at RP2D	At RP2D: 70% ORR with ≥ VGPR 60%	No mature data
Cevostamab (BFCR4350A)[2]	▪ FcRH5/CD3 bispecific T-cell engager ▪ Q3W IV infusions	53	▪ Median of 6PL ▪ 72% triple refractory ▪ 45% penta refractory	▪ Thrombocytopenia 32%, G3-4 25% ▪ CRS 76%, G3-4 2% ▪ Neurotoxicity 28%, no G3-4	ORR in ≥3.6/20-mg cohorts: 53% (18/34) in all pts 63% (5/8) in pts with prior anti-BCMA	No mature data

1. Berdeja JG, et al. ASCO 2021. Abstract 8008. 2. Cohen A, et al. ASH 2020. Abstract 292.

Courtesy of Noopur Raje, MD

Phase 1 First-in-Human Study of Teclistamab in Patients With RRMM

Study Design and Patients

Teclistamab is a B-cell Maturation Antigen (BCMA) x CD3 bispecific antibody

Key eligibility criteria
- RR or intolerant to established MM therapies
- No prior BCMA-targeted therapy

Dosing Overview
- Premedications[a] were limited to step-up dosing and first full dose
  - No steroid requirement after first full dose
- Step-up dose[b]: week -1
- Initial Q2W IV dosing switched to weekly IV or SC ± step-up dosing

IV Teclistamab (N=84)
0.3-720 µg/kg
(+ step-up dosing[b])

SC Teclistamab (N=73)
80-3000 µg/kg
RP2D: 1500 µg/kg[c]

Key objectives: RP2D (Part 1), RP2D safety/tolerability (Part 2)
Antitumor activity, PK, PD

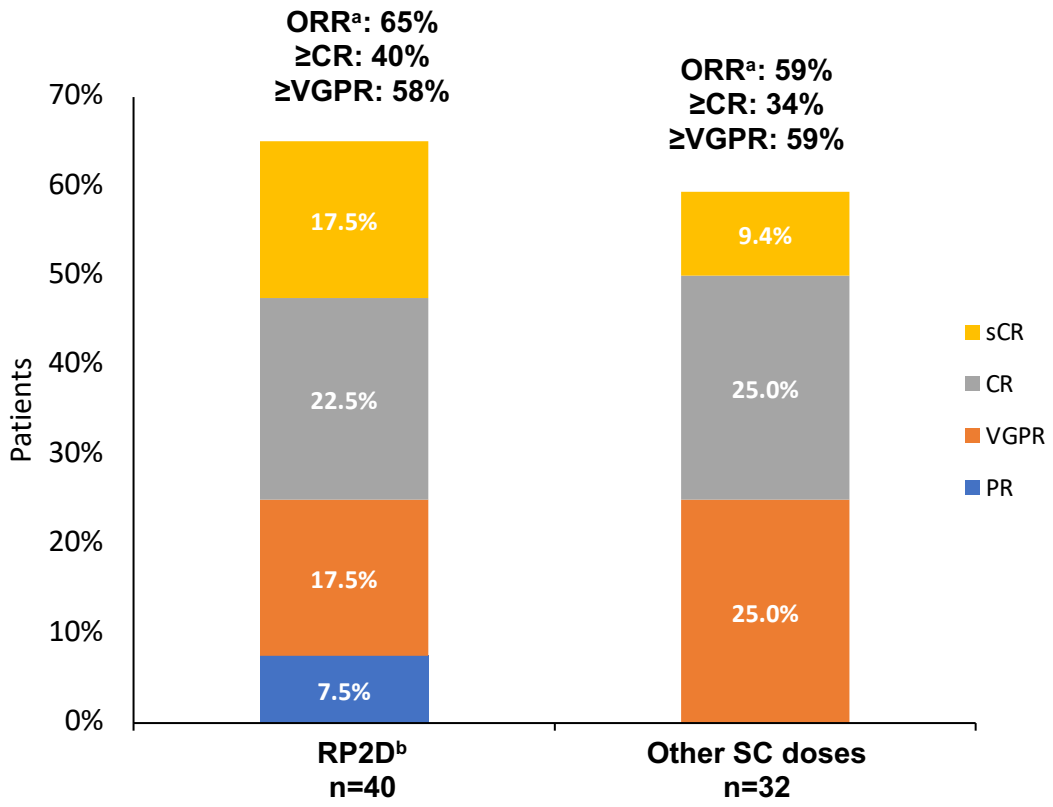
Patient Characteristics		SC Total (N=73)	RP2D (n=40)
Median age (range), years		64 (39–84)	62.5 (39–84)
Extramedullary plasmacytomas ≥1, n (%)		11 (15)	8 (20)
Median time since diagnosis (range), years		5.9 (0.8–23.5)	5.7 (0.8–17.4)
High-risk cytogenetics,[d] n (%)		16 (30)	10 (37)
Prior transplantation, n (%)		63 (86)	34 (85)
Median prior lines of therapy (range), n		5 (2–14)	5 (2–11)
Triple-class exposed,[e] n (%)		71 (97)	40 (100)
Penta-drug exposed,[f] n (%)		50 (68)	26 (65)
Refractory status, n (%)	Carfilzomib	49 (67)	27 (68)
	Pomalidomide	55 (75)	28 (70)
	Anti-CD38 antibody	68 (93)	39 (98)
	Triple-class	58 (79)	33 (83)
	Penta-drug	28 (38)	15 (38)
Refractory to last line of therapy, n (%)		64 (88)	33 (83)

•[a]Glucocorticoid, antihistamine, and antipyretic. [b]1-3 step-up doses given within 1 week before a full dose. [c]With 60 and 300 µg/kg step-up doses given within 1 week before a full dose.
[d]Defined as del(17p), t(4;14), t(14;16), t(14;20).[e]PI, IMiD, and anti-CD38, [f]2 PIs, 2 IMiDs, and anti-CD38., PK, pharmacokinetics; q2w, once every 2 weeks; RP2D, recommended phase 2 dose.

•Usmani SZ. *Lancet 2021*

Courtesy of Noopur Raje, MD

Phase 1 First-in-Human Study of Teclistamab in Patients With RRMM: Efficacy



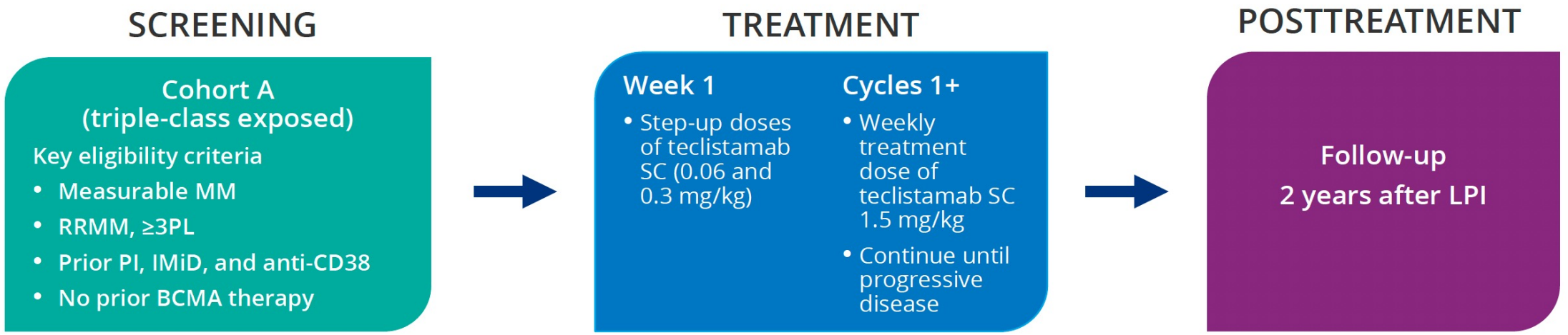
- RP2D mF/U: 6.1 months (range: 1.2-12.2)
  - Median time to first response: 1.0 month (range: 0.2-3.1)
  - ORR in 33 triple-class refractory patients: 61%
- Of 6 evaluable patients in RP2D cohort, all achieved MRD-negative CR/sCR at 10^{-6} (n=5) and 10^{-5} (n=1)
- Median DOR was not reached

