Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Chimeric Antigen Receptor T-Cell Therapy in Multiple Myeloma

Thursday, June 24, 2021
5:00 PM – 6:00 PM ET

Faculty

Noopur Raje, MD
Alli McClanahan, MSN, APRN, ANP-BC

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

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

Alli McClanahan, MSN, APRN, ANP-BC
Nurse Practitioner
Division of Hematology
Mayo Clinic
Rochester, Minnesota

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Commercial Support

This activity is supported by an educational grant from Bristol-Myers Squibb Company.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, Genentech, a member of the Roche Group, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Raje — Disclosures

Consulting Agreements	Amgen Inc, bluebird bio, Celgene Corporation

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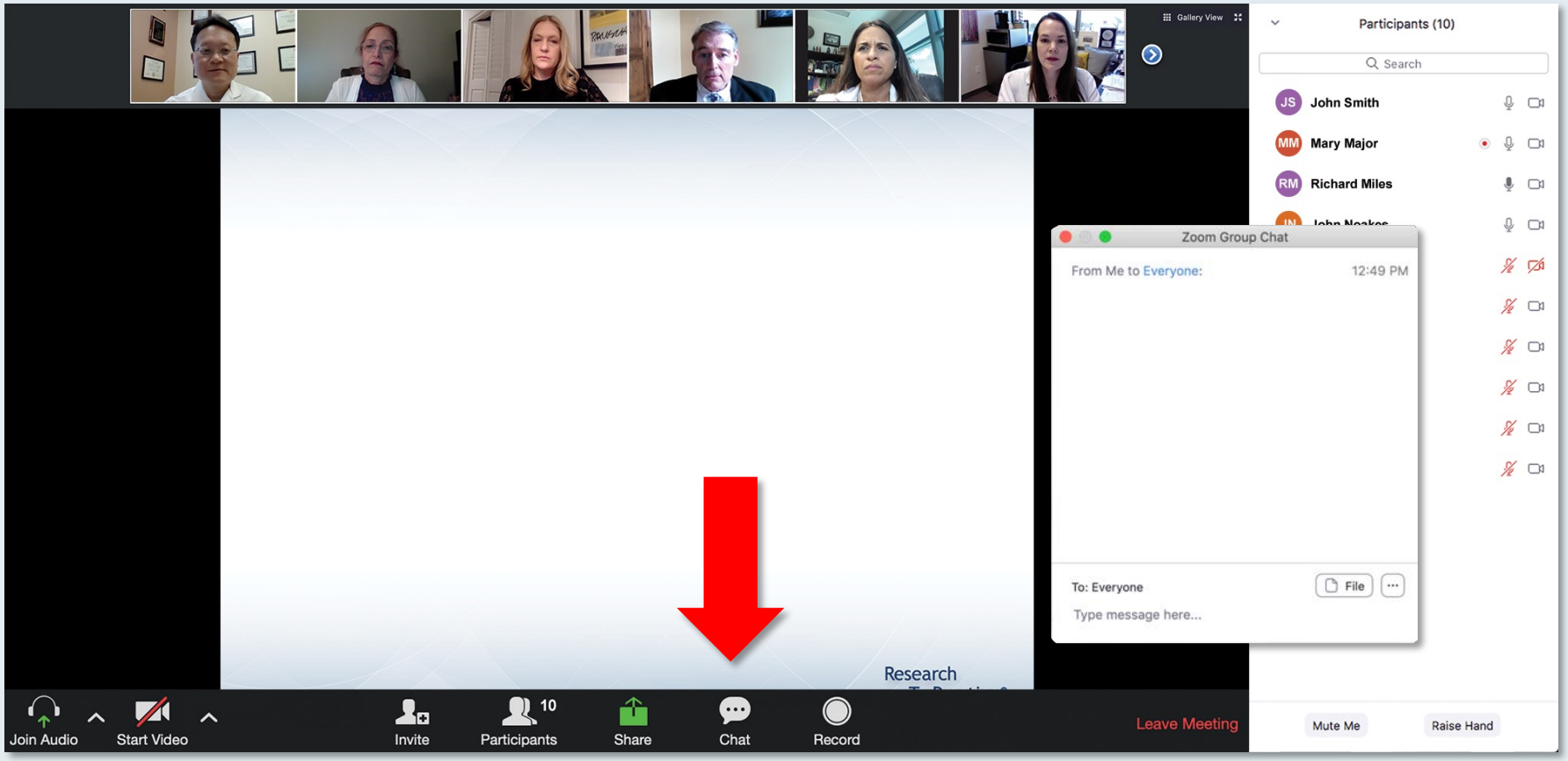
Ms McClanahan — Disclosures

No relevant conflicts of interest to disclose.

We Encourage Clinicians in Practice to Submit Questions



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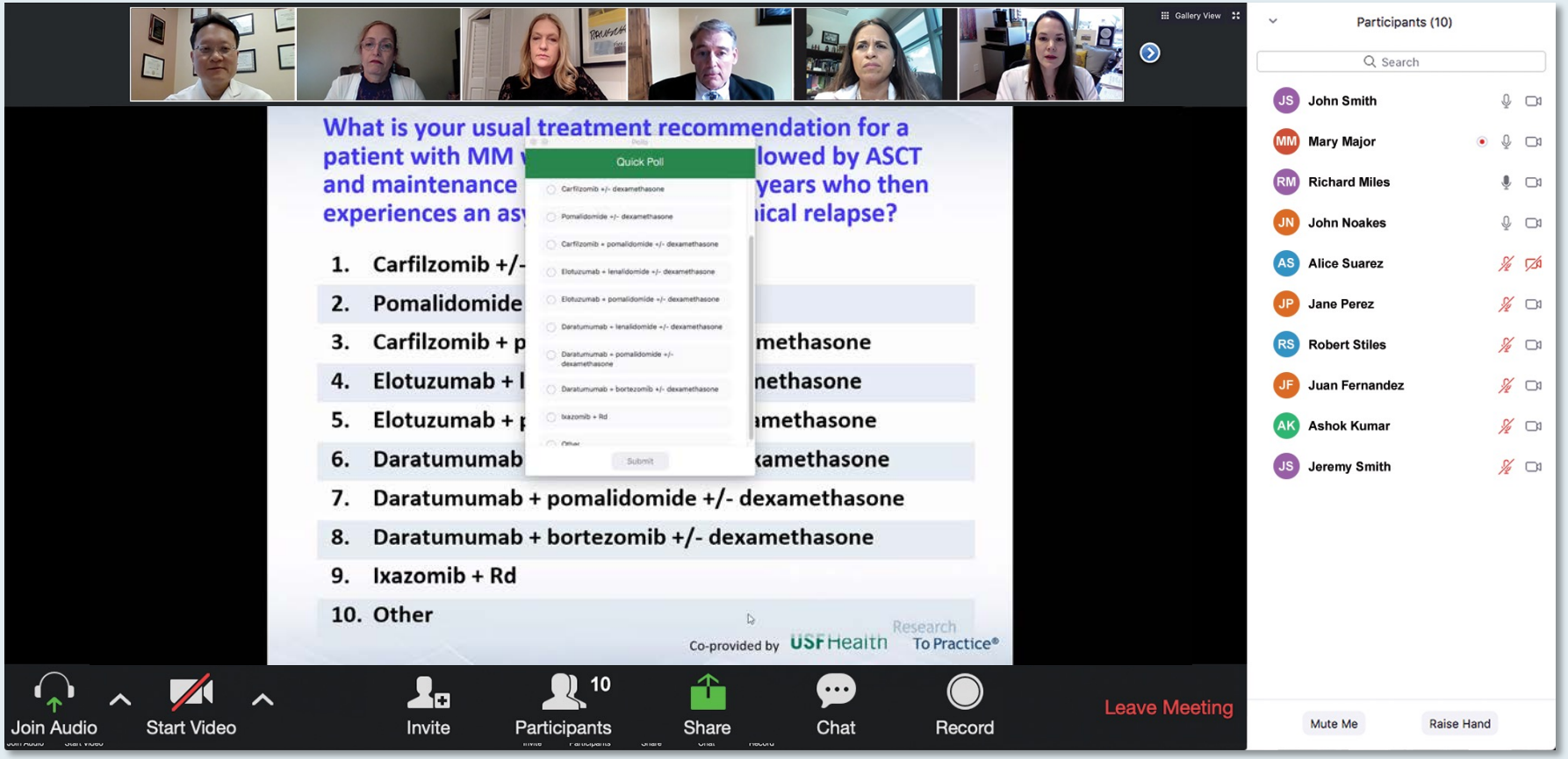
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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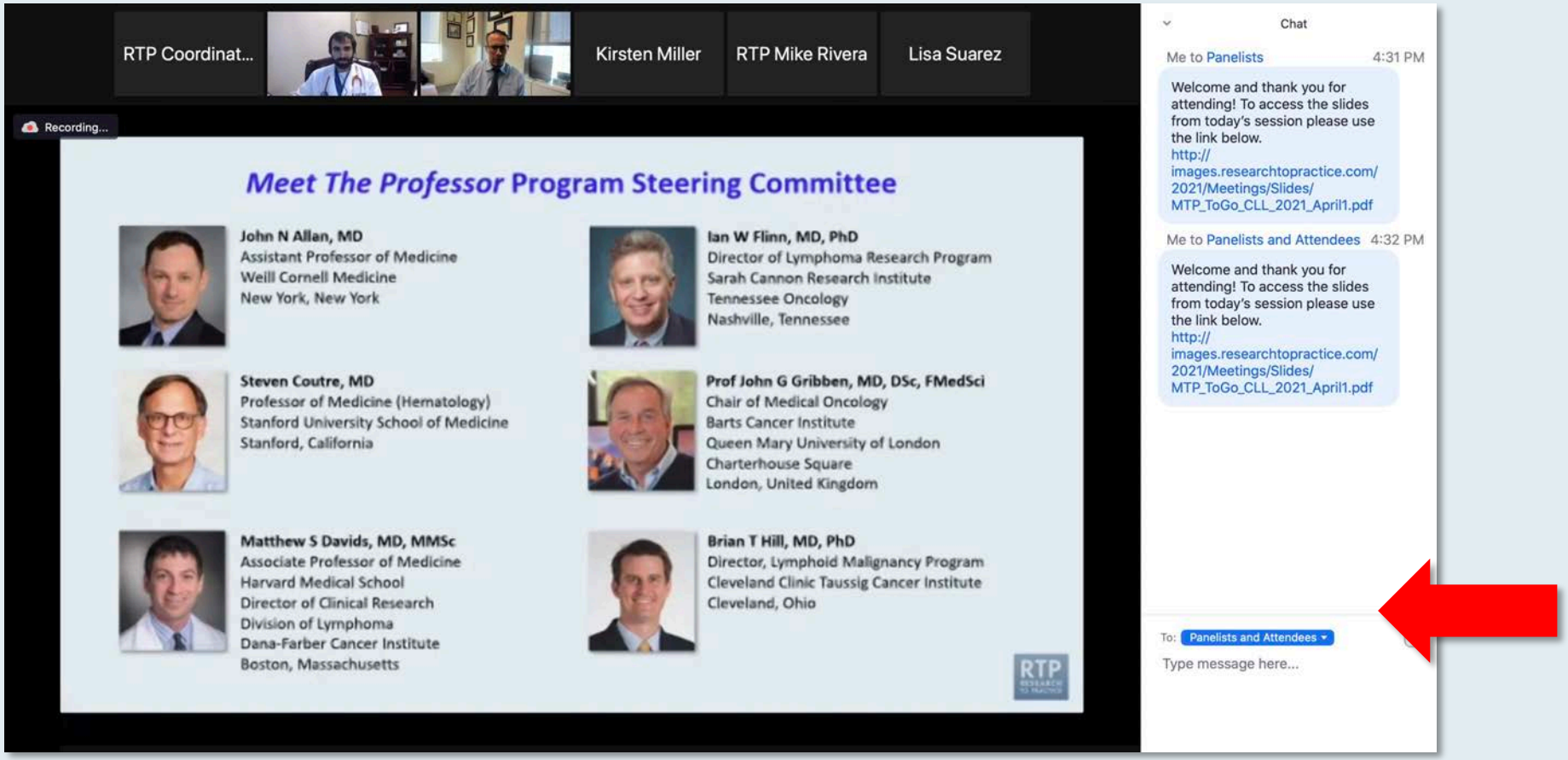
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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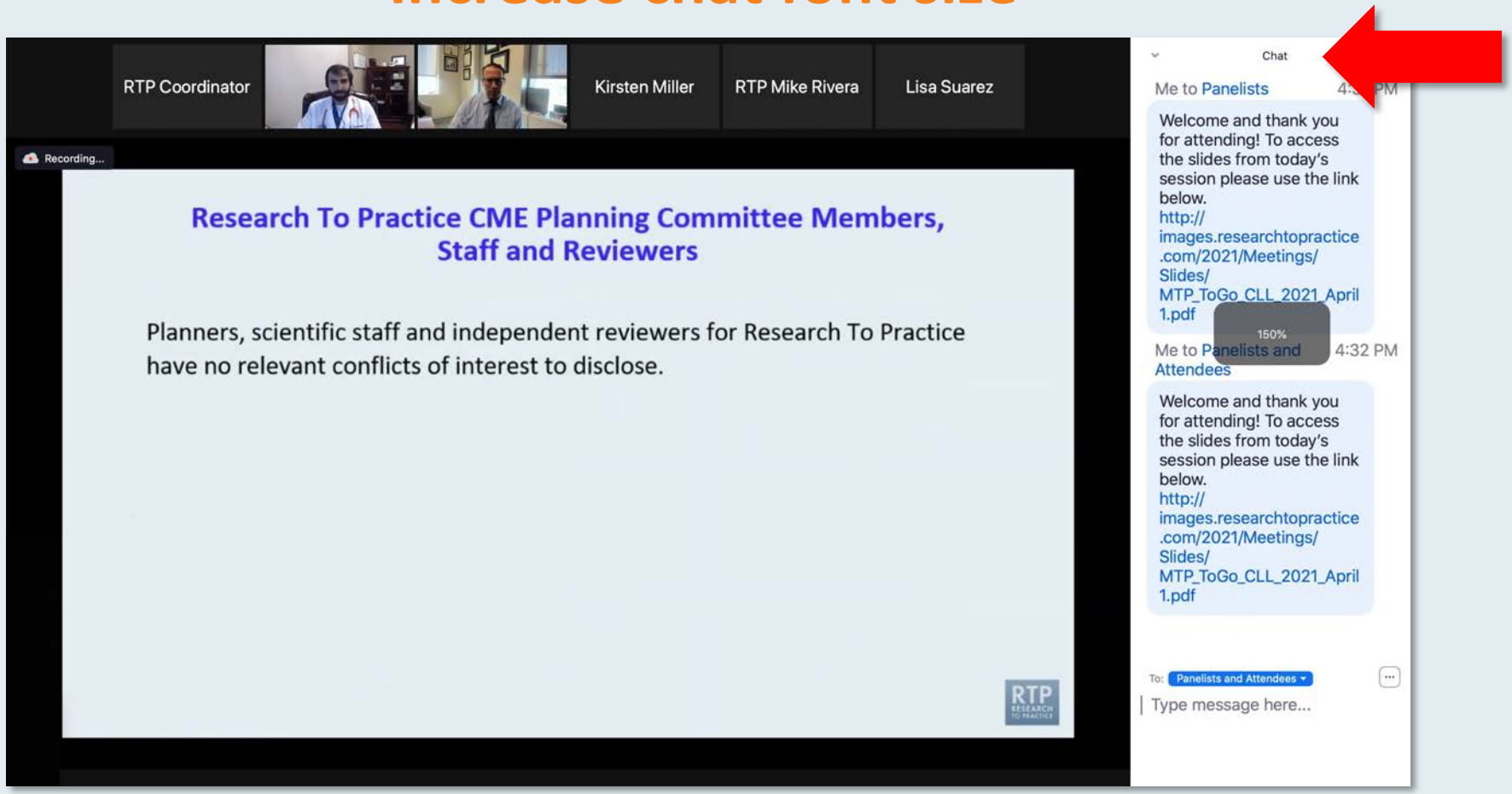
Familiarizing Yourself with the Zoom Interface

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.

