Data + Perspectives: Investigators Discuss the Current and Future Roles of Chimeric Antigen Receptor T-Cell Therapy and Bispecific Antibodies in the Care of Patients with Hematologic Cancers

A CE/NCPD-Accredited Virtual Event in Partnership with the 2022 Pan Pacific Lymphoma Conference

Tuesday, August 9, 2022

5:00 PM – 6:30 PM ET

Faculty

Ajai Chari, MD
Ian W Flinn, MD, PhD
Nikhil C Munshi, MD
Laurie H Sehn, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Ajai Chari, MD
Professor of Medicine (Hematology and Medical Oncology)
Icahn School of Medicine at Mount Sinai
Director, Clinical Research
Multiple Myeloma Program
Associate Medical Director
The Tisch Cancer Institute Clinical Trials Office
New York, New York

Ian W Flinn, MD, PhD
Director of Lymphoma Research Program
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee

Nikhil C Munshi, MD
Kraft Family Chair
Director of Basic and Correlative Science
Jerome Lipper Multiple Myeloma Center
Professor of Medicine
Harvard Medical School
Dana-Farber Cancer Institute
Boston, Massachusetts

Laurie H Sehn, MD, MPH
Chair, Lymphoma Tumour Group
BC Cancer Centre for Lymphoid Cancer
Clinical Professor of Medicine
Division of Medical Oncology
University of British Columbia
Associate Editor, Blood
Vancouver, British Columbia, Canada

MODERATOR
Neil Love, MD
Research To Practice

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from Genentech, a member of the Roche Group, and Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC.

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, ADC Therapeutics, 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, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, 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, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

RTP
RESEARCH
TO PRACTICE

The University of Nebraska Medical Center (UNMC) and Research To Practice (RTP) Planners, Staff and Reviewers

The below planning committee members have nothing to disclose: Neil Love, MD — RTP President and Planner, Atif Hussein, MD — RTP Reviewer, Renee Paulin, MSN, RN, CWOCN — UNMC Planner and Reviewer, Brenda Ram, CMP, CHCP — UNMC Planner, Michele Williams, DNP, AGPCNP-BC — RTP Reviewer and Kathryn Ault Ziel, PhD — RTP Staff and Planner.

Accreditation Information

In support of improving patient care, this activity has been planned and implemented by University of Nebraska Medical Center and Research To Practice. University of Nebraska Medical Center is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Physicians

The University of Nebraska Medical Center designates this live activity for a maximum of 1.5 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurses

The University of Nebraska Medical Center designates this activity for 1.5 ANCC contact hours. Nurses should only claim credit for the actual time spent participating in the activity.

Support Statement

This activity is supported by educational grants from Genentech, a member of the Roche Group, and Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC.

RTP RESEARCH TO PRACTICE

Dr Chari — Disclosures

Advisory Committee	Amgen Inc, Celgene Corporation, Janssen Biotech Inc, Karyopharm Therapeutics, Sanofi Genzyme, Seagen Inc, Takeda Pharmaceuticals USA Inc
Consulting Agreements	Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, Janssen Biotech Inc, Karyopharm Therapeutics, Takeda Pharmaceuticals USA Inc
Contracted Research	Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Celgene Corporation, GlaxoSmithKline, Janssen Biotech Inc, Novartis, Oncoceutics Inc, Pharmacyclics LLC, an AbbVie Company, Seagen Inc, Takeda Pharmaceuticals USA Inc

Dr Flinn — Disclosures

Consulting Agreements (to Sarah Cannon Research Institute)	AbbVie Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Century Therapeutics, Genentech, a member of the Roche Group, Genmab, Hutchison MediPharma, Iksuda Therapeutics, InnoCare Pharma, Janssen Biotech Inc, Kite, A Gilead Company, MorphoSys, Myeloid Therapeutics, Novartis, Nurix Therapeutics Inc, Pharmacyclics LLC, an AbbVie Company, Roche Laboratories Inc, Secura Bio, Servier Pharmaceuticals LLC, Takeda Pharmaceuticals USA Inc, TG Therapeutics Inc, Verastem Inc, Vincerx Pharma, Xencor
Research Grants (to Sarah Cannon Research Institute)	2seventy bio, AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Agios Pharmaceuticals Inc, ArQule Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bio-Path Holdings Inc, Bristol-Myers Squibb Company, CALGB, Calibr, Celgene Corporation, City of Hope National Medical Center, Constellation Pharmaceuticals, CTI BioPharma Corp, Curis Inc, Epizyme Inc, Fate Therapeutics, FORMA Therapeutics, Forty Seven Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, IGM Biosciences Inc,Incyte Corporation, Infinity Pharmaceuticals Inc, InnoCare Pharma, Janssen Biotech Inc, Kite, A Gilead Company, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, MorphoSys, Myeloid Therapeutics, Novartis, Nurix Therapeutics Inc, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Portola Pharmaceuticals Inc, Rhizen Pharmaceuticals AG, Roche Laboratories Inc, Seagen Inc, Takeda Pharmaceuticals USA Inc, TCR2 Therapeutics, Tessa Therapeutics, TG Therapeutics Inc, Trillium Therapeutics Inc, Triphase Research and Development Corporation, Unum Therapeutics, Verastem Inc