- [a] Investigator assessment of evaluable patients who had ≥1 postbaseline disease evaluation per 2011 IMWG response criteria, includes unconfirmed response
  [b] 1500 µg/kg SC QW, with step-up doses of 60 and 300 µg/kg
- Usmani SZ et al. *Lancet 2021*
- CR, complete response; DOR, duration of response; MRD, minimal residual disease; mF/U, median follow up; ORR, overall response rate; PR, partial response; RP2D, recommended phase 2 dose; sCR, stringent complete response; VGPR, very good partial response

Courtesy of Noopur Raje, MD

MajesTEC-1: Phase 2 Study Design

MajesTEC-1 is a first-in-human, phase 1/2, open-label, multicohort, multicenter, dose escalation study to evaluate teclistamab in patients with RRMM who previously received ≥3 prior lines of therapy and were triple-class exposed



Primary endpoint: ORR

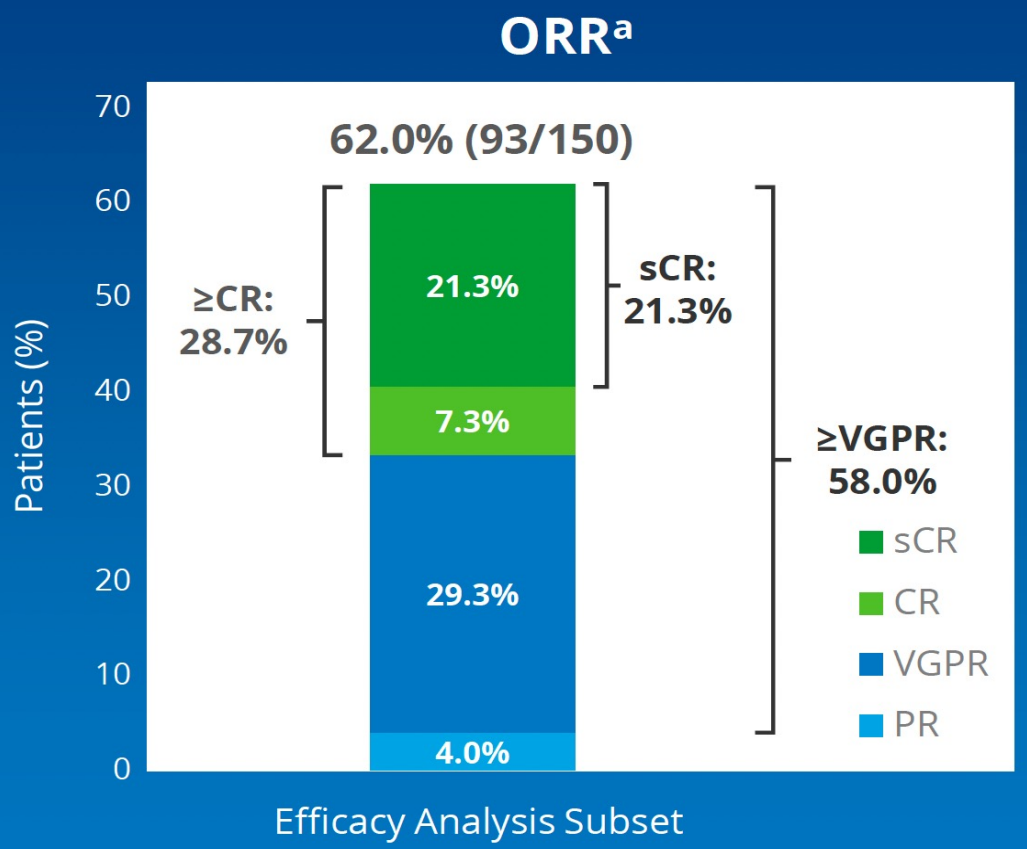
Key secondary endpoints: DOR, ≥VGPR, ≥ CR, sCR, TTR, MRD status, PFS, OS, safety, pharmacokinetics, immunogenicity, PRO

BCMA, B-cell maturation antigen; CR, complete response; DOR, duration of response; IMiD, immunomodulatory drug; LPI, last patient in; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PL, prior line; PRO, patient reported outcomes; RR, relapsed/refractory; sCR, stringent CR; SC subcutaneous; TTR, time to response; VGPR, very good partial response

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual.

Moreau et al, ASH 2021, Abstract 896

MajesTEC-1: Overall Response Rate for Teclistamab Monotherapy



- At a median follow-up of 7.8 months (range: 0.5+–18):
  - ORR of 62.0% (95% CI: 53.7–69.8) represents a substantial benefit for patients with triple-class exposed disease
- Median time to first response: 1.2 months (range: 0.2–5.5)
- MRD negativity rate[b]
  - 24.7% (37/150; 95% CI: 18.0–32.4) at a threshold of 10^{-5}
  - 16.7% (25/150; 95% CI: 11.1–23.6) at a threshold of 10^{-6}[,c]
- In patients who achieved ≥CR, the MRD-negativity rate was 41.9%

[a]PR or better, IRC assessed; ORR was assessed in efficacy analysis population, which includes all patients who received their first dose on or before March 18, 2021 (n=150); [b] Baseline clones were obtained for all patients All MRD assessments were done by next-generation sequencing; [c]Patients who were not negative at the 10^{-6} threshold were indeterminate.

CR, complete response; IRC, independent review committee; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual.

Moreau et al, ASH 2021, Abstract 896

MagnetisMM-1: Phase 1 Study of Elranatamab (PF-06863135), a BCMA-targeted CD3-Engaging Bispecific Molecule, for Patients with RRMM

Prior treatments

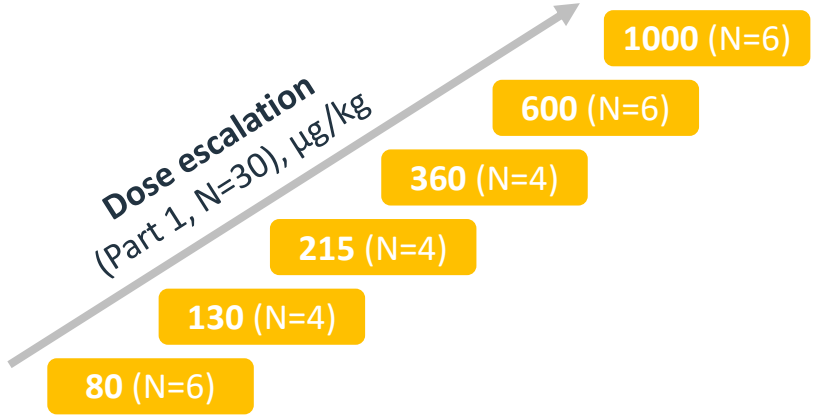
	N=55
Number of prior therapies, median (range)	6.0 (2-15)
Triple-class exposed, n (%)	54 (98)
Triple-class refractory,[a] n (%)	50 (91)
Prior BCMA-targeted therapy, n (%) Anti-BCMA ADC CAR-T	12 (22) 7 (13) 5 (9)

[a]Refractory to ≥1 PI, 1 IMiD, and 1 anti-CD38 mAb

Efficacy summary

- Elranatamab 1000 µg/kg Q2W achieved exposure associated with anti-myeloma efficacy
- Confirmed ORR was 69% (9/13) at the recommended dose of 1000 µg/kg Q1W
- 70% (7/10) of patients with prior BCMA-directed therapy achieved response

Study design



- Heavily pretreated population
- Good efficacy rates
- Small study population

Data cut-off: July 26, 2021

Sebag M, et al. ASH 2021;Abstract 895

Courtesy of Noopur Raje, MD

MagnetisMM-1: Phase 1 Study of Elranatamab (PF-06863135), a BCMA-targeted CD3-Engaging Bispecific Molecule, for Patients with RRMM