ONCOLOGY TODAY

WITH DR NEIL LOVE

CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY IN NON-HODGKIN LYMPHOMA

DR TANYA SIDDIQI

CITY OF HOPE NATIONAL MEDICAL CENTER

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ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

A Daylong Multitumor Educational Webinar in Partnership with the Texas Society of Clinical Oncology (TxSCO)

Saturday, June 26, 2021
8:00 AM – 3:00 PM Central Time
(9:00 AM – 4:00 PM Eastern Time)

RTP RESEARCH TO PRACTICE

Video Consensus or Controversy? Chronic Lymphocytic Leukemia and Follicular Lymphoma

Tuesday, June 29, 2021
5:00 PM – 6:00 PM ET

Faculty

Nathan H Fowler, MD
Prof John G Gribben, MD, DSc, FMedSci
Brad S Kahl, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Video Consensus or Controversy? Multiple Myeloma

Wednesday, June 30, 2021
5:00 PM – 6:00 PM ET

Faculty

Natalie S Callander, MD
Shaji K Kumar, MD
Additional faculty to be announced

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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Prostate Cancer: Session 1

Thursday, July 1, 2021
5:00 PM – 6:00 PM ET

Faculty

Charles J Ryan, MD
Brenda Martone, MSN, NP-BC, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

In Partnership with Project Echo® and Florida Cancer Specialists

Tuesday, July 6, 2021
5:00 PM – 6:00 PM ET

Faculty

David I Quinn, MBBS, PhD

Moderator

Neil Love, MD

A Conversation with the Investigators: Ovarian Cancer

Wednesday, July 7, 2021
5:00 PM – 6:00 PM ET

Faculty

Michael J Birrer, MD, PhD
Kathleen Moore, MD
Additional faculty to be announced

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Non-Small Cell Lung Cancer

Thursday, July 8, 2021
5:00 PM – 6:00 PM ET

Faculty

Zofia Piotrowska, MD, MHS
Tara Plues, APRN, MSN

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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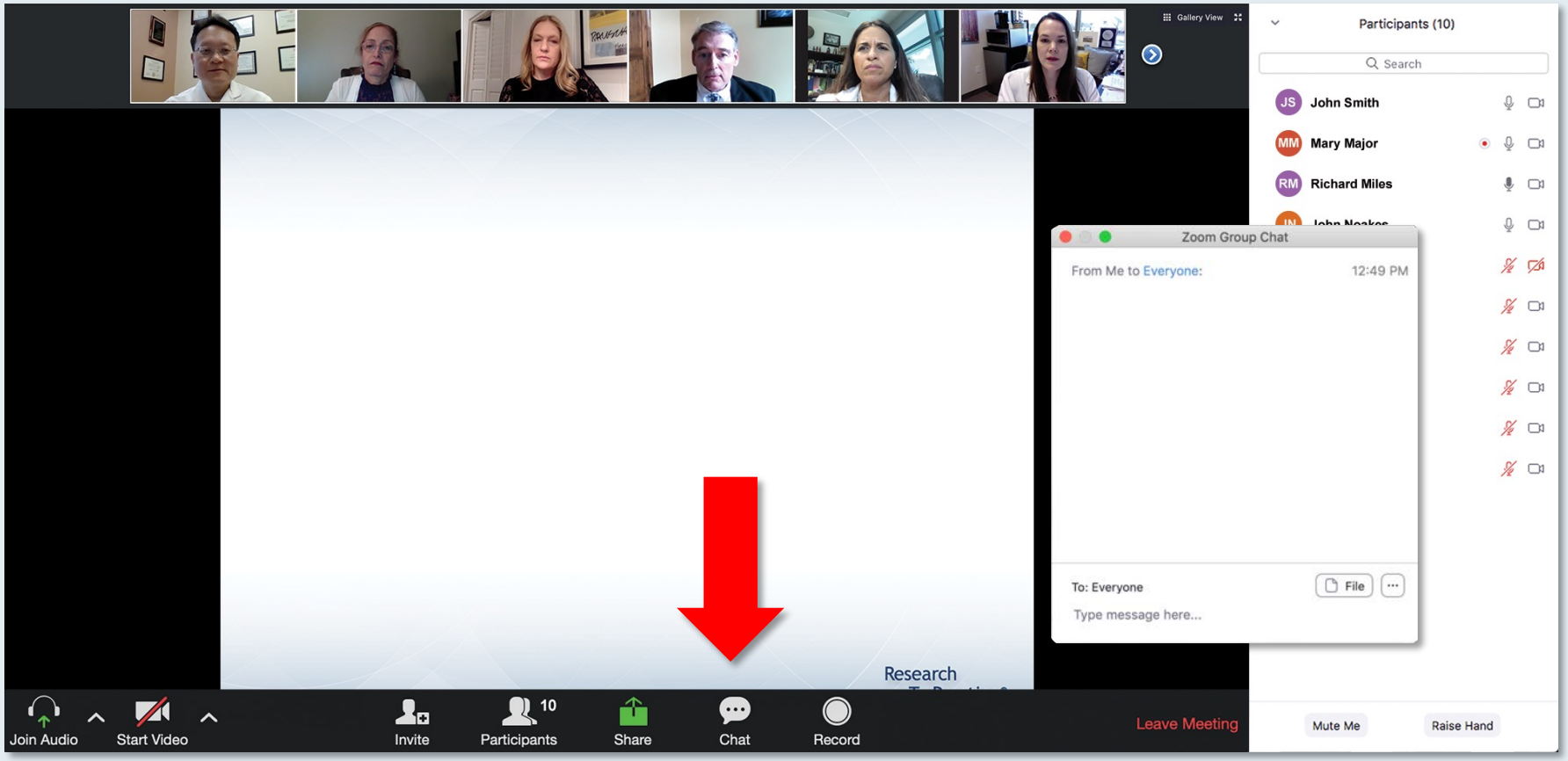

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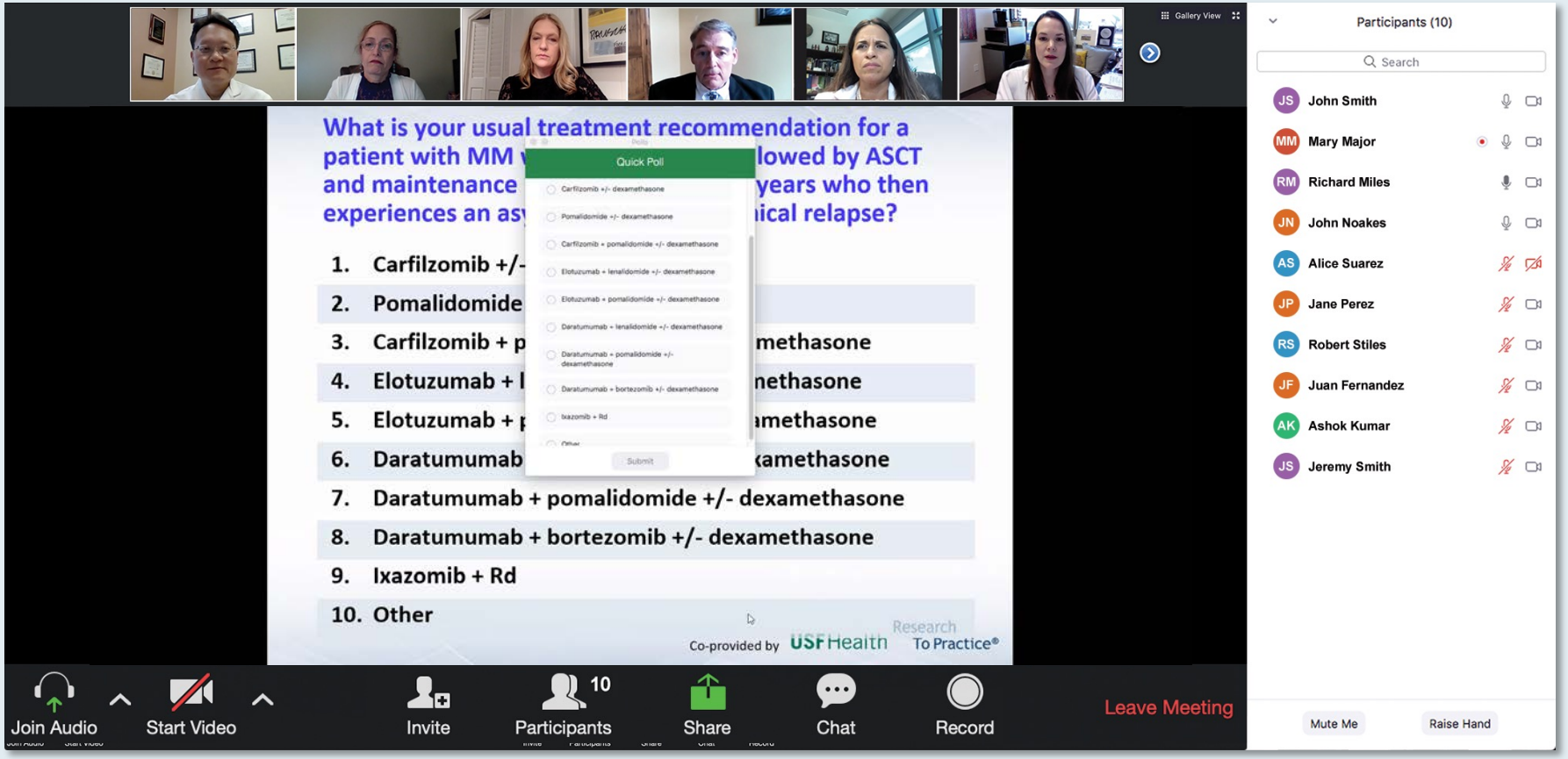

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RTP RESEARCH TO PRACTICE

Oncology Grand Rounds Nursing Webinar Series

April 2021

Monday	Tuesday	Wednesday	Thursday	Friday
19	20 Breast Ca 8:30 AM Lung Ca 5:00 PM	21 AML 12:00 PM CRC and GE Ca 4:45 PM	22 Prostate Ca 8:30 AM Lymphomas 5:00 PM	23
26	27 Multiple Myeloma 8:30 AM Gynecologic Ca 5:00 PM	28 Bladder Ca 12:00 PM	29 CLL 8:30 AM CAR-T 5:00 PM	30

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13th Annual Oncology Grand Rounds

A Complimentary NCPD Live Webinar Series
Held During the 46th Annual ONS Congress

Chimeric Antigen Receptor T-Cell Therapy

Thursday, April 29, 2021
5:00 PM – 6:30 PM ET

Medical Oncologists

Jeremy Abramson, MD
Caron Jacobson, MD
Noopur Raje, MD

Oncology Nurse Practitioners

Sonia Glennie, ARNP, MSN, OCN
Alli McClanahan, MSN, APRN, ANP-BC
Elizabeth Zerante, MS, AGACNP-BC

Moderator

Neil Love, MD

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Elizabeth Zerante MS, AGACNP-BC


Alli McClanahan, MSN, APRN, ANP-BC


Sonia Glennie, ARNP MSN OCN

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Agenda

Module 1: Management of Multiple Myeloma (MM)

- Dr Raje: A 56-year-old man with IgA kappa MM
- Ms McClanahan: A 65-year-old man with IgA kappa MM

Module 2: Clinical Use of BCMA-Targeted CAR T-Cell Therapy in MM

- Dr Raje: A 78-year-old woman with IgA kappa MM and a p53 mutation
- Ms McClanahan: A 68-year-old man with multiregimen-refractory IgA kappa MM