RTP
RESEARCH
TO PRACTICE

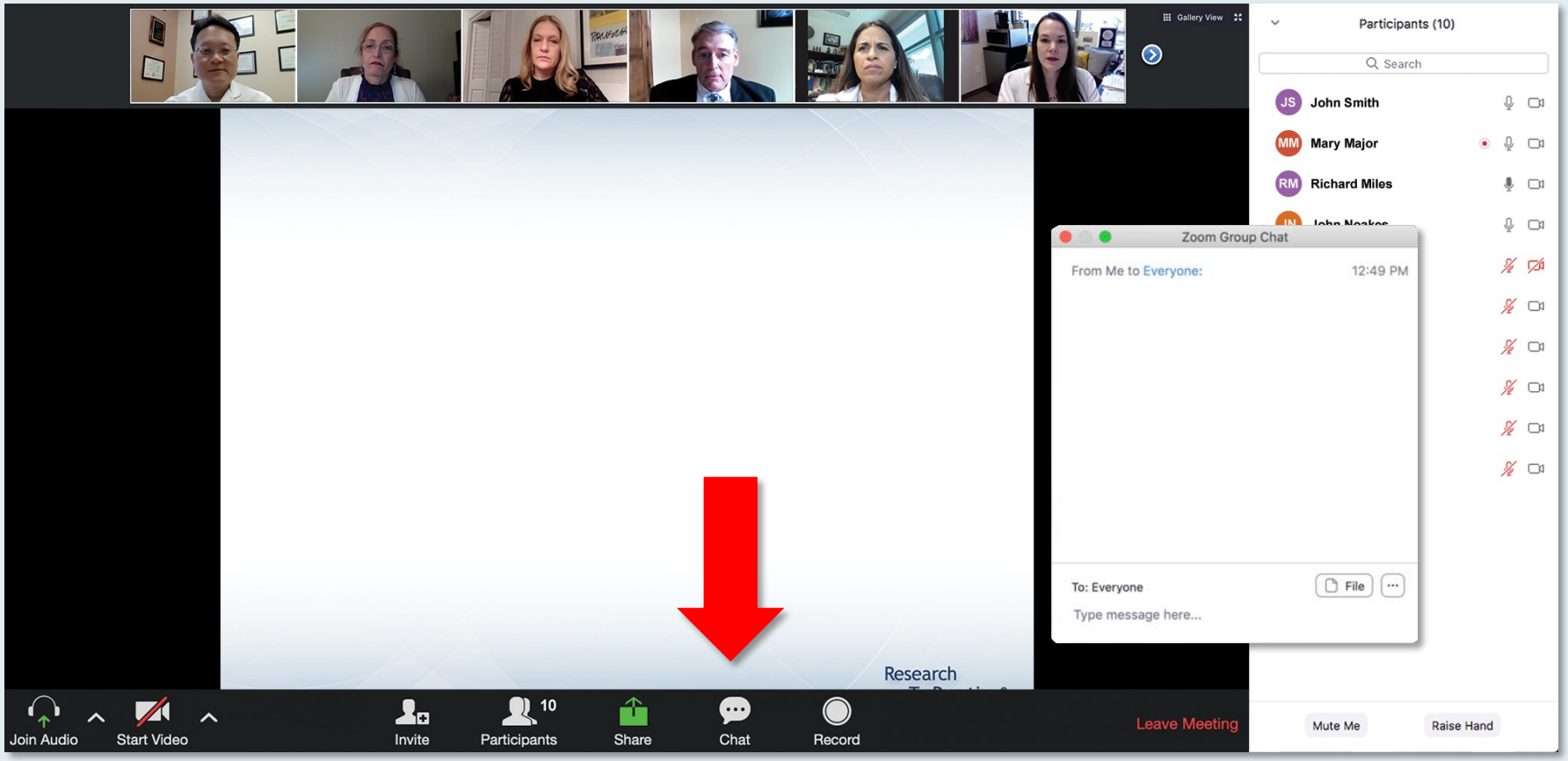
Dr Munshi — Disclosures

Consulting Agreements	AbbVie Inc, Amgen Inc, Bristol-Myers Squibb Company, GlaxoSmithKline, Janssen Biotech Inc, Legend Biotech, Novartis, Oncopeptides, Pfizer Inc, Takeda Pharmaceuticals USA Inc
Stock Ownership	C4 Therapeutics

Dr Sehn — Disclosures

Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Incyte Corporation, Janssen Biotech Inc, Kite, A Gilead Company, Merck, Seagen Inc, Takeda Pharmaceuticals USA Inc, TG Therapeutics Inc
Contracted Research	Genentech, a member of the Roche Group, Teva Oncology

We Encourage Clinicians in Practice to Submit Questions