Treatment-emergent AEs

AE, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Total
Hematologic					
Neutropenia	0	2 (3.6)	13 (23.6)	24 (43.6)	39 (70.9)
Anemia	2 (3.6)	8 (14.5)	25 (45.5)	1 (1.8)	36 (65.5)
Lymphopenia	0	0	3 (5.5)	25 (45.5)	28 (50.9)
Thrombocytopenia	6 (10.9)	6 (10.9)	5 (9.1)	10 (18.2)	27 (49.1)
Leukopenia	2 (3.6)	4 (7.3)	9 (16.4)	4 (7.3)	19 (34.5)
Non-hematologic					
CRS	28 (50.9)	20 (36.4)	0	0	48 (87.3)
Injection site reactions	27 (49.1)	4 (7.3)	0	0	31 (56.4)
Fatigue	6 (10.9)	12 (21.8)	3 (5.5)	0	21 (38.2)
Diarrhea	11 (20.0)	7 (12.7)	2 (3.6)	0	20 (36.4)
Hypophosphatemia	0	6 (10.9)	13 (23.6)	1 (1.8)	20 (36.4)
Decreased appetite	12 (21.8)	6 (10.9)	1 (1.8)	0	19 (34.5)
Dry skin	17 (30.9)	2 (3.6)	0	0	19 (34.5)

Occurring in ≥33% of patients

Effect of priming and pre-medication on CRS

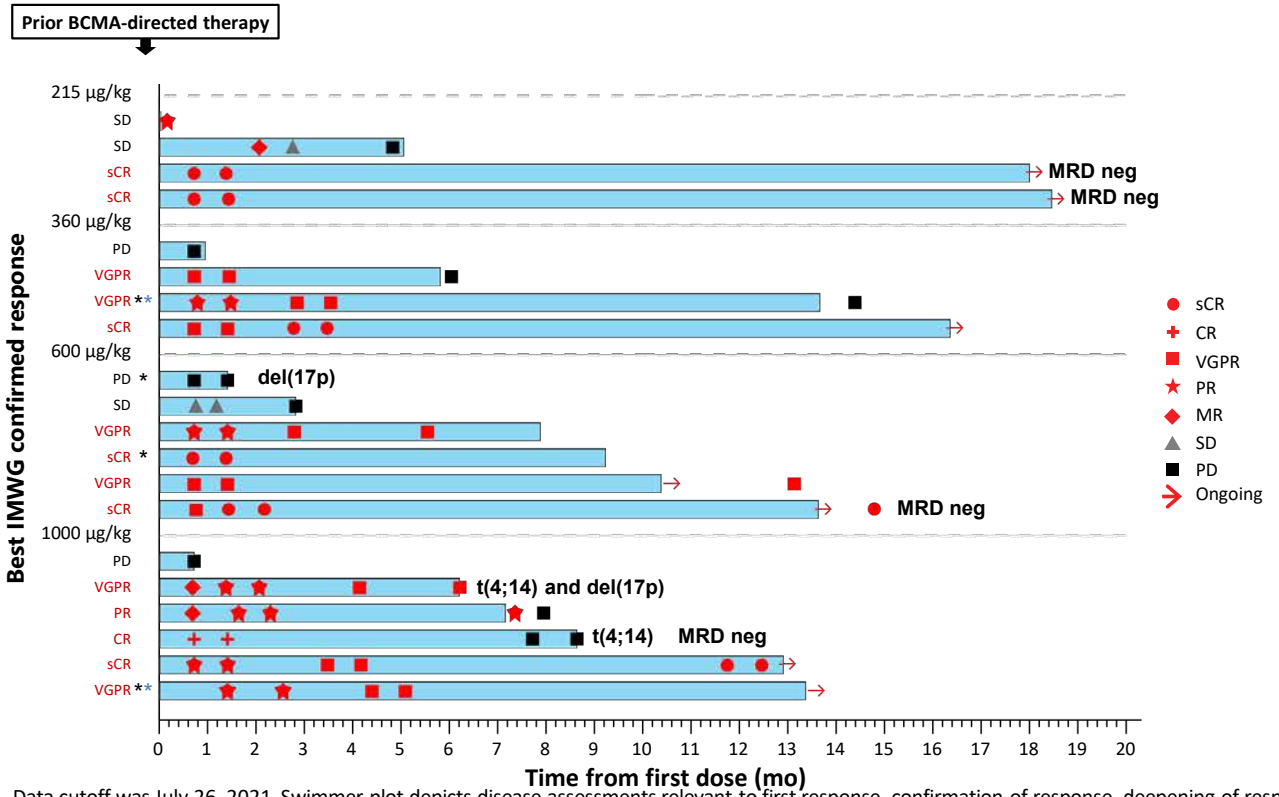
	Elranatamab SC at recommended monotherapy dose		
	Dose escalation Part 1 (N=6)	Priming cohorts Part 1.1 (N=20)	Expansion Part 2A (N=15)
Priming/Pre-medication	**No / No**	**Yes / No**	**Yes / Yes**
Overall incidence of CRS, n (%)	6 (100)	20 (100)	10 (66.7)
Grade 1	4 (66.7)	10 (50)	5 (33.3)
Grade 2	2 (33.3)	10 (50)	5 (33.3)
Duration, days, median (range)	4.0 (1–10)	3.0 (2–7)	3.0 (1–4)

Sebag M, et al. ASH 2021;Abstract 895

Courtesy of Noopur Raje, MD

MagnetisMM-1: Phase 1 Study of Elranatamab (PF-06863135), a BCMA-targeted CD3-Engaging Bispecific Molecule, for Patients with RRMM

Escalation (Part 1, ≥215 µg/kg, N=20) – Duration of Treatment



- Median follow-up was 12.5 months.
- 75% (3/4) of patients with prior BCMA-directed therapy achieved response including 1 sCR and 2 VGPR.
- 100% (4/4) of patients assessed were MRD negative.

Data cutoff was July 26, 2021. Swimmer plot depicts disease assessments relevant to first response, confirmation of response, deepening of response, and best response.
MRD status, available for 4 patients, was assessed by next-generation sequencing at a sensitivity of $1x10^{-5}$ in accordance with IMWG criteria for MRD assessment.
* Prior anti-BCMA ADC. * Prior BCMA-targeted CAR-T.
sCR=stringent complete response; CR=complete response; VGPR=very good partial response; PR=partial response; MR=minimal response; SD=stable disease; PD=progressive disease; BCMA=B-cell maturation antigen; MRD=minimal residual disease; neg=negative; IMWG=International Myeloma Working Group; ADC=antibody drug conjugate; CAR-T=chimeric antigen receptor T-cell therapy.

Sebag et al.ASH 2021

Courtesy of Noopur Raje, MD

Five anti-BCMA bispecific antibodies presented at ASH 2020

Updated Phase 1 Results of Teclistamab, a B-cell Maturation Antigen (BCMA) × CD3 Bispecific Antibody, in Relapsed and/or Refractory Multiple Myeloma (RRMM)

Alfred L. Garfall[1], Saad Z. Usmani[2], María-Victoria Mateos[3], Hareth Nahi[4], Niels W.C.J. van de Donk[5], Jesus F. San-Miguel[6], Albert Oriol[7], Laura Rosinol[8], Ajai Chari[9], Manisha Bhutani[2], Lixia Pei[10], Raluca Verona[10], Suzette Girgis[10], Tara Stephenson[10], Jenna D. Goldberg[10], Arnob Banerjee[10], Amrita Krishnan[11]

[1]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [2]Levine Cancer Institute-Atrium Health, Charlotte, NC, USA; [3]Hospital Clinico Universitario de Salamanca, Salamanca, Spain; [4]Karolinska University Hospital at Huddinge, Stockholm, Sweden; [5]Amsterdam University Medical Center, Location VU University Medical Center, Amsterdam, The Netherlands; [6]Clínica Universidad de Navarra, Navarra, Spain; [7]Institut Català d'Oncologia and Institut Josep Carreras. Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain; [8]Hospital Clínic, Barcelona, Spain; [9]Mt. Sinai School of Medicine, New York, NY, USA; [10]Janssen R&D, Spring House, PA, USA; [11]City of Hope, Duarte, CA, USA

A phase 1 FIH study of AMG 701, an anti-BCMA half-life extended (HLE) BiTE® (bispecific T-cell engager) molecule, in relapsed / refractory multiple myeloma