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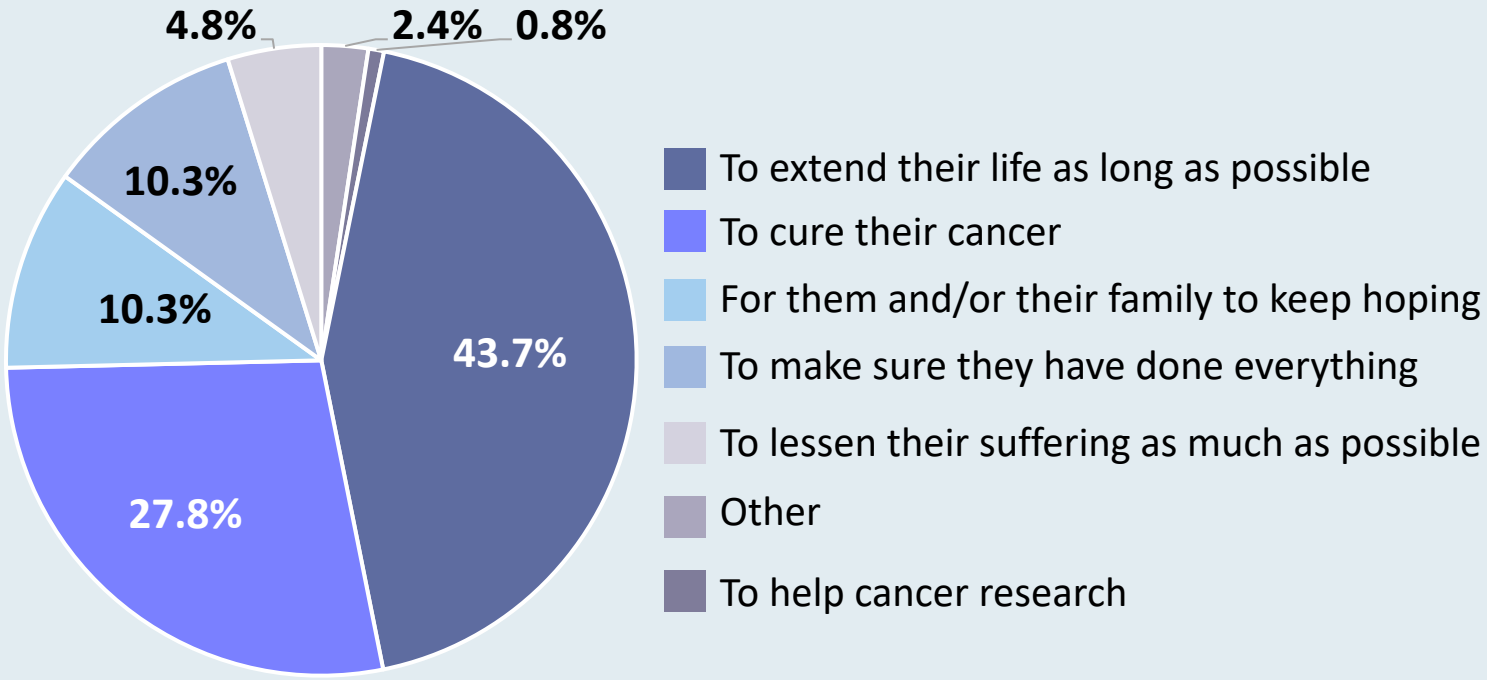
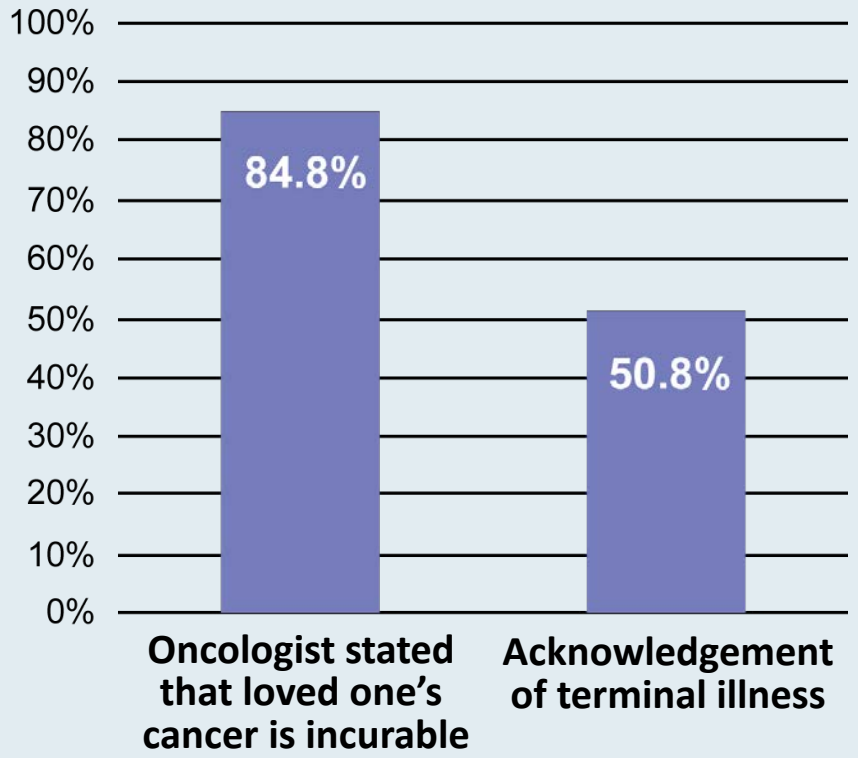
Perceptions of Prognosis in Caregivers of Patients with MM

Caregiver-Reported Primary Goal of Patient's Treatment



Caregiver Acknowledgement of the Curability of Patient's Illness



Shapiro YN et al. ASCO 2021;Abstract 12082.

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How many patients, if any, in your practice have received some form of chimeric antigen receptor (CAR) T-cell therapy?

1. None
2. 1 patient
3. 2 patients
4. 3 patients
5. >3 patients

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The antitumor component of chimeric antigen receptor (CAR) T-cell therapy is…

1. Re-transplanted marrow cells
2. Chemotherapy
3. The patient's T cells
4. I don't know

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The antitumor component of autologous stem cell transplantation (ASCT) is…

1. Re-transplanted marrow cells
2. Chemotherapy
3. The patient's T cells
4. I don't know

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CAR T-cell therapy is commonly associated with…

1. Cytokine release syndrome (CRS)
2. Neurotoxicity
3. Rash
4. Peripheral neuropathy
5. Both CRS and neurotoxicity
6. I don’t know

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Case Presentation – Dr Raje: A 56-year-old man with IgA kappa multiple myeloma

- 2010: Diagnosed with IgA kappa MM
  - Initially treated with RVd → lenalidomide maintenance
- 2014: Patient's disease progressed; treated with carfilzomib/pomalidomide/dex
- 2016: Progression with bone disease; treated with carfilzomib + daratumumab
- 2018: Patient again experienced disease progression
- Treated with bortezomib + cyclophosphamide
  - Planned to initiate CAR T-cell therapy
- Patient treated with idecabtagene vicleucel (ide-cel) → progression after 18 months
- Patient is currently receiving selinexor + carfilzomib

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How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Case Presentation – Ms McClanahan: A 65-year-old man with IgA kappa multiple myeloma

- 2019: Diagnosed with IgA kappa MM
  - Initially treated with ixazomib/daratumumab/lenalidomide/dex → ASCT
- Day 60 PET scan revealed disease progression
  - 2nd transplant versus CAR T-cell therapy discussed; patient opted for the latter
- Prior to CAR T patient developed RSV and influenza and was hospitalized
  - Patient received dara/pom/dex bridging therapy
- Ultimately treated with anti-BCMA CAR T-cell therapy on a clinical trial
  - Attained a very good partial response
  - Experienced mild cytokine release syndrome; did not require any intervention
- Recent mild reactive axillary nodes on PET scan follow-up
  - Likely secondary to recent COVID-19 vaccine
  - Repeat labs and imaging have been reassuring

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How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Overview of the Management of Multiple Myeloma (MM)

Strategy of MM treatment

- Depth of response, continuous treatment, cure
- Up-front treatment: Higher versus standard risk
  - Combination therapy – 3- versus 4-drug regimens
    - Proteasome inhibitors, IMiDs, anti-CD38 antibodies
  - Minimal residual disease (MRD) – Role of maintenance therapy
  - New agents: Belantamab mafadotin, selinexor, melflufen, iberdomide

Immuno-oncology 2021

- Checkpoint inhibitors
- Cellular therapy: Chimeric antigen receptor (CAR) T-cell therapy
- Bispecific antibodies

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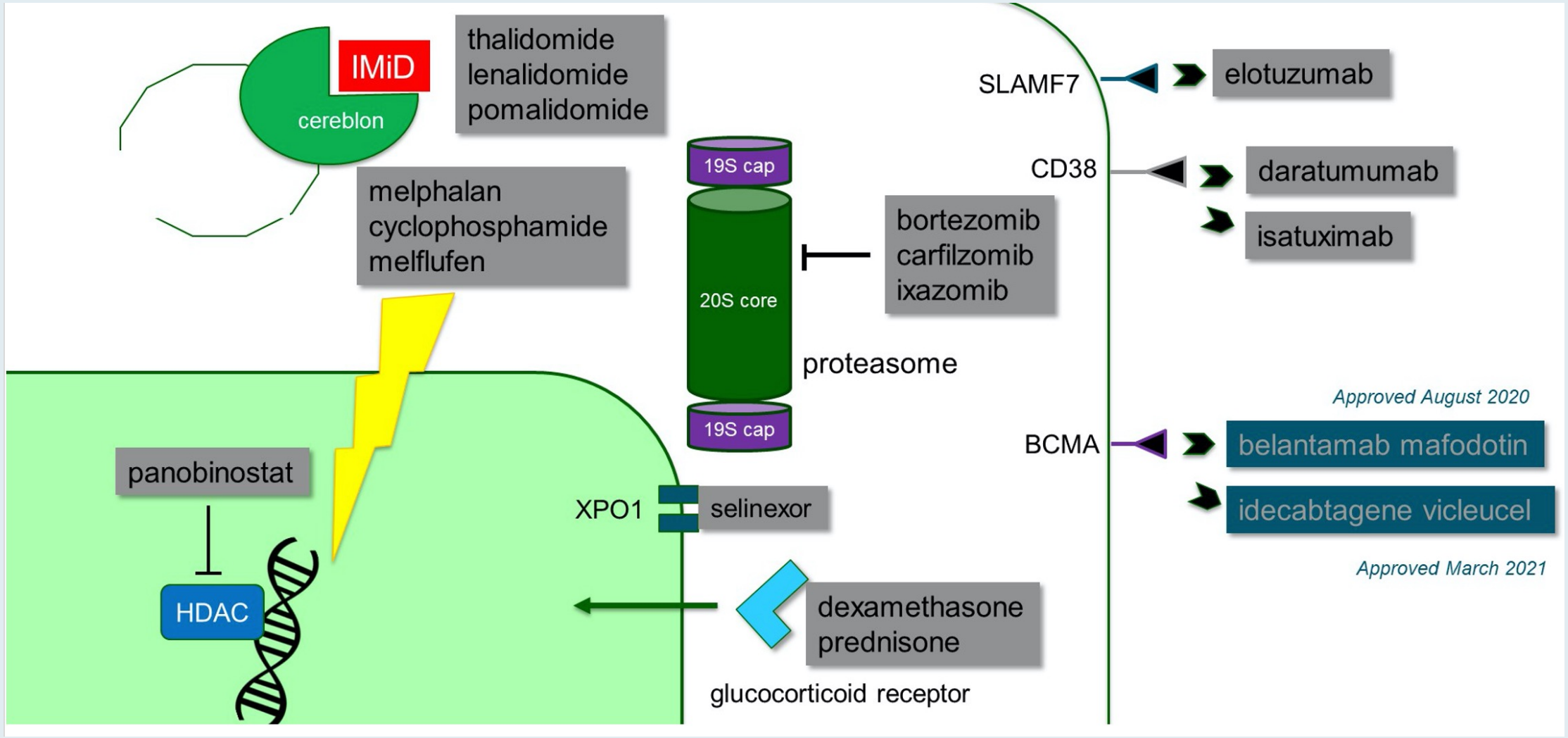
Therapeutic Options for Relapsed/Refractory MM



Raje N. ASCO 2021;Education Session – How to Treat High-Risk Myeloma at Diagnosis and Relapse.

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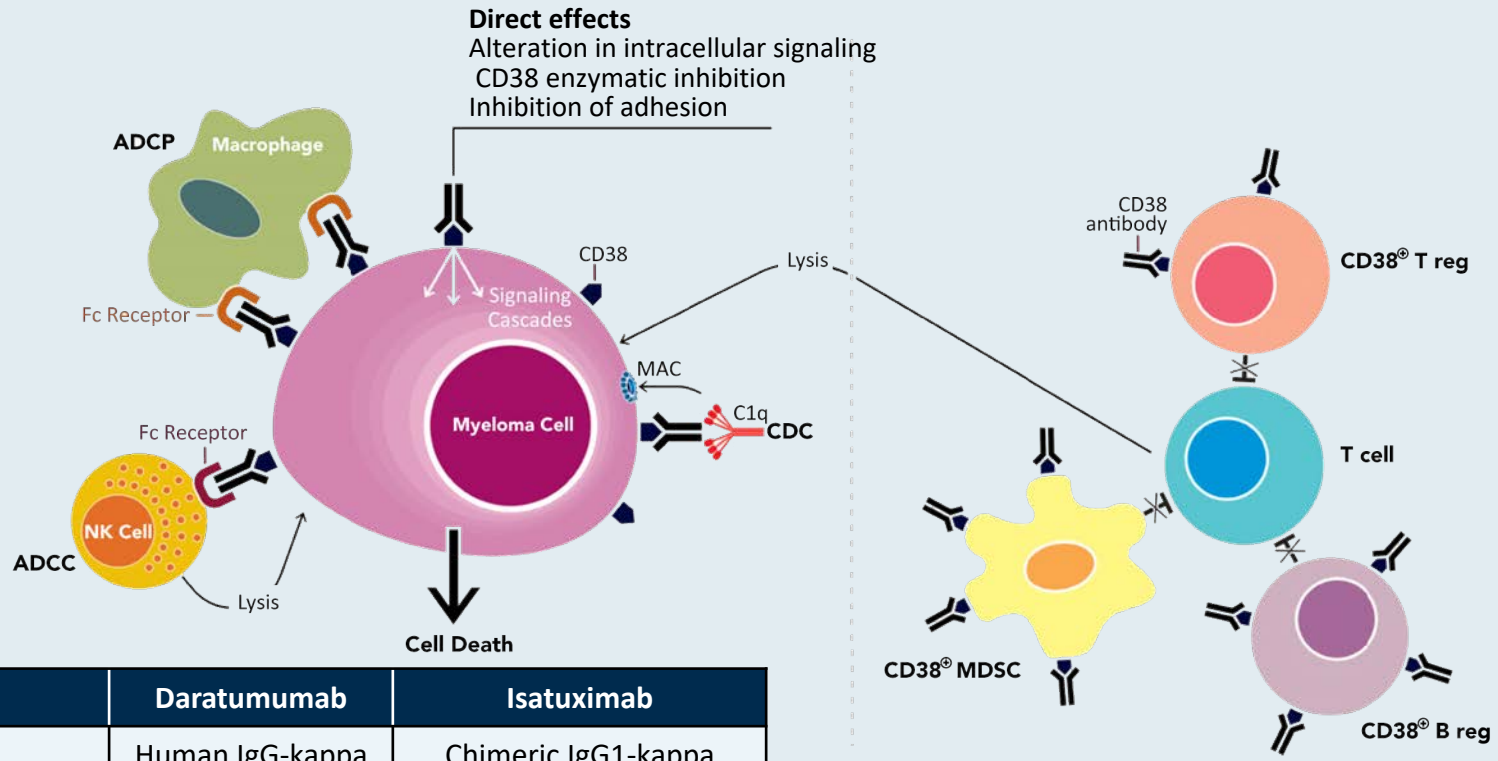
Anti-CD38 Antibodies: Mechanism of Action, Structural and Pharmacologic Similarities and Differences

Fc-dependent immune effector mechanisms and direct effects **Immunomodulatory effects**



Mechanism of action	Daratumumab	Isatuximab
Origin, isotype	Human IgG-kappa	Chimeric IgG1-kappa
CDC	+++	+
ADCC	++	++
ADCP	+++	Not determined
PCD direct	—	++
PCD cross linking	+++	+++
Modulation ectoenzyme function	+	+++

van de Donk NWCJ et al. *Blood* 2018;131(1):13-29.