Simon J. Harrison,[1] Monique C. Minnema,[2] Hans C. Lee,[3] Andrew Spencer,[4] Prashant Kapoor,[5] Deepu Madduri,[6] Jeremy Larsen,[7] Sikander Ailawadhi,[8] Jonathan Kaufman,[9] Marc S. Raab,[10] Parameswaran Hari,[11] Shinsuke Iida,[12] Ravi Vij,[13] Faith E. Davies,[14] Robin Lesley,[15] Vijay V. Upreti,[16] Zhao Yang,[17] Anjali Sharma,[18] Alex C. Minella,[18] Suzanne Lentzsch[19]

[1]Clinical Haematology, Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, Australia, Sir Peter MacCallum Dept of Oncology, Melbourne University, Melbourne, Australia, [2]University Medical Center Utrecht, University Utrecht, Utrecht, Netherlands, [3]The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA, [4]Alfred Hospital-Monash University, Melbourne, Australia, [5]Mayo Clinic, Rochester, MN, USA, [6]Icahn School of Medicine at Mount Sinai, New York, NY, USA, [7]Mayo Clinic, Phoenix, AZ, USA, [8]Mayo Clinic, Jacksonville, FL, USA, [9]Emory University, Atlanta, GA, USA, [10]Heidelberg University Hospital, Heidelberg, Germany, [11]Medical College of Wisconsin, Milwaukee, WI, USA, [12]Nagoya City University Hospital, Nagoya, Japan, [13]Washington University School of Medicine, St. Louis, MO, USA, [14]NYU Langone, New York, NY, USA, [15]Clinical Biomarkers and Diagnostics, Amgen Inc., South San Francisco, CA, USA, [16]Clinical Pharmacology, Modeling & Simulation, Amgen Inc., South San Francisco, CA, USA, [17]Global Biostatistical Science, Amgen Inc., Thousand Oaks, CA, USA, [18]Early Development, Oncology, Amgen Inc., Thousand Oaks, CA, USA, [19]Columbia University Medical Center, New York, NY, USA

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PRESENTED BY: PROFESSOR SIMON J. HARRISON

Initial results of a phase I study of TNB-383B, a BCMA x CD3 bispecific T-cell redirecting antibody, in relapsed/refractory multiple myeloma

Cesar Rodriguez, Anita D'Souza, Nina Shah, Peter M. Voorhees, Ben Buelow, Ravi Vij, and Shaji Kumar

ASH Annual Meeting, 05 Dec 2020


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Phase 1 First-in-human Study of REGN5458, a BCMA x CD3 Bispecific Monoclonal Antibody, in Patients With Relapsed/Refractory Multiple Myeloma

Deepu Madduri, MD,[1] Ashley Rosko, MD,[2] Jason Brayer, MD, PhD,[3] Jeffrey A. Zonder, MD,[4] James E. Hoffman, MD,[5] William I. Bensinger, MD,[6] Jingjin Li, PhD,[7] Linzhi Xu, PhD,[7] Lieve Adriaens, PharmD,[7] Dhruti Chokshi, BS,[7] Weijiang Zhang, PhD,[7] Ruben G. W. Quek, PhD,[7] Anita Boyapati, PhD,[7] Manish Sharma, MD,[7] Frank Seebach, MD,[7] L. Andres Sirulnik, MD, PhD,[7] Israel Lowy, MD, PhD,[7] David M. Weinreich, MD,[7] George D. Yancopoulos, MD, PhD,[7] Madhav V. Dhodapkar, MD,[8] Suzanne Lentzsch, MD, PhD,[9] Dennis Cooper, MD,[10] Sundar Jagannath, MD[1]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [3]H. Lee Moffitt Cancer Center, Tampa, FL, USA; [4]Karmanos Cancer Institute, Detroit, MI, USA; [5]University of Miami Health System, Miami, FL, USA; [6]Swedish Center for Blood Disorders and Stem Cell Transplants, Seattle, WA, USA; [7]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [8]Emory University School of Medicine, Atlanta, GA, USA; [9]Columbia University Medical Center, New York, NY, USA; [10]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA

ClinicalTrials.gov ID: NCT03761108

This study was funded by Regeneron Pharmaceuticals, Inc.
Medical writing support was provided by Bu Reinen, PhD, of Prime (Knutsford, UK) and funded by Regeneron Pharmaceuticals, Inc.

Presented at the 62nd ASH Annual Meeting, December 5–8, 2020, San Diego, CA, USA. Abstract #291

1


Page 1

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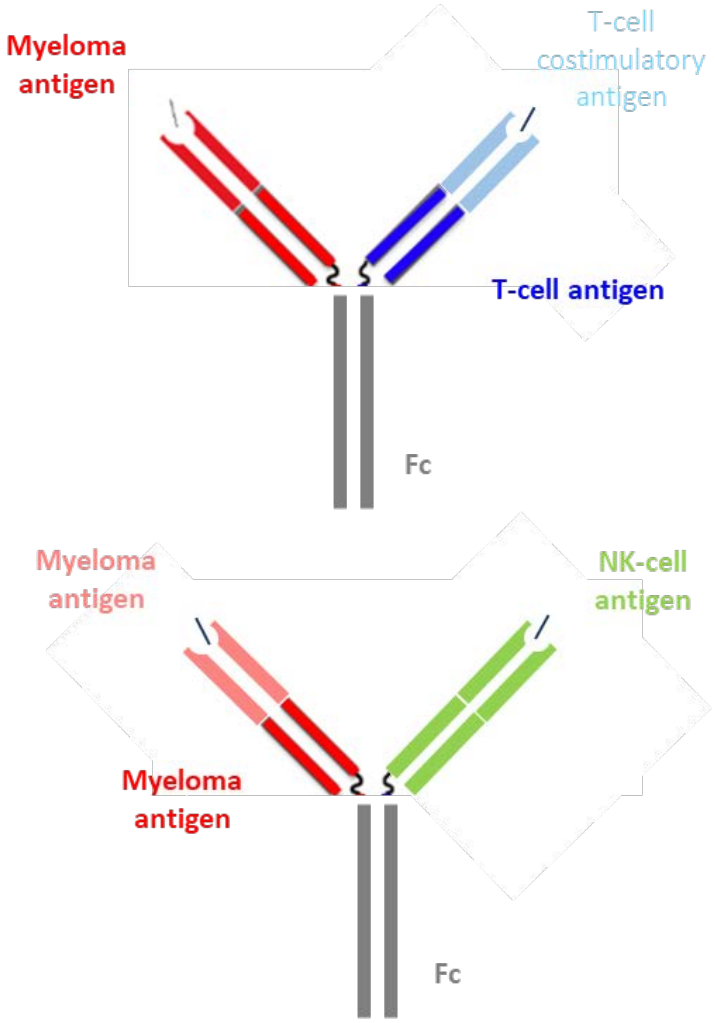
Preliminary Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of Subcutaneously (SC) Administered PF-06863135, a B-Cell Maturation Antigen (BCMA)–CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma (RRMM)

Alexander M. Lesokhin, Moshe Y. Levy, Andrew P. Dalovisio, Nizar J. Bahlis, Melhem Solh, Michael Sebag, Andrzej Jakubowiak, Yogesh S. Jethava, Caitlin L. Costello, Michael P. Chu, Michael R. Savona, Cristina Gasparetto, Suzanne Trudel, Jeffrey Chou, Chandrasekhar Udata, Cynthia Basu, Heike I. Krupka, and Noopur S. Raje

Poster # 3206 Presented at the American Society of Hematology Annual Meeting 2020 (ASH Virtual), December 5-8, 2020

Courtesy of Noopur Raje, MD

The Future: Trispecific Antibodies



- Still in pre-clinical stages of development
- With bispecifics, in absence of T cell co-stimulation higher likelihood of anergy, leading to a suboptimal anti-tumor response
- Wu, et al. recently demonstrated a **trispecific T cell engager** targeting CD38, CD3, and CD28 (co-stimulatory protein on T-cells) very potent killing of CD38+ MM cell lines, 3- to 4-log higher than daratumumab
- Also suppressed MM growth in mice and promoted proliferation of memory and effector T-cells and downregulation of regulatory T-cells in primates
- **Trispecific NK cell engagers** also being developed, targeting CD16A on NK cell as well as the MM antigens BCMA and CD200