Co-provided by USF Health
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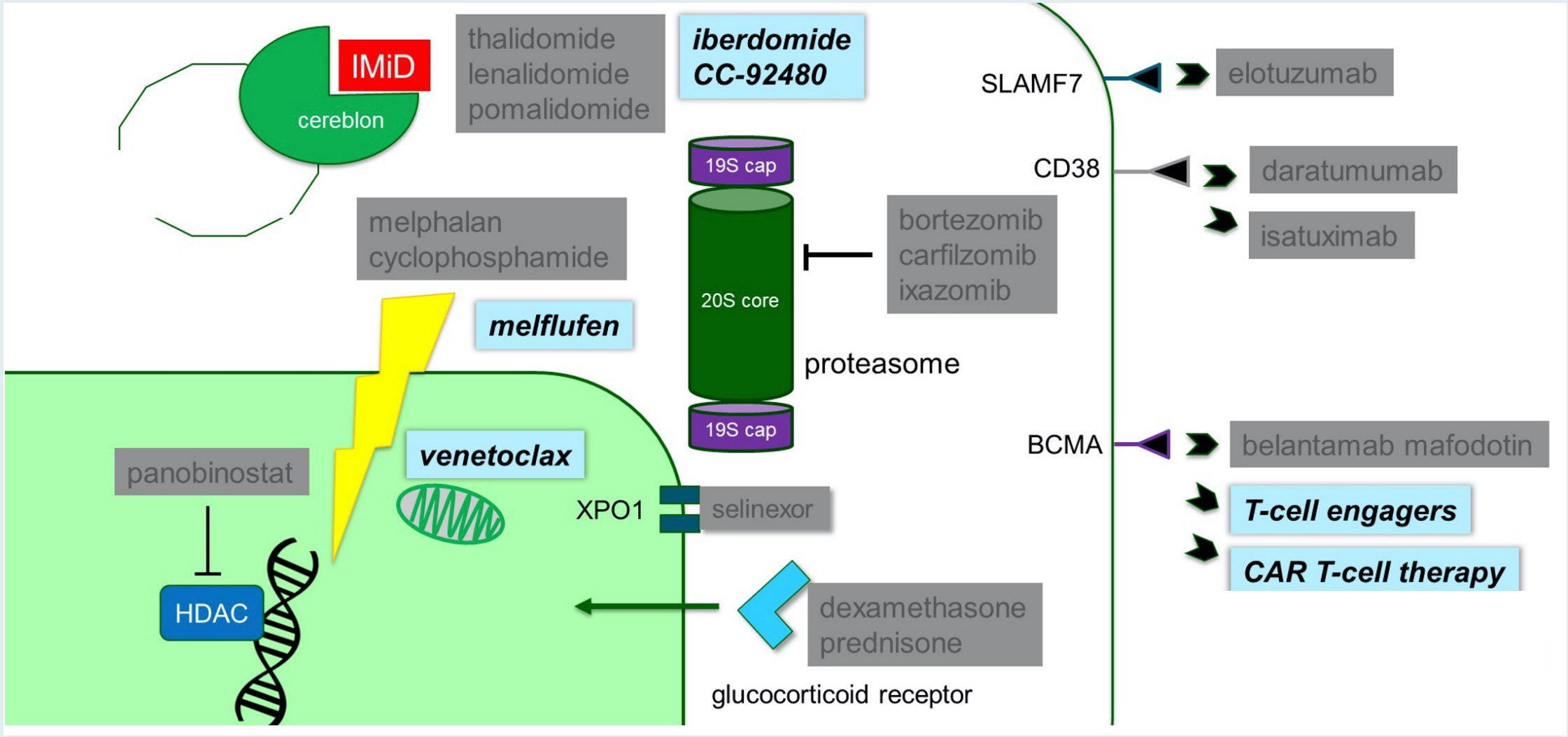
Therapeutic Options for R/R MM – What's New?



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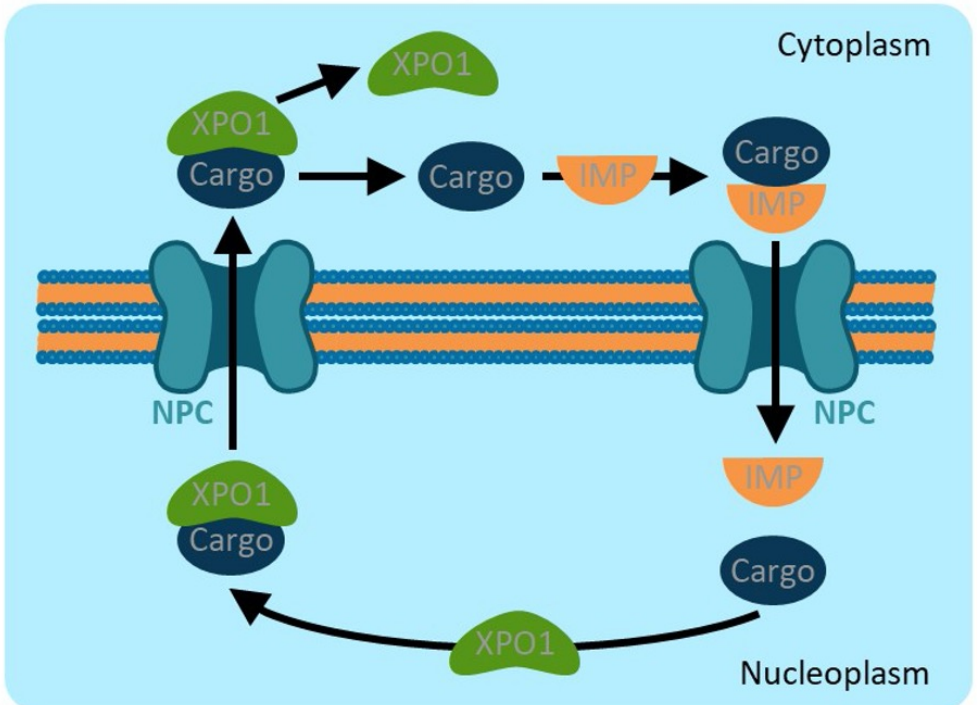
Selinexor: Mechanism of Action

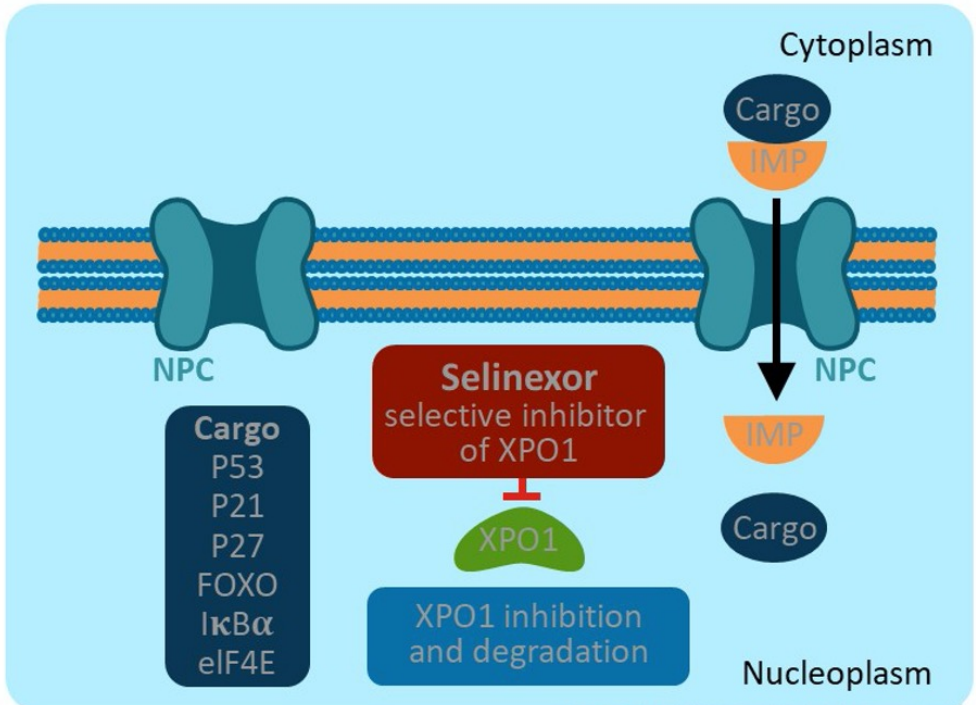
Exportin 1 is the major nuclear export protein for:

- Tumor suppressor proteins, eIF4E-bound oncoprotein mRNAs, glucocorticoid receptor



XPO1 is overexpressed in MM

- Selinexor is an oral XPO1 inhibitor



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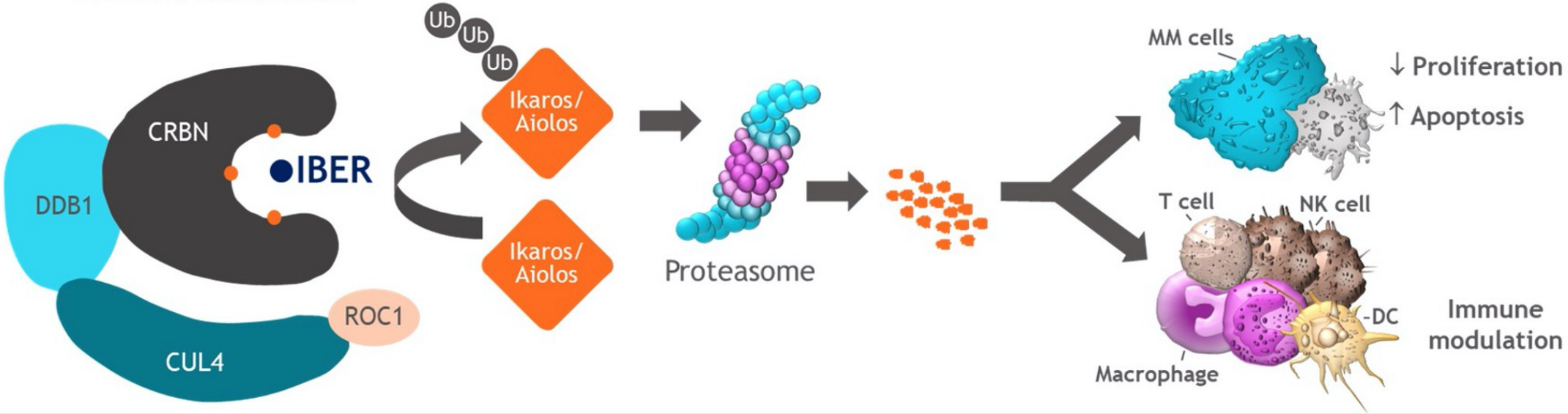
Iberdomide: Mechanism of Action

- IBER is an oral, potent novel CRBN E3 ligase modulator (CELMoD) compound that co-opts CRBN to enable enhanced degradation of target proteins, including Ikaros and Aiolos[1,2]
  - IBER induces potent direct antimyeloma and immune-stimulatory activity in preclinical models[1]
  - IBER is active in LEN- and POM-resistant myeloma cell lines and enhances cell-mediated killing through immune stimulation[1,2]



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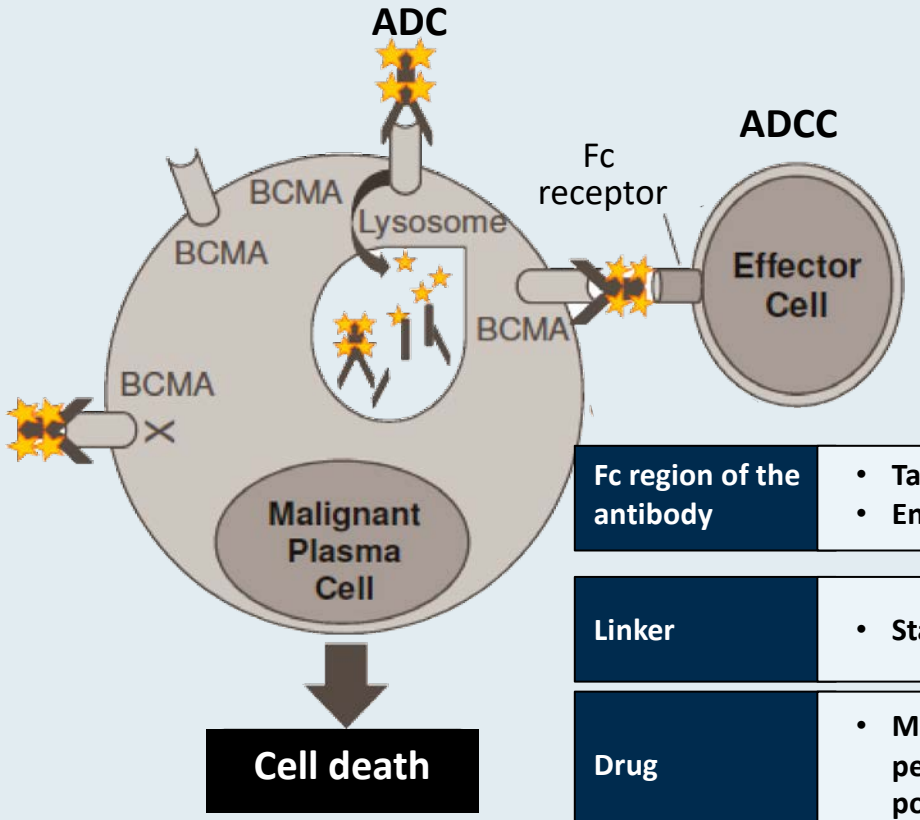
Belantamab Mafodotin: Anti-BCMA Antibody-Drug Conjugate

- B-cell maturation factor (BCMA) expression is restricted to B cells at later stages of differentiation and is required for survival of plasma cells
- BCMA is broadly expressed at variable levels on malignant plasma cells
- Belantamab mafodotin is a humanized, afucosylated IgG1 anti-BCMA antibody conjugated to microtubule disrupting agent MMAF via a stable, protease-resistant maleimidocaproyl linker



Fc region of the antibody	• **Target specific** • **Enhanced ADCC**
Linker	• **Stable in circulation**
Drug	• **MMAF (non cell permeable, highly potent auristatin)**

Mechanisms of action:
- ADC mechanism
- ADCC mechanism
- Immunogenic cell death
- BCMA receptor signaling inhibition

Tai YT et al. *Blood* 2014;123(20):3128-38.