Lancman, et al. ASH 2020
Wu, et al. *Nature Cancer* 2019

Courtesy of Noopur Raje, MD

Slide Courtesy of Dr. Ajai Chair

Current Understanding and Future Directions

- The immune system is important across the spectrum of myeloma
- BCMA is a validated target
- Antibody drug conjugates, bispecific T-cell engagers, and cellular products all show efficacy
- Future will be to define how to combine/sequence these
- Next generation approaches will focus on improving efficacy and DOR

Courtesy of Noopur Raje, MD

Agenda

Introduction: Monday Night with Research To Practice

MODULE 1: Targeting BCMA

MODULE 2: CAR T-Cell Therapy

MODULE 3: Bispecific Antibodies

MODULE 4: Belantamab Mafodotin

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Case Presentation – Dr Berdeja: A 78-year-old man with multiregimen-relapsed MM who receives belantamab mafodotin

- 78-yr-old male diagnosed with ISS/R-ISS stage II multiple myeloma with standard-risk cytogenetics
- Initial treatment: lenalidomide/dexamethasone; achieved a VGPR
- After 24 mos, his M spike increased consistent with PD. At this time, he was also noted to have a Cr 2.5.
- Treated with cyclophosphamide/bortezomib/dex; achieved a PR, lasting 12 mos
- Treated with daratumumab/bortezomib/dexamethasone; achieved VGPR, lasting 12 mos
- Treated with elotuzumab, pomalidomide, dex; achieved a PR

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

Case Presentation – Dr Berdeja: A 78-year-old man with multiregimen-relapsed MM who receives belantamab mafodotin (continued)

- 8 mos later, patient presents with increasing back pain and found to have a new pathological fracture with an increase in M protein to 1 g/dL.
- Given his age and renal insufficiency, he was not felt to be a CART candidate.
- He underwent treatment with belantamab mafodotin 2.5 mg/kg IV q 3 wks.
- He achieved VGPR after 3 cycles. Tolerated therapy well except for mild eye irritation.
- Prior to cycle 4 he was found to have G3 keratopathy on ophtho exam but no changes in visual acuity. Dose was held for 2 mos. Repeat evaluation revealed G1 keratopathy. Cycle 4 proceeded with dose reduction to 1.9 mg/kg IV. Tolerated well.

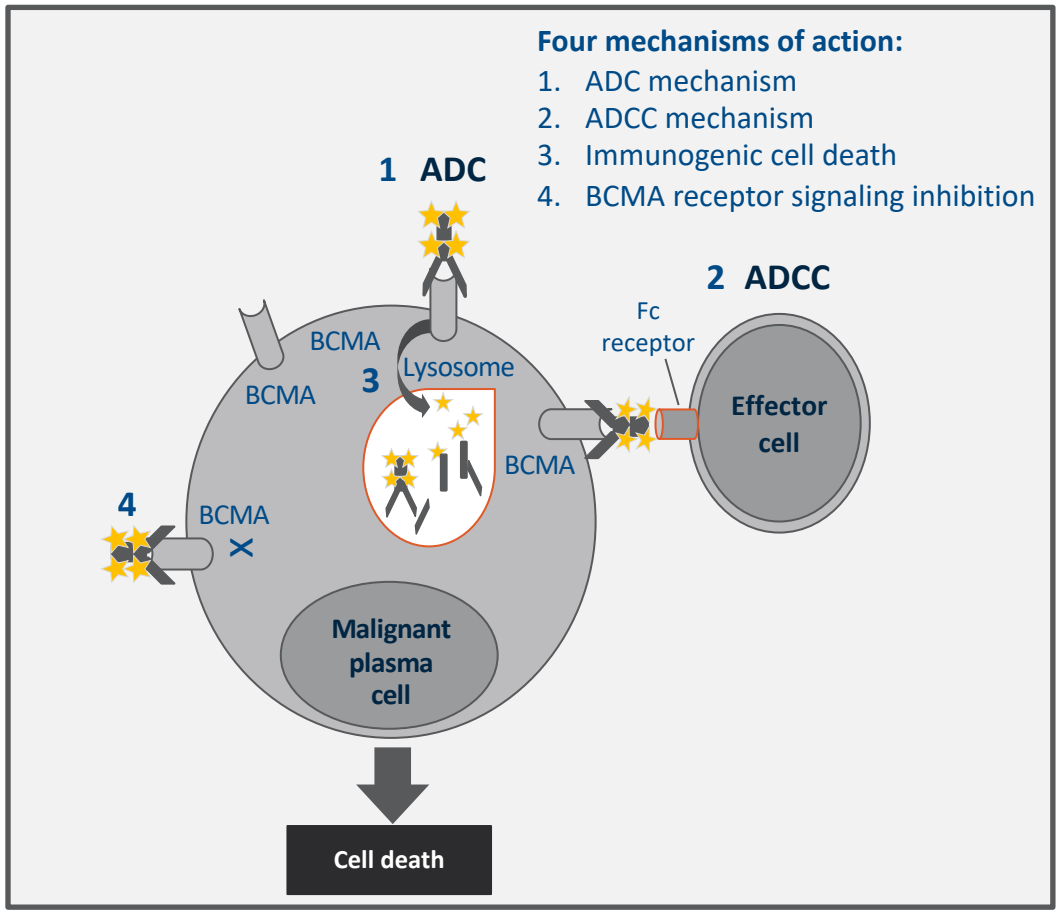
SARAH CANNON

Courtesy of Jesús G Berdeja, MD

Belantamab mafodotin (GSK2857916)

Background

- Antibody
  - Humanized, afucosylated IgG1
- Antibody-Target
  - BCMA
- Payload
  - MMAF (monomethyl auristatin-F)



[1]Tai YT, et al. Blood 2014;123(20):3128-38.

Trudel et al. The Lancet Oncology. 2018 Dec 1;19(12):1641-53

ADC, antibody-drug conjugate; ADCC, antibody-dependent cell-mediated cytotoxicity; BCMA, B-cell maturation antigen; IgG, immunoglobulin G; MMAF, monomethyl auristatin-F

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

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

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.

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

DREAMM-6: Investigator-Assessed Best Confirmed Response for Belantamab Mafodotin + Vd