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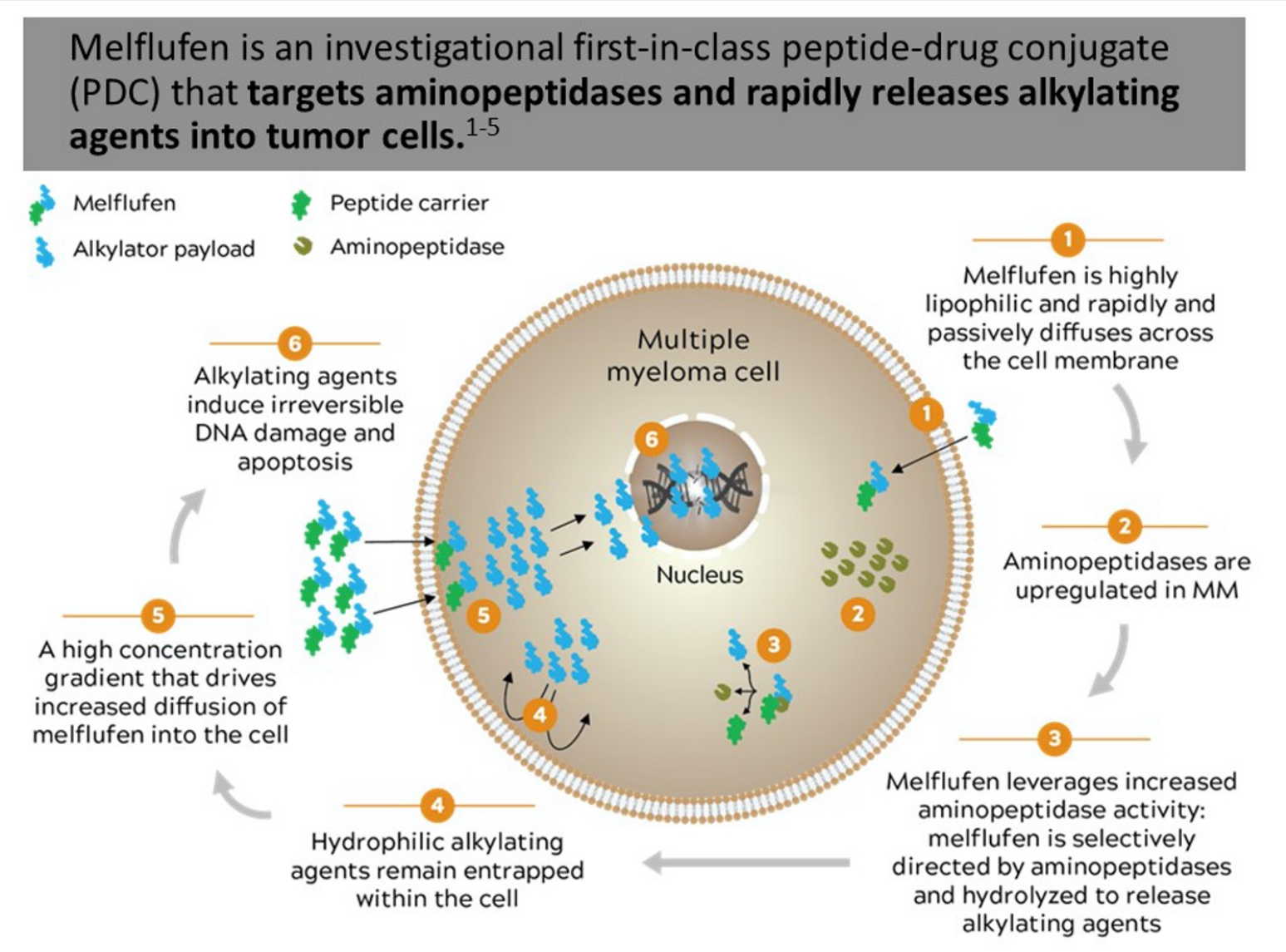
Melflufen: Mechanism of Action



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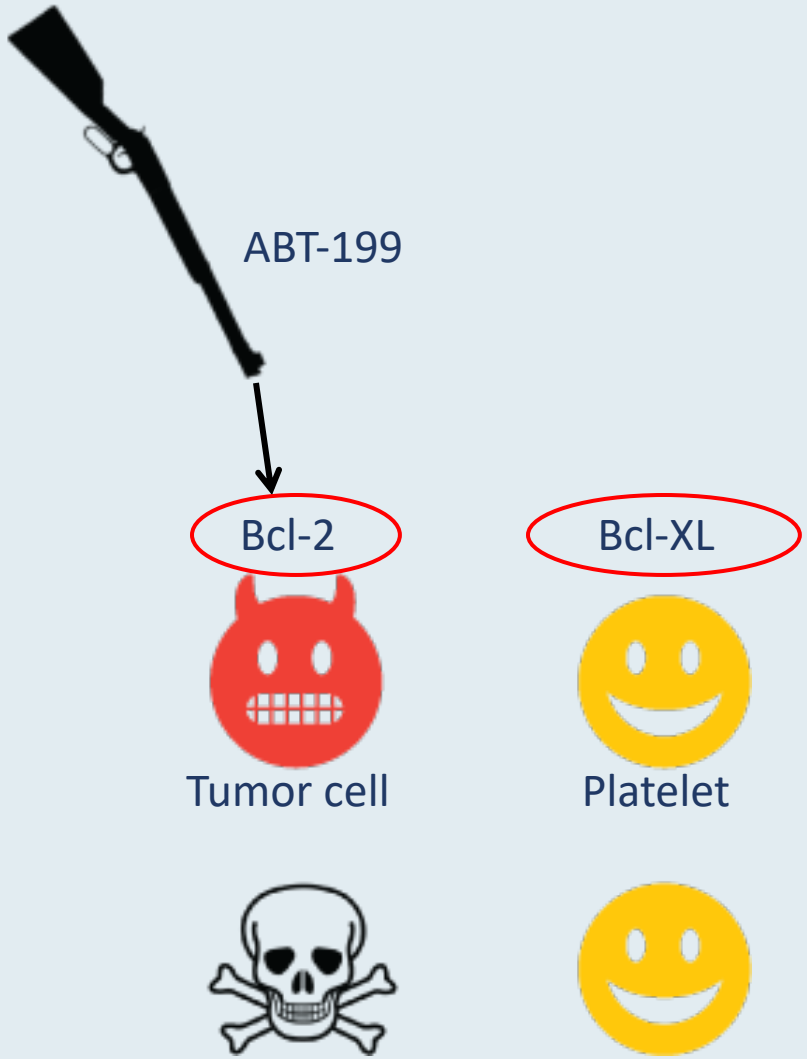
Mechanism of Action of Venetoclax



- **Bcl-2 functions to prevent cell death by apoptosis**
- **Venetoclax is specific for Bcl-2 and inhibits its function, thereby removing the block on apoptosis**

Adapted from Davids MS, Letai A. *Cancer Cell* 2013;23(2):139-41.

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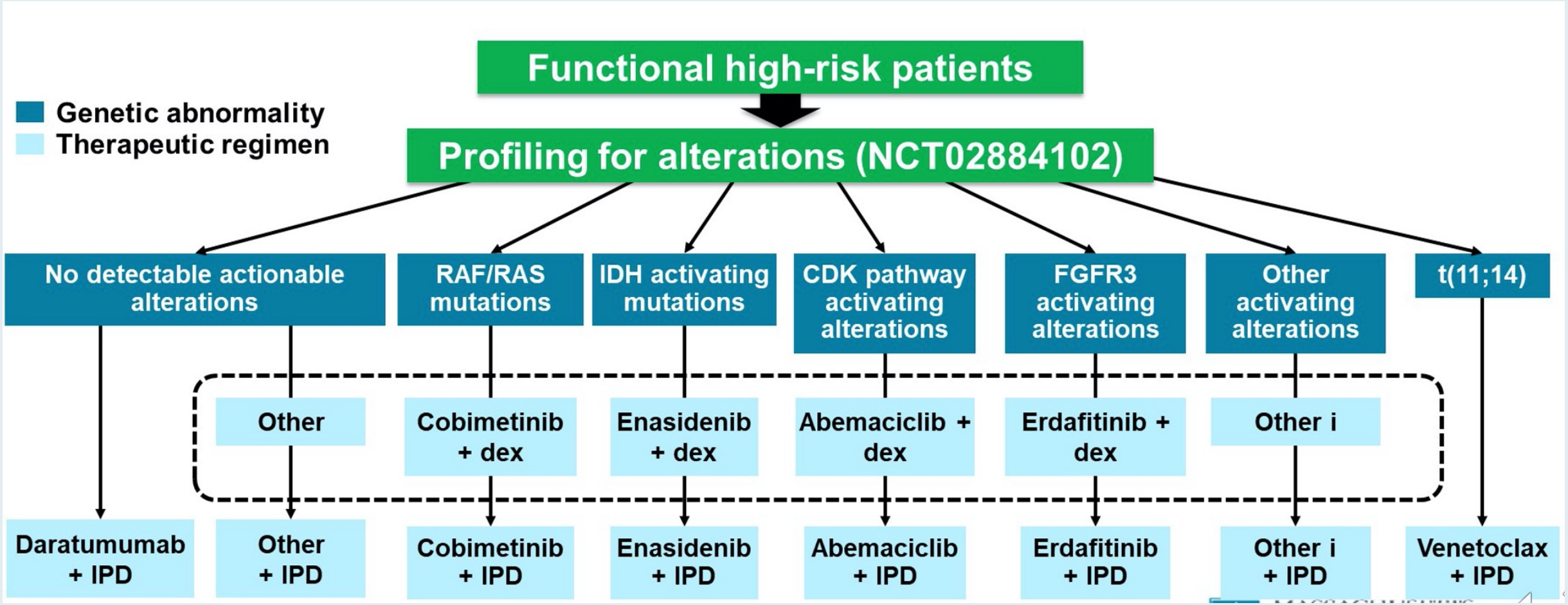
MyDRUG: Mutation-Specific Approach



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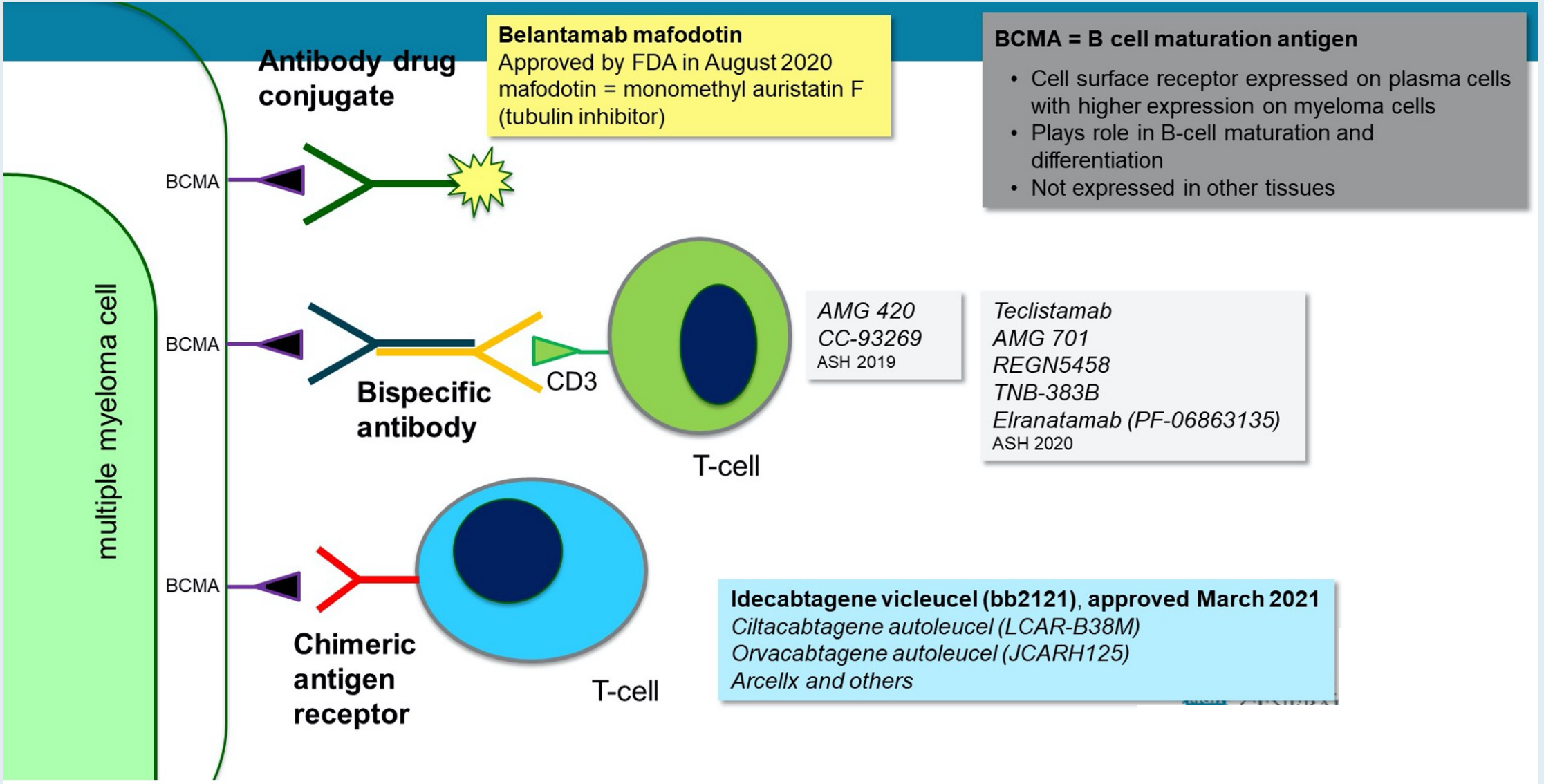
Therapies Targeting BCMA



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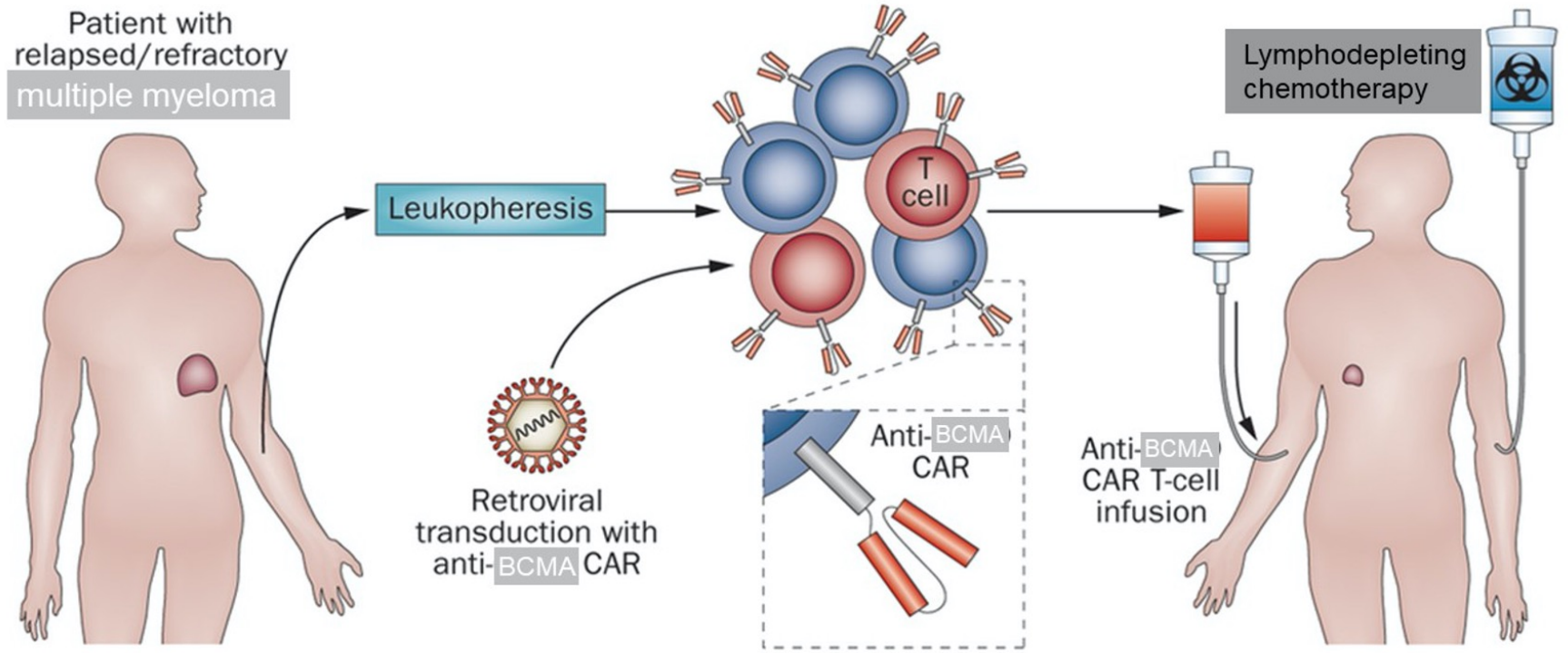
CAR T-Cell Therapy: Mechanism of Action



Klebanoff et al., *Nature Rev. Clin. Oncol* 2014

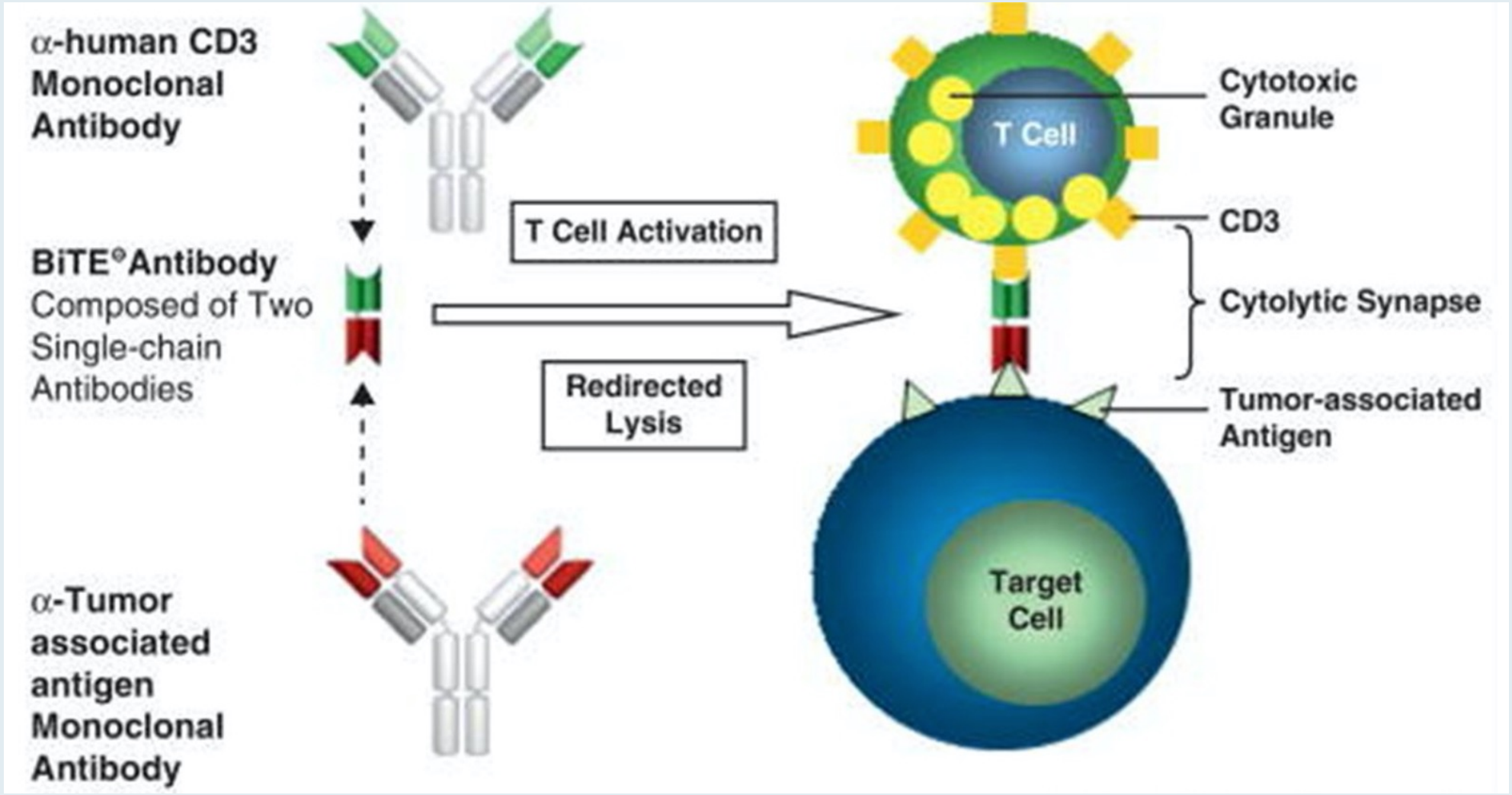
In ALL and lymphoma, patient's T-cells are collected and engineered to target CD19

In myeloma, CAR T-cells target myeloma-specific antigens, e.g. BCMA

Raje N. ASCO 2021;Education Session – How to Treat High-Risk Myeloma at Diagnosis and Relapse.

RTP RESEARCH TO PRACTICE

Bispecific T-Cell Engagers



Raje N. ASCO 2021;Education Session – How to Treat High-Risk Myeloma at Diagnosis and Relapse.

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Agenda

Module 1: Management of Multiple Myeloma (MM)

- Dr Raje: A 56-year-old man with IgA kappa MM
- Ms McClanahan: A 65-year-old man with IgA kappa MM

Module 2: Clinical Use of BCMA-Targeted CAR T-Cell Therapy in MM

- Dr Raje: A 78-year-old woman with IgA kappa MM and a p53 mutation
- Ms McClanahan: A 68-year-old man with multiregimen-refractory IgA kappa MM

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At this point, responses to CAR T-cell therapy in patients with MM appear very similar to those seen with CD19-directed CAR T-cell therapy for diffuse large B-cell lymphoma.

1. Agree
2. Disagree
3. I don’t know

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Case Presentation – Dr Raje: A 78-year-old woman with IgA kappa multiple myeloma and a p53 mutation

- 2015: Diagnosed with IgA kappa MM
  - Initially treated with RVd → lenalidomide/bortezomib maintenance
- 2016: Patient's disease progressed; treated with daratumumab/pomalidomide/dex
  - Attained a partial response
- 2018: Patient again experienced disease progression
- Treated with carfilzomib + cyclophosphamide
  - Planned to initiate CAR T-cell therapy
- Patient treated with ciltacabtagene autoleucel (JNJ-4528)
  - Remains MRD negative at 20 months

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How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Case Presentation – Ms McClanahan: A 68-year-old man with multiregimen-refractory IgA kappa multiple myeloma

- 2012: Diagnosed with IgA kappa MM
  - Treated with approximately 9 regimens over the next 8 years
- **Clinical condition prior to undergoing CAR T-cell therapy**: ECOG PS 1; transfusion dependent
- 2020: Anti-BCMA CAR T-cell therapy preparation:
- High risk of CRS (Pre-CART bone marrow biopsy [BMBX]: 90% involvement, IgA level ~ 5000)
  - Treated prophylactically with anakinra (3 hours prior and then daily x 5 days after CART with plans to increase to BID with CRS)
  - Also admitted to hospital following CAR T-cell infusion
- **Day of CAR T-cell infusion**: By that evening patient was febrile to 39.3°C → anakinra increased to BID
  - Remained febrile 5 hours later with hypotension not responsive to 2L IV fluids
  - Transferred to ICU with grade 3 CRS requiring norepinephrine and vasopressin; tocilizumab + dexamethasone
- Symptoms promptly resolved with no signs of neurotoxicity
- **Current status of patient:** Over 1 year post-CART remains in CR with recent BMBX – MRD negative

RTP RESEARCH TO PRACTICE

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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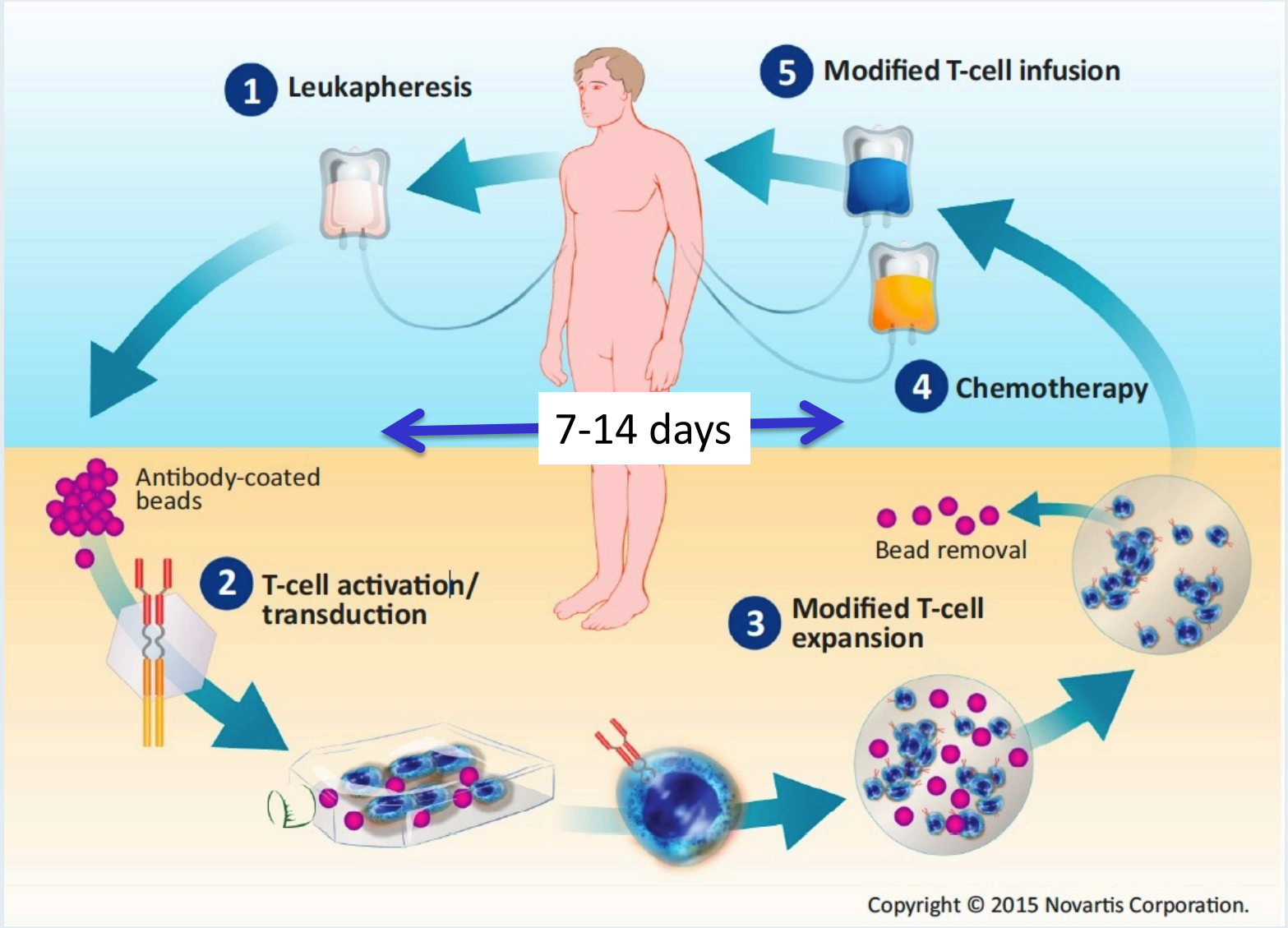
Overview of CAR T-Cell Therapy