Figure 3. Investigator-assessed* best confirmed response

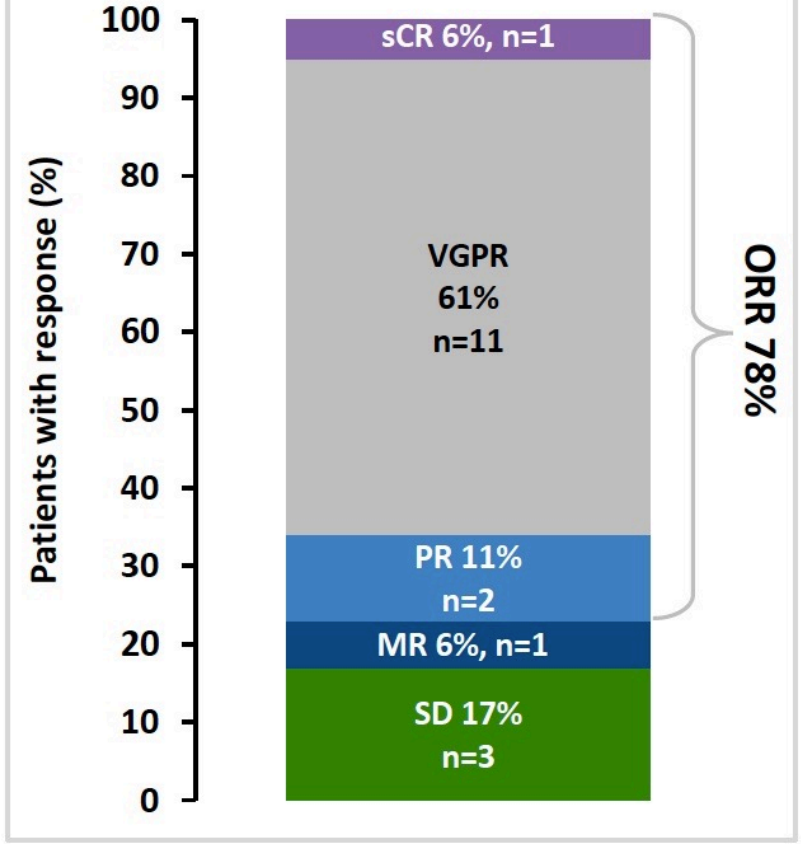
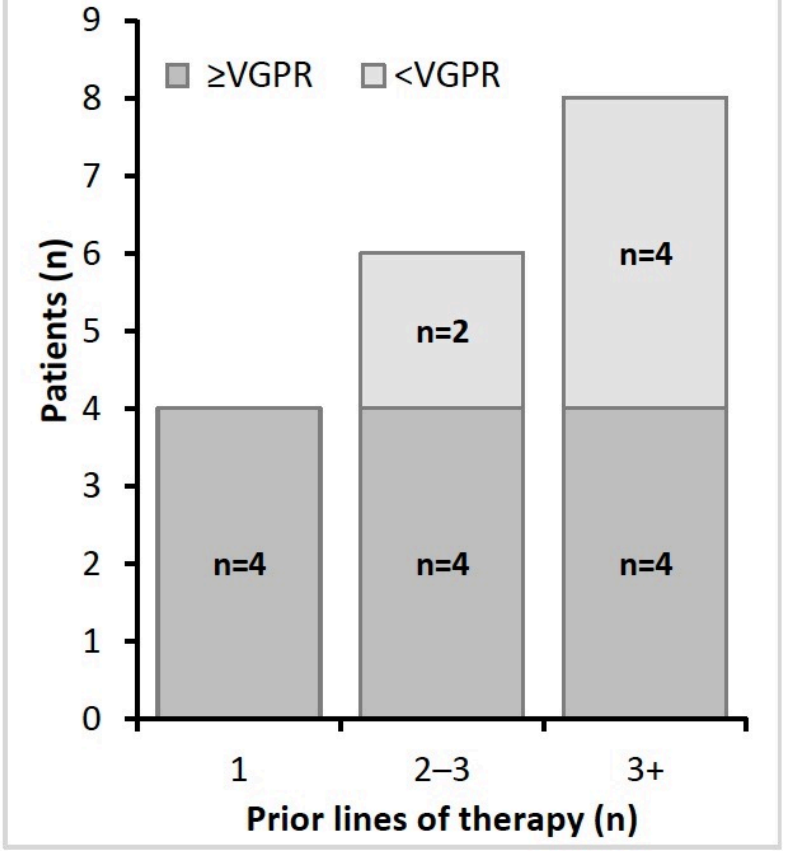


Figure 4. Investigator-assessed* best confirmed response per prior number of LOT



Popat R et al. ASH 2020;Abstract 1419.

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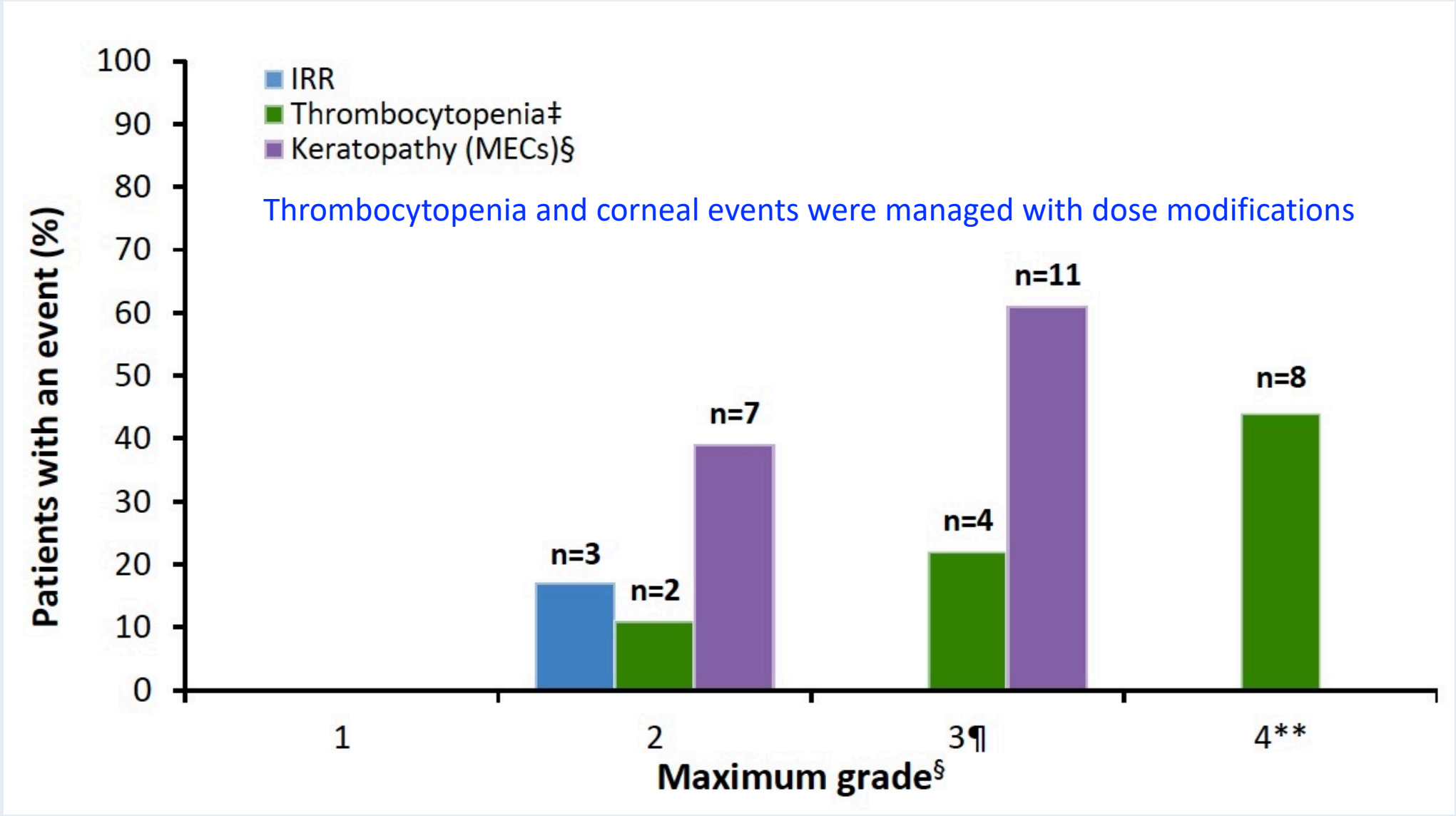
DREAMM-6: Adverse Events of Special Interest



Popat R et al. ASH 2020;Abstract 1419.

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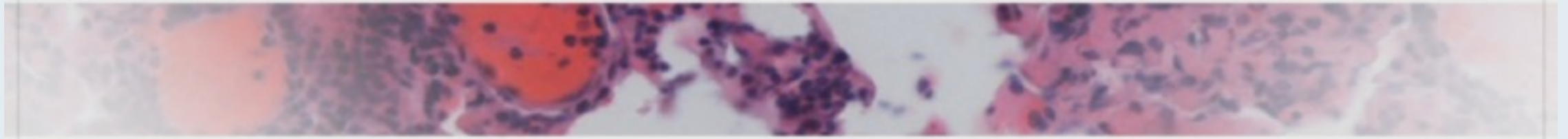

DREAMM-5 Study: Investigating the Synergetic Effects of Belantamab Mafodotin plus Inducible T-cell Co-Stimulator Agonist (aICOS) Combination Therapy in Patients with Relapsed/Refractory Multiple Myeloma

Natalie S. Callander, MD[1], Vincent Ribrag, MD[2], Paul G. Richardson, MD[3], Ajay K. Nooka, MD, MPH, FACP[4], Kevin Song, MD, FRCPC[5], Katarina Uttervall, MD, PhD[6], Monique C. Minnema, MD, PhD[7], Katja Weisel, MD[8], Hang Quach, MD[9], Chang-Ki Min, MD, PhD[10], Marc S. Ballas, MD, MPH[11], Xiaofang Li[11], Nirav Ratia[12], Morrys Kaisermann, MD, PhD[11], Beata Holkova, MD[11], Suzanne Trudel, MD[13]

[1]Carbone Cancer Center, University of Wisconsin, Madison, WI, USA; [2]Institut Gustave Roussy, Villejuif, France; [3]Dana-Farber Cancer Institute, Boston, MA, USA; [4]Emory University, Winship Cancer Institute, Atlanta, GA, USA; [5]Vancouver General Hospital, Vancouver, BC, Canada; [6]Karolinska University Hospital, Stockholm, Sweden; [7]University Medical Center Utrecht, Utrecht, Netherlands; [8]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [9]University of Melbourne, St. Vincent's Hospital Melbourne, Melbourne, VIC, Australia; [10]Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea; [11]GlaxoSmithKline, Upper Providence, PA, USA; [12]GlaxoSmithKline, Brentford, Middlesex, United Kingdom; [13]Princess Margaret Cancer Centre, Toronto, ON, Canada

Presentation No. 897 | Presented at the 63rd American Society of Hematology Annual Meeting and Exposition, Atlanta, Georgia | December 11–14, 2021

Preliminary Efficacy Outcomes

The preliminary overall response rate (ORR) for the total population was 52% (n=13; 95% CI: 31.3–72.2).