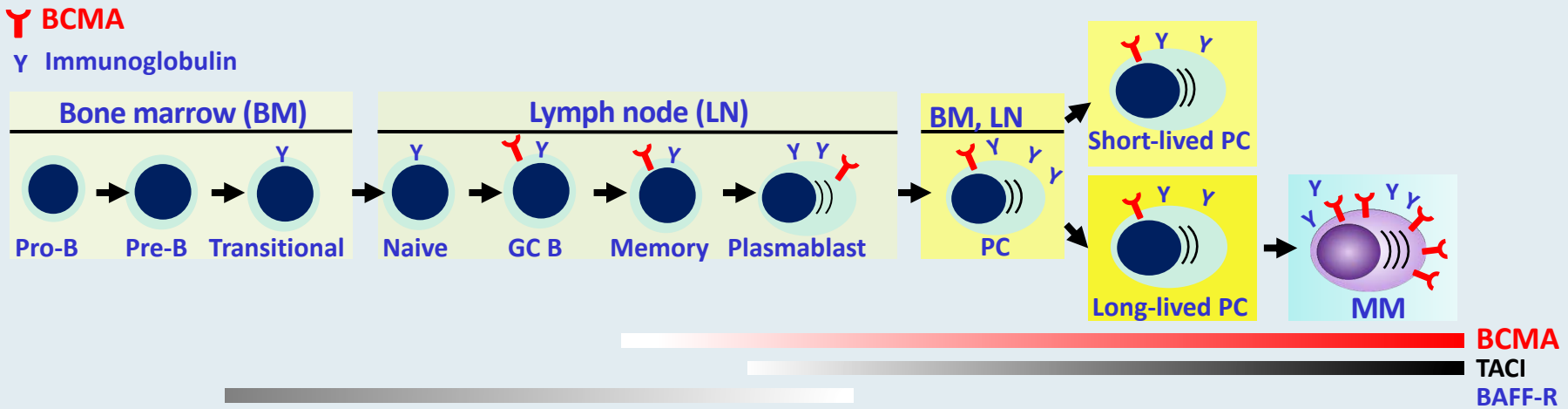


Modification, Courtesy, David Porter, MD

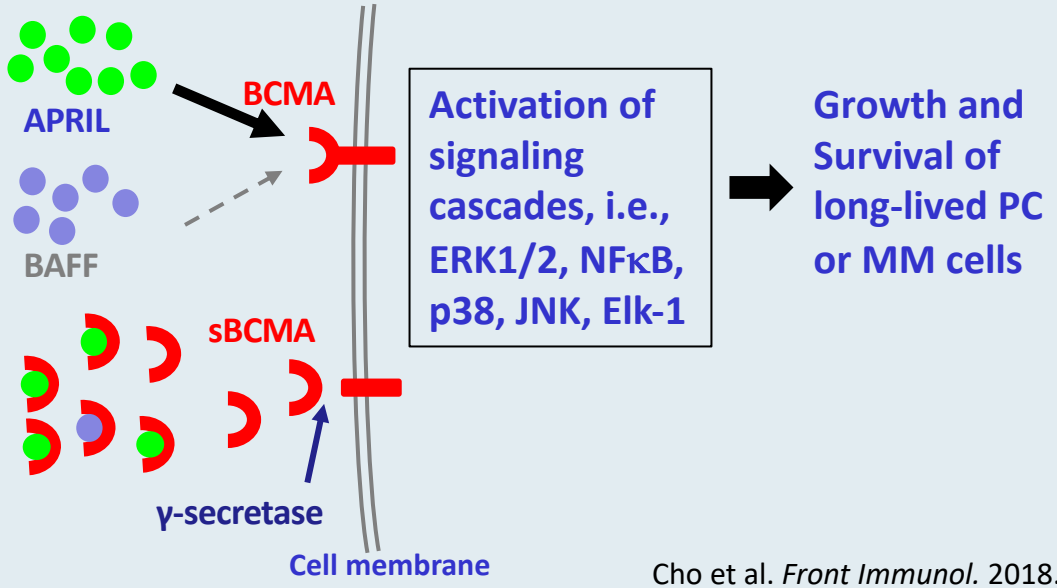
RTP RESEARCH TO PRACTICE

B-Cell Maturation Antigen (BCMA)
A Promising Target in Multiple Myeloma

A



B



- **BCMA is member of the TNF receptor superfamily**
  Expressed nearly universally on MM cells
  Expression largely restricted to plasma cells and some mature B cells
- **BCMA support survival of long-lived PCs, Ig Class switch and Ab Production**
- **Promotes proliferation, survival and associated with immunosuppressive BM microenvironment**

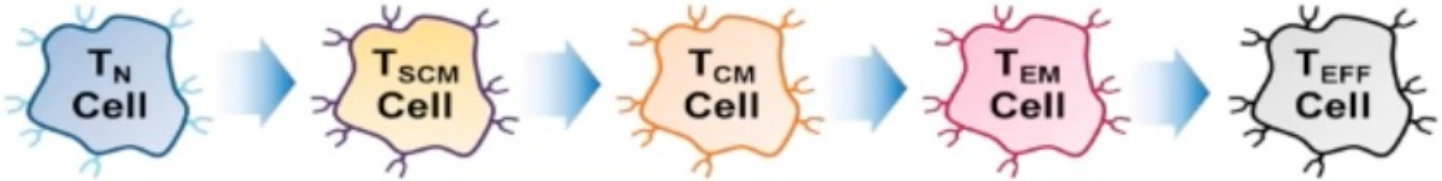
Cho et al. *Front Immunol.* 2018.

Courtesy of Nikhil C Munshi, MD

RTP RESEARCH TO PRACTICE

bb21217: Mechanism of Action

- bb21217 uses the same CAR molecule as bb2121,[1] but is cultured with the PI3K inhibitor, bb007, to enrich for T cells displaying a memory-like phenotype
- CAR T cells enriched for this phenotype may persist and function for longer than non-enriched CAR T cells[2]
- Persistence of functional CAR T cells after infusion may be one determinant of duration of response[3]



Memory-like phenotype
T-cell plasticity
Long-lived
Self-renewal

Effector-like phenotype
Terminally differentiated
Short-lived
No self-renewal

- When cultured in the presence of the PI3K inhibitor bb007, donor cells become enriched for memory-like CAR T cells and the percentage of senescent CAR T cells decreases.

Alsina M et al. ASH 2020;Abstract 130.

RTP RESEARCH TO PRACTICE

FDA Approves Idecabtagene Vicleucel for Multiple Myeloma

Press Release – March 26, 2021

"On March 26, 2021, the FDA approved idecabtagene vicleucel for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. This is the first FDA-approved cell-based gene therapy for multiple myeloma.

Idecabtagene vicleucel is a BCMA-directed genetically modified autologous chimeric antigen receptor (CAR) T-cell therapy. Each dose is customized using a patient's own T-cells, which are collected and genetically modified, and infused back into the patient.

Efficacy was evaluated in 100 patients who received idecabtagene vicleucel in the dose range of 300 to 460 x 106 CAR-positive T cells. Efficacy was established based on overall response rate (ORR), complete response (CR) rate, and duration of response (DOR), as evaluated by an Independent Response committee using the International Myeloma Working Group Uniform Response Criteria for Multiple Myeloma."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-idecabtagene-vicleucel-multiple-myeloma

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N Engl J Med 2021;384(8):705-16

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma

Nikhil C. Munshi, M.D., Larry D. Anderson, Jr., M.D., Ph.D., Nina Shah, M.D., Deepu Madduri, M.D., Jesús Berdeja, M.D., Sagar Lonial, M.D., Noopur Raje, M.D., Yi Lin, M.D., Ph.D., David Siegel, M.D., Ph.D., Albert Oriol, M.D., Philippe Moreau, M.D., Ibrahim Yakoub-Agha, M.D., Ph.D., Michel Delforge, M.D., Michele Cavo, M.D., Hermann Einsele, M.D., Hartmut Goldschmidt, M.D., Katja Weisel, M.D., Alessandro Rambaldi, M.D., Donna Reece, M.D., Fabio Petrocca, M.D., Monica Massaro, M.P.H., Jamie N. Connarn, Ph.D., Shari Kaiser, Ph.D., Payal Patel, Ph.D., Liping Huang, Ph.D., Timothy B. Campbell, M.D., Ph.D., Kristen Hege, M.D., and Jesús San-Miguel, M.D., Ph.D.

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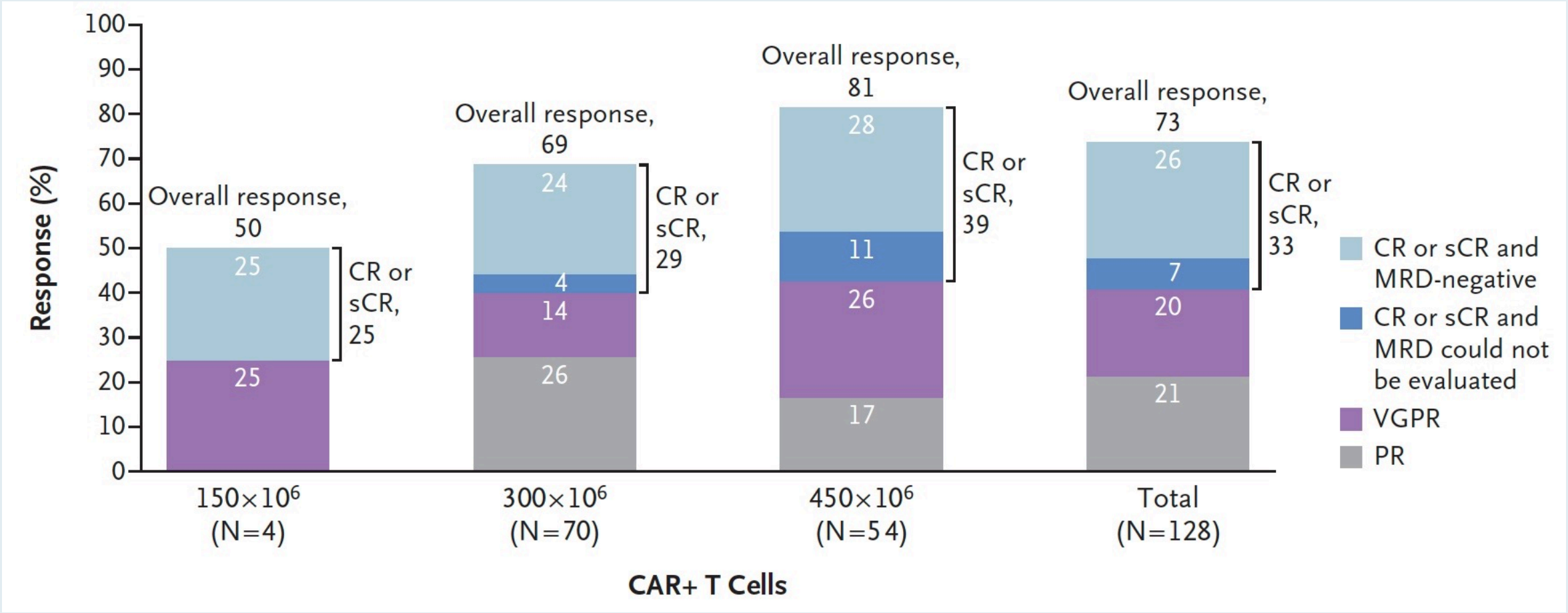
KarMMa: Tumor Response, Overall and According to Target Dose



Munshi NC et al. *N Engl J Med* 2021;384(8):705-16.

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KarMMa: Select Adverse Events

Variable	Any Grade	Grade 3 or 4
	no. of patients (%)	
Adverse event*		
Any	128 (100)	127 (99)
Hematologic		
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)
Febrile neutropenia	21 (16)	20 (16)
Cytokine release syndrome†	107 (84)	7 (5)
Neurotoxic effect‡	23 (18)	4 (3)

Munshi NC et al. *N Engl J Med* 2021;384(8):705-16.

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Updated Results from CARTITUDE-1 – Ciltacabtagene Autoleucel (Cilta-cel): ASCO 2021

- **At a longer median follow-up of 18 months, a single dose of cilta-cel led to early, deep, and durable responses in heavily pretreated patients with MM**
  - ORR: 98%; sCR: 80%; MRD 10^{-5} negativity: 92% in evaluable patients
  - 18-month PFS rate: 66%; OS rate: 81%
- **Cilta-cel has a manageable safety profile consistent with its mechanism of action; no new safety signals were observed with longer follow-up**
  - Successful new patient management strategies have been implemented in the CARTITUDE program to prevent and reduce the incidence of neurotoxicity
- **Cilta-cel is being investigated in the ongoing phase 2 CARTITUDE-2[a] and phase 3 CARTITUDE-4[b] studies in earlier line settings**

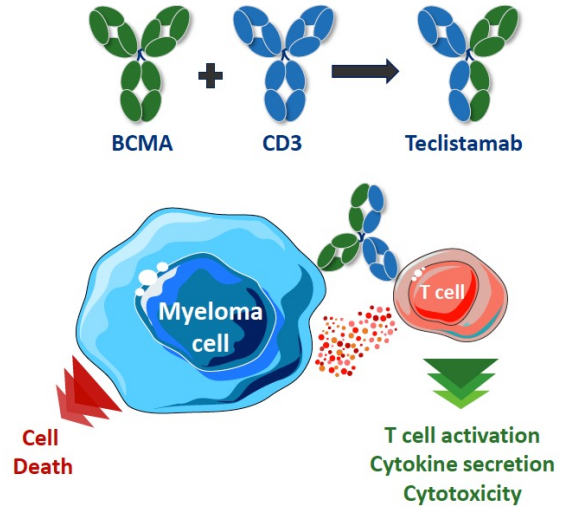
Usmani SZ et al. ASCO 2021;Abstract 8005.

RTP RESEARCH TO PRACTICE

Bispecific Antibodies for R/R MM

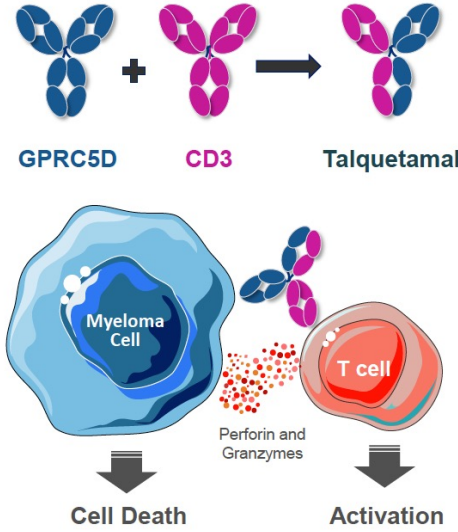
Teclistamab: BCMA × CD3 DuoBody® Antibody

- Prognosis is poor for patients who progress on available classes of therapies, with ORR ~30%, mPFS of ~3 months, and mOS between 6–11 months[1]
- Teclistamab (JNJ-64007957)[a] is a humanized BCMA × CD3 bispecific IgG-4 antibody that redirects CD3+ T cells to BCMA-expressing myeloma cells
- Teclistamab induces T cell-mediated killing of myeloma cells from heavily-treated patients and in xenograft models[2-4]
- Updated results from an ongoing phase 1 study of teclistamab administered IV or SC in patients with RRMM (NCT03145181) are presented here[5]



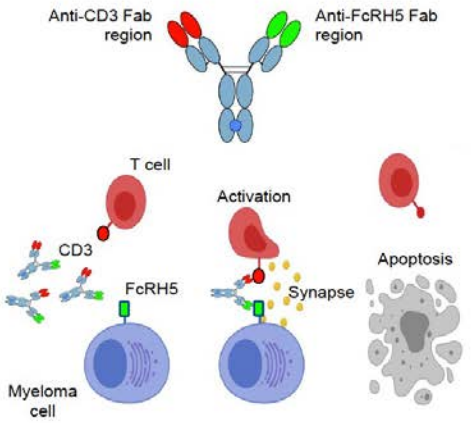
Talquetamab: GPRC5D x CD3 Bispecific Antibody

- Talquetamab is a first-in-class DuoBody® IgG4 PAA antibody that binds to both GPRC5D and CD3
- Talquetamab redirects T cells to GPRC5D-expressing myeloma cells to mediate cell killing
- Antitumor activity was demonstrated in primary myeloma cells and xenograft models of MM[1-3]
- Talquetamab's pharmacokinetic profile presents an opportunity for less frequent SC dosing
- First-in-human phase 1 study is ongoing to evaluate talquetamab in patients with RRMM (NCT03399799)



Cevostamab: FcRH5xCD3 bispecific antibody

- Fc receptor-homolog 5 (FcRH5)
  - Expressed on myeloma cells with near 100% prevalence[1]
  - Expression on myeloma and plasma cells > normal B cells[1]
- Cevostamab
  - Humanized IgG-based T-cell-engaging bispecific antibody[1]
  - Targets FcRH5 on myeloma cells and CD3 on T cells[1]
- Ongoing Phase I dose-escalation and expansion trial (NCT03275103) is evaluating the safety and activity of cevostamab monotherapy in patients with RRMM[2]



Garfall AL et al. ASH 2020;Abstract 180;
Chari A et al. ASH 2020;Abstract 290;
Cohen AD et al. ASH 2020;Abstract 292.