A very good partial response or better (≥VGPR) was achieved for 32% of patients (n=8), or 57% of responders (8/14).

Overview of Efficacy*, n (%)	Cohort A Belamaf 1.9 mg/kg + aICOS 8 mg N=9	Cohort B Belamaf 2.5 mg/kg + aICOS 8 mg N=10	Cohort C Belamaf 2.5 mg/kg + aICOS 24 mg N=6	Total Population N=25
Stringent complete response	0	1 (10)	0	1 (4)
Complete response	1 (11)	0	0	1 (4)
Very good partial response	2 (22)	1 (10)	3 (50)	6 (24)
Partial response	1 (11)	3 (30)	1 (17)	5 (20)
Minimal response	0	0	1 (17)	1 (4)
Stable disease	4 (44)	2 (20)	1 (17)	7 (28)
Progressive disease	1 (11)	1 (10)	0	2 (8)
Not evaluable	0	2 (20)	0	2 (8)
Overall response rate (%; 95% CI†) sCR+CR+VGPR+PR	**4 (44; 13.7–78.8)**	**5 (50; 18.7–81.3)**	**4 (67; 22.3–95.7)**	**13 (52; 31.3–72.2)**
Clinical benefit rate (%; 95% CI) sCR+CR+VGPR+PR+MR	4 (44; 13.7–78.8)	5 (50; 18.7–81.3)	5 (83; 35.9–99.6)	14 (56; 34.9–75.6)

Callander NS et. al, ASH 2021, Abstract 897

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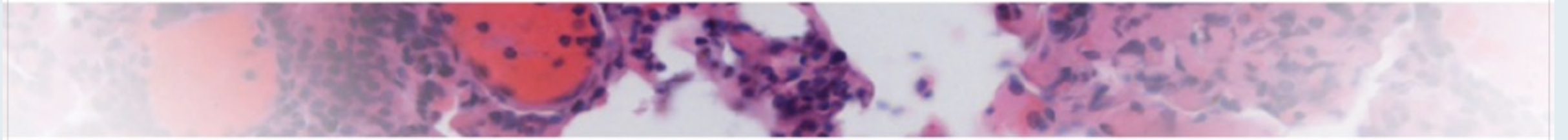


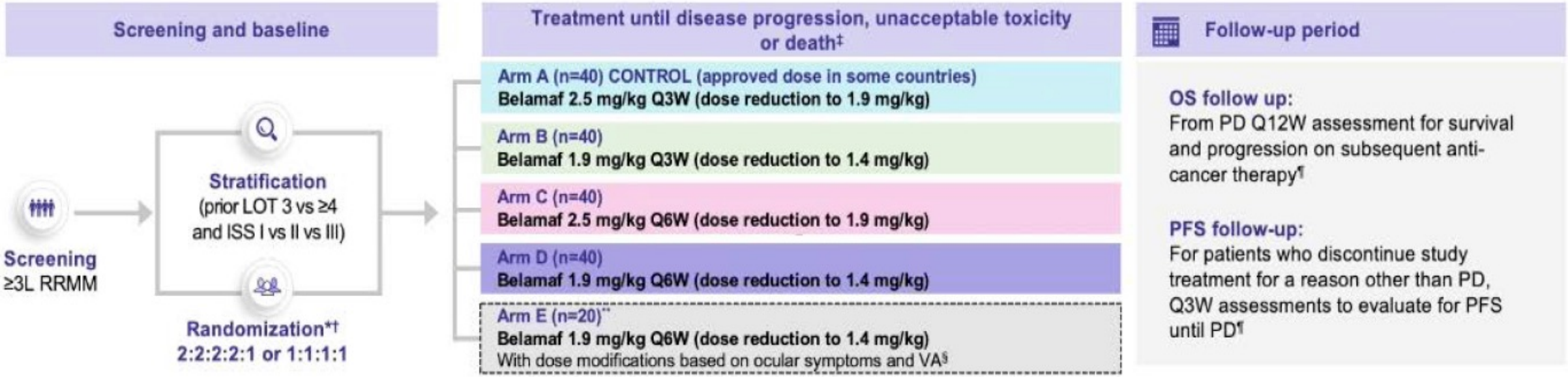
Exploring Alternative Dosing Regimens of Single-Agent Belantamab Mafodotin on Safety and Efficacy in Patients with Relapsed or Refractory Multiple Myeloma: DREAMM-14

Malin Hultcrantz, MD, PhD[1], David Kleinman, MD[2], Pavandeep Ghataorhe, MD, PhD[3], Astrid McKeown, PhD[3], Wei He, PhD[4], Thomas Ling, BSc (Hons)[3], Roxanne C. Jewell, PhD[5], Julie Byrne, PhD[6], Laurie Eliason, MPH[6], Emma Scott, MD[6], Joanna Opalinska, MD[6]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]University of Rochester, Rochester, NY, USA; [3]GlaxoSmithKline, London, England, UK; [4]GlaxoSmithKline, Cambridge, Boston, MA, USA; [5]GlaxoSmithKline, Research Triangle Park, NC, USA; [6]GlaxoSmithKline, Upper Providence, PA, USA

Methods

DREAMM-14 (NCT05064358) is a Phase 2, 5-arm, randomized, parallel, open-label multicenter study evaluating efficacy and safety of belantamab mafodotin at different doses and administration schedules (Figure 1) in a patient population with RRMM similar to that of DREAMM-2.



Hultcrantz M et al, SH 2021, Abstract 1645

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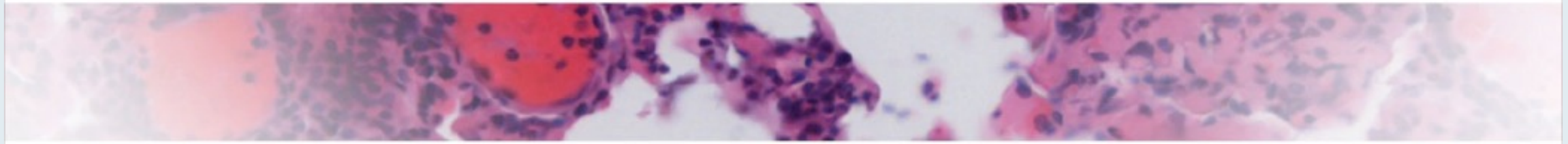

DREAMM-9: Phase I Study of Belantamab Mafodotin Plus Standard of Care in Patients with Transplant-Ineligible Newly Diagnosed Multiple Myeloma

Saad Z. Usmani, MD[1], Aránzazu Alonso Alonso, MD[2], Hang Quach, MD[3], Youngil Koh, MD[4], Andreas Guenther, MD[5], Chang-Ki Min, MD[6], Xavier Leleu, MD, PhD[7], Al-Ola Abdallah, MD, PhD[8], Albert Oriol, MD[9], Britta Besemer, MD[10], Mamta Garg, MD, FRCP, FRCPath[11], Irwindeep Sandhu, MD, FRCPC[12], Katja Weisel, MD, PhD[13], Enrique M. Ocio San Miguel, MD, PhD[14], Michele Cavo, MD[15], Xiaoou L. Zhou, MD, PhD[16], Morrys C. Kaisermann, MD, PhD[17], Lukasz M. Mis, MSc[18], Danaè Williams, MSc[17], Anne Yeakey, MD[19] Geraldine Ferron-Brady, PhD[17], David J. Figueroa, BA[17], Brandon E. Kremer, MD, PhD[17], Ira V. Gupta, MD[17], Wojciech Janowski, MD[20]

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Results

Efficacy

Preliminary data on efficacy of belamaf combination treatments are encouraging.

ORR was 100% in Cohorts 1 (12 patients), 3, and 5 (6 patients each), and 83% in Cohorts 2 and 4 (5/6 patients each; **Table 4**).

At least half of patients in each cohort achieved ≥VGPR; the highest rates were seen in Cohorts 1 and 5 (**Table 4**).

- Based on real-time capture from the clinical database, VGPR were observed in some patients as early as 4 weeks into treatment
- As of data cut-off, 3/12 patients in Cohort 1, 2/6 patients in Cohort 4, and 1/6 patients each in Cohorts 3 and 5 remained in complete response (CR); with 6/12 patients in Cohort 1 and 1/6 patient in Cohort 5 in stringent complete response (sCR) with a median follow-up of 12.7 and 4.0 months, respectively.

In Cohort 1, as of data cut-off, 9 of 12 patients with best response of ≥VGPR had an MRD assessment; 7 of the 9 patients who achieved ≥VGPR achieved minimal residual disease (MRD)-negative status at the first test after VGPR.

Table 4. Efficacy Data for Patients Treated with Belamaf + VRd

Clinical response	Cohort 1 belamaf 1.9 mg/kg Q3/4W, every cycle of SOC n=12	Cohort 2 belamaf 1.4 mg/kg Q6/8W, every other cycle of SOC n=6	Cohort 3 belamaf 1.9 mg/kg Q6/8W, every other cycle of SOC n=6	Cohort 4 belamaf 1.0 mg/kg Q3/4W, every cycle of SOC n=6	Cohort 5 belamaf 1.4 mg/kg Q3/4W, every cycle of SOC n=6
ORR, n (%; 95% CI)	12 (100; 73.5–100)	5 (83; 35.9–99.6)	6 (100; 54.1–100)	5 (83; 35.9–99.6)	6 (100; 54.1–100)
sCR, n (%)	6 (50)	0	0	0	1 (17)
CR, n (%)	3 (25)	0	1 (17)	2 (33)	1 (17)
VGPR, n (%)	3 (25)*	4 (67)	2 (33)	1 (17)	4 (67)
PR, n (%)	0	1 (17)	3 (50)	2 (33)	0
SD, n (%)	0	1 (17)	0	0	0

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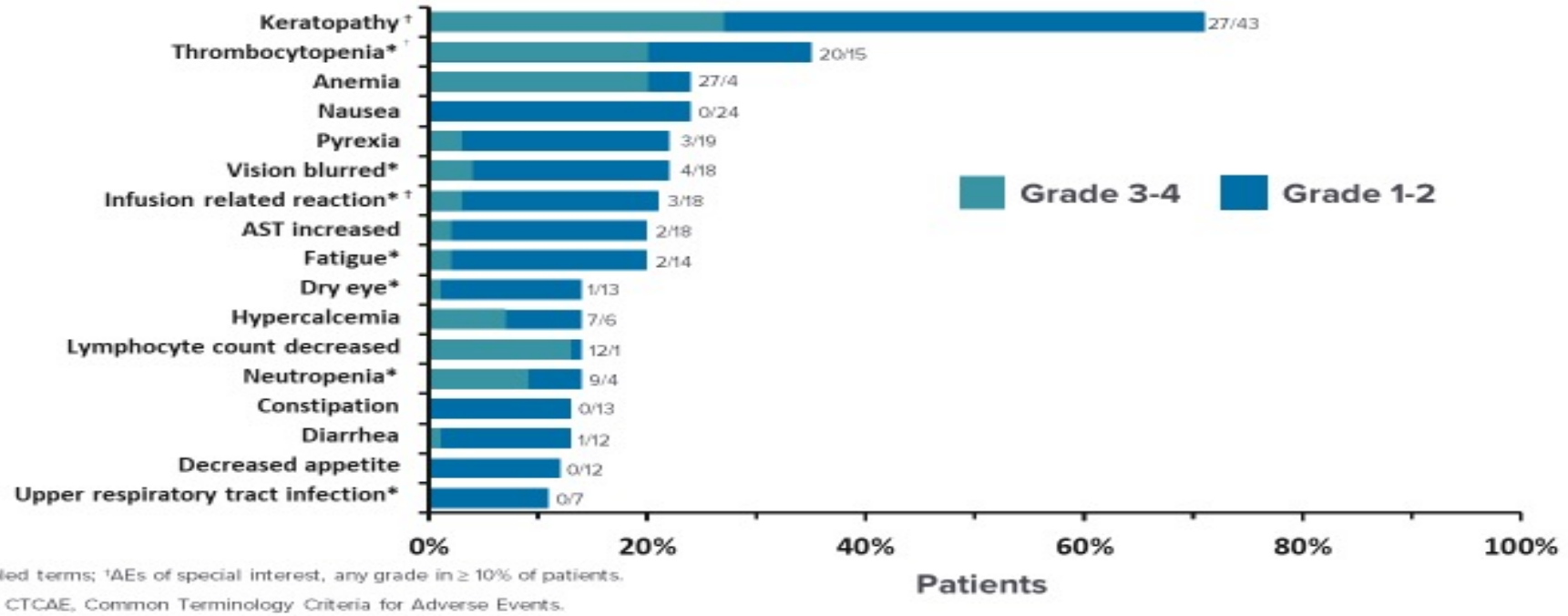
Usmani SZ et al, ASH 2021, Abstract 2738

Belantamab mafodotin toxicity

DREAMM-2
Most Common AEs by CTCAE Grade for belamaf 2.5 mg/kg, %



*AEs based on pooled terms; †AEs of special interest, any grade in ≥ 10% of patients.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events.
Lonial S, et al. Lancet Oncol. 2020;21:207-221.

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

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

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

Belantamab mafodotin development

- Approved in RRMM with at least 4 prior LOT including PI/IMID/antiCD38
- DREAMM studies underway in various combinations in earlier lines of therapy and frontline settings
  - DREAMM 9 BelaMaf +VRD in TI NDMM early results – feasible[1]
- Canadian Myeloma Research Group[2]
  - Belantamab in combination with pomalidomide and dexamethasone in pts with ≥ 1 LOT
  - Various BM dosing cohorts
    - 1.92 or 2.5 mg/kg IV on D1 q 4wks and 2.5 or 3.4 split dosing IV on D1 and D8 q 4 wks
    - MTD BM 2.5mg/kg D1 or split over D1 and D8 (2.5mg/kg total) IV Q4wks – DLTs were Gr 3 keratopathy
    - Promising early efficacy: ORR 88% all 34 pts, ORR 100% in 11 pts with triple refractory disease

[1] Usmani et al, ASH 2021.
[2]Trudel et al, ASH 2020

SARAH CANNON

Courtesy of Jesús G Berdeja, MD

Targeting BCMA ~~may be~~ is a new standard

	Antibody drug conjugate	Bispecific antibody	CAR T-cell
Approved product	Belantamab mafodotin (August 2020)	Several in phase II	Ide-cel (March 2021)
Efficacy	++ (as single agent; higher in combinations)	+++	++++
How given	IV, q3 weeks, until progression	IV or SC, weekly or q2 weeks until progression	One-and-done
Where given	Community	Academic medical centers	Academic medical centers
Notable adverse events	Ocular (corneal)	CRS and neurotoxicity	CRS and neurotoxicity
CRS	Not seen	++	+++
Neurotoxicity	Not seen	+	++
Availability	Off-the-shelf; after ophthalmology evaluation	Off-the-shelf	Wait time for manufacturing

Courtesy of Noopur Raje, MD

Key Considerations in the Optimal Clinical Care of Patients with Small Cell Lung Cancer

Wednesday, February 9, 2022
5:00 PM – 6:00 PM ET

Faculty

Luis Paz-Ares, MD, PhD
Jared Weiss, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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