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An early indicator of neurotoxicity from CAR T-cell therapy is…

1. Somnolence
2. Seizures
3. Altered handwriting
4. Hyperactivity
5. I don’t know

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CAR T-Cell Therapy-Associated Cytokine Release Syndrome (CRS)

CRS — May be mild or life-threatening

- Occurs with CART19 activation and expansion
- Dramatic cytokine elevations (IL-6, IL10, IFNɣ, CRP, ferritin)
- Fevers initially (can be quite high: 105˚F)
- Myalgias, fatigue, nausea/anorexia
- Capillary leak, headache, hypoxia and hypotension
- CRS-related mortality 3% to 10%

Varadarajan I, Lee DW. *Cancer J* 2019;25(3):223-30.
Abramson JS et al. ASCO 2019 Education Book.

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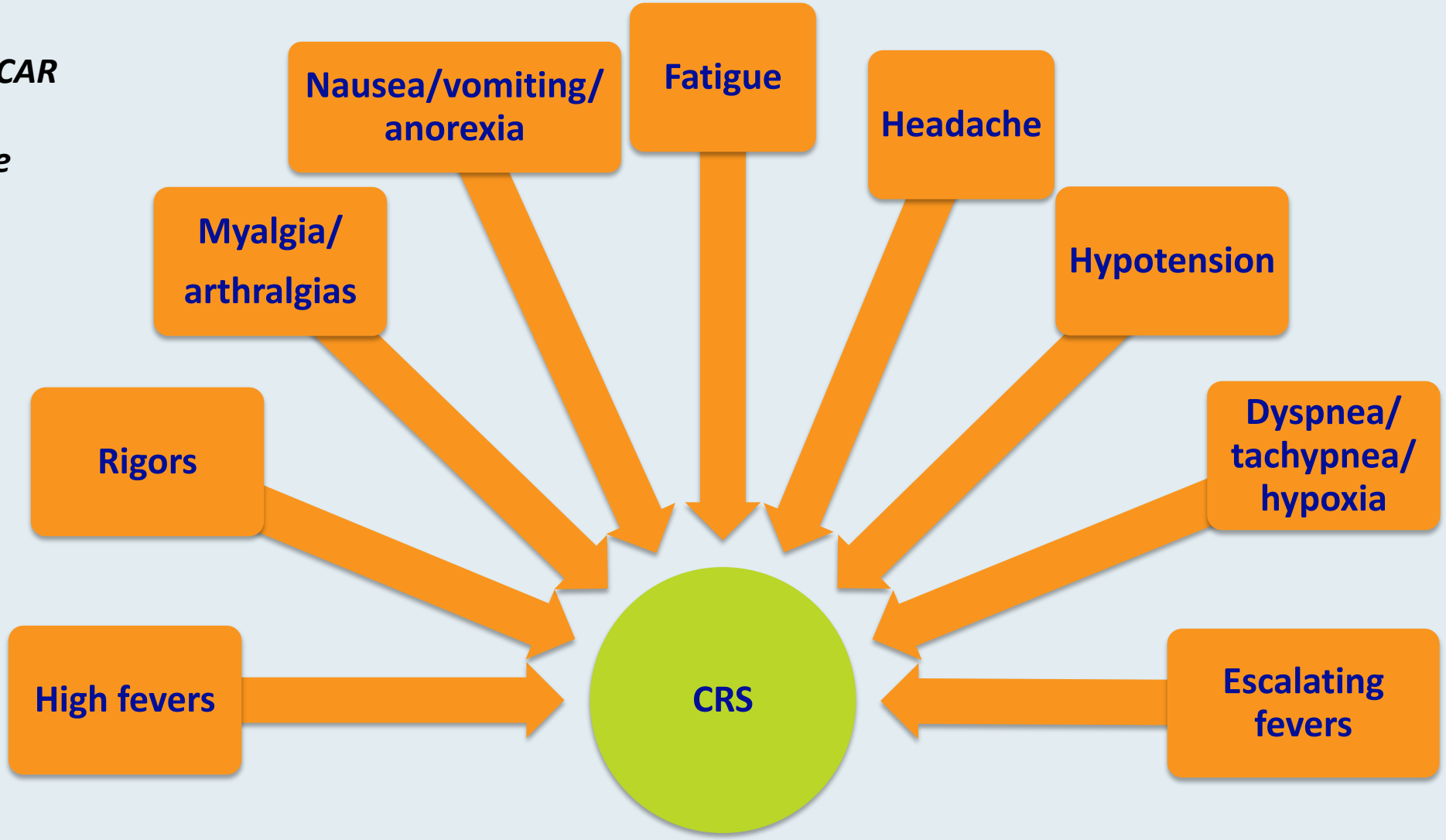
Cytokine Release Syndrome (CRS): Common Symptoms

Based on CAR T-cell experience



Diagnosis based on <u>clinical</u> symptoms and events

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CAR T-Cell Therapy-Associated Neurologic Toxicity

Neurologic toxicity — May be mild or life-threatening

- Mechanism unclear, referred to as immune effector cell-associated neurotoxicity syndrome (ICANS)
- Encephalopathy
- Seizures
- Delirium, confusion, aphasia, agitation, sedation, coma

Varadarajan I, Lee DW. *Cancer J* 2019;25(3):223-30.
Abramson JS et al. ASCO 2019 Education Book.

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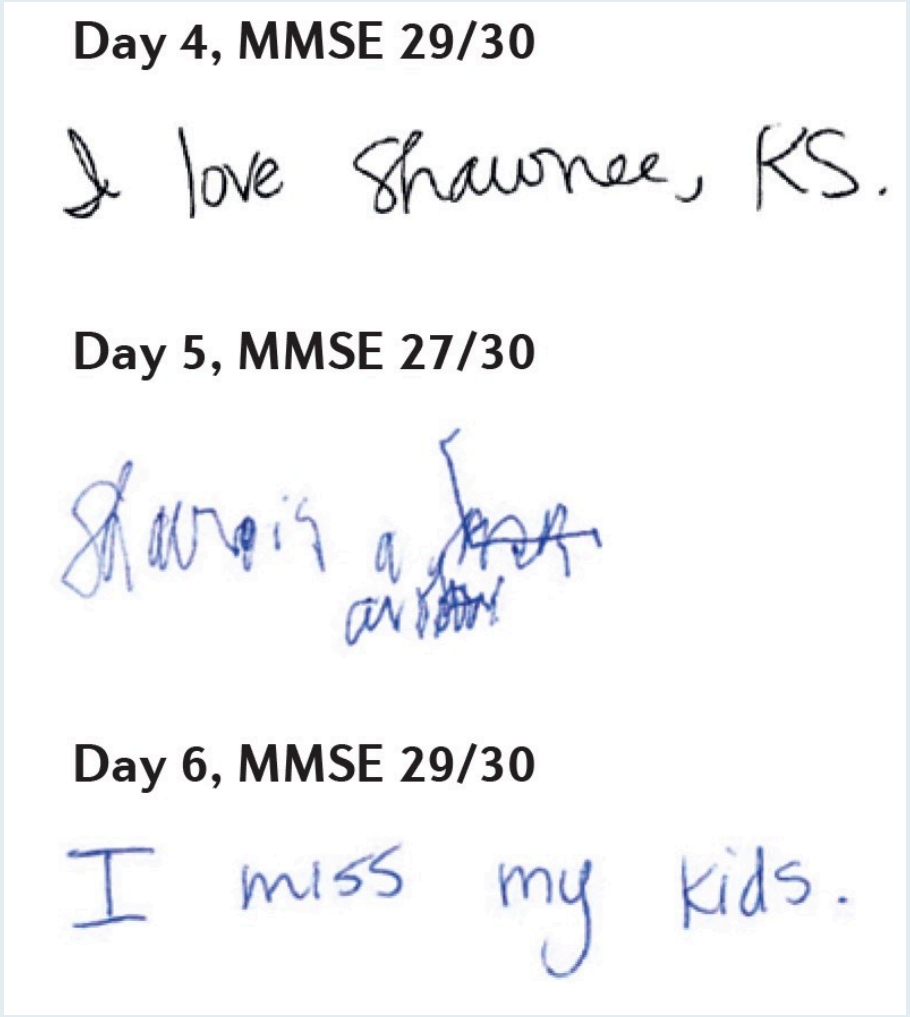
Handwriting Samples and MMSE After CAR T-Cell Therapy



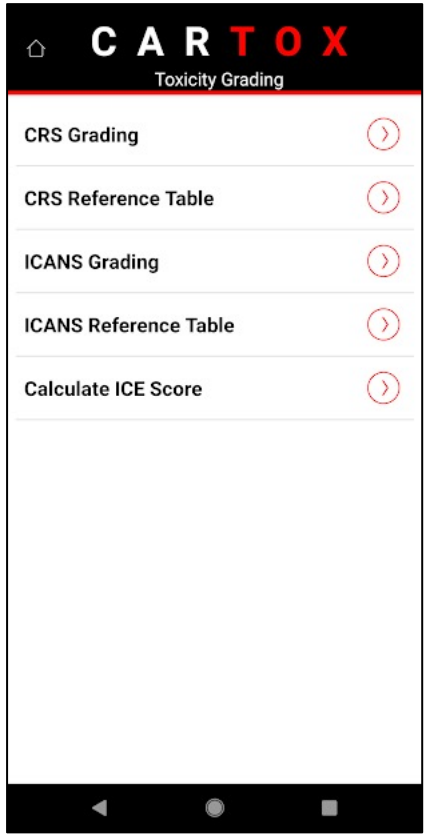
- Handwriting samples and mini mental status exam (MMSE) scores obtained on days 4, 5, and 6 after CAR T-cell therapy
- Note how the patient's handwriting was markedly impaired on day 5, despite only a small decrease in their MMSE score.

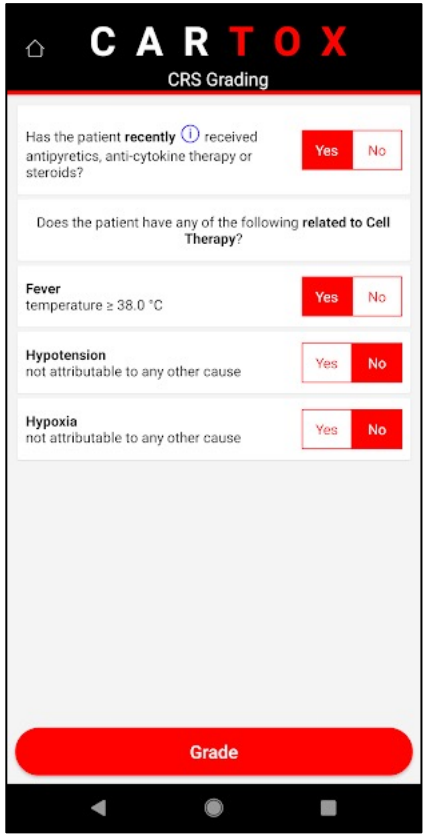
Neelapu SS et al. *Nat Rev Clin Oncol* 2018;15(1):47-62.

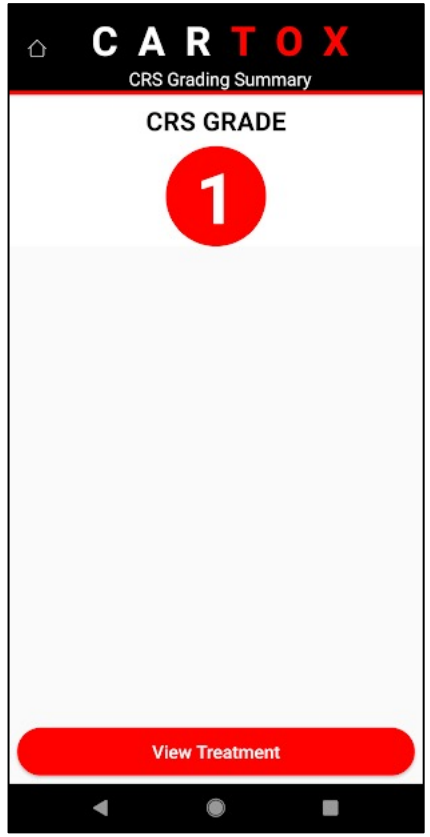
RTP RESEARCH TO PRACTICE

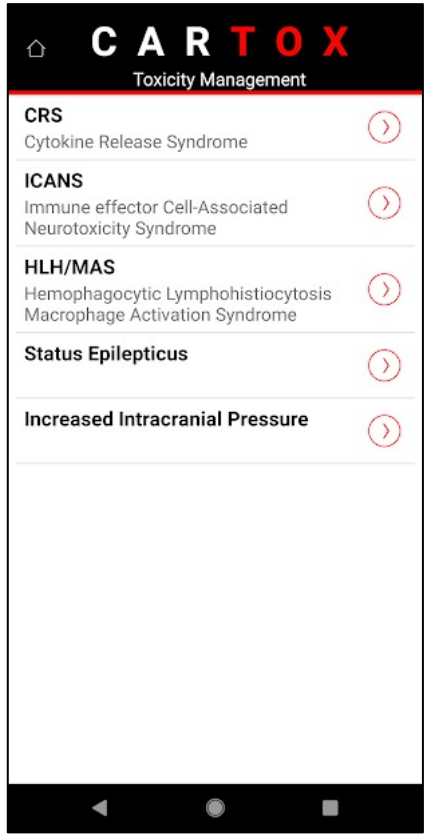
CARTOX App for Grading and Management of CRS and ICANS

Smart phone app available free on both App Store (iPhone) and Google Play (Android)









Sherry Adkins

Courtesy of Sattva S Neelapu, MD

Neelapu et al. *Nat Rev Clin Oncol,* Jan 2018

Lee et al. *Biol Blood Marrow Transplant,* 2019 Apr;25 (4):625-638

Patient Education Regarding CAR T-Cell Therapy

CRS	Neurotoxicity	Management of Toxicities
• Fever • Hypotension • Tachycardia • Hypoxia • Chills	• Tremors • Dizziness • Delirium • Confusion • Agitation • Cerebral Edema	• Tocilizumab • Steroids

Adkins, S. (2019). Car T cell therapy: adverse events and management. J. Adv Pract Onco Supple3. 21-28..

ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

A Daylong Multitumor Educational Webinar in Partnership with the Texas Society of Clinical Oncology (TxSCO)

Saturday, June 26, 2021
8:00 AM – 3:00 PM Central Time
(9:00 AM – 4:00 PM Eastern Time)

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Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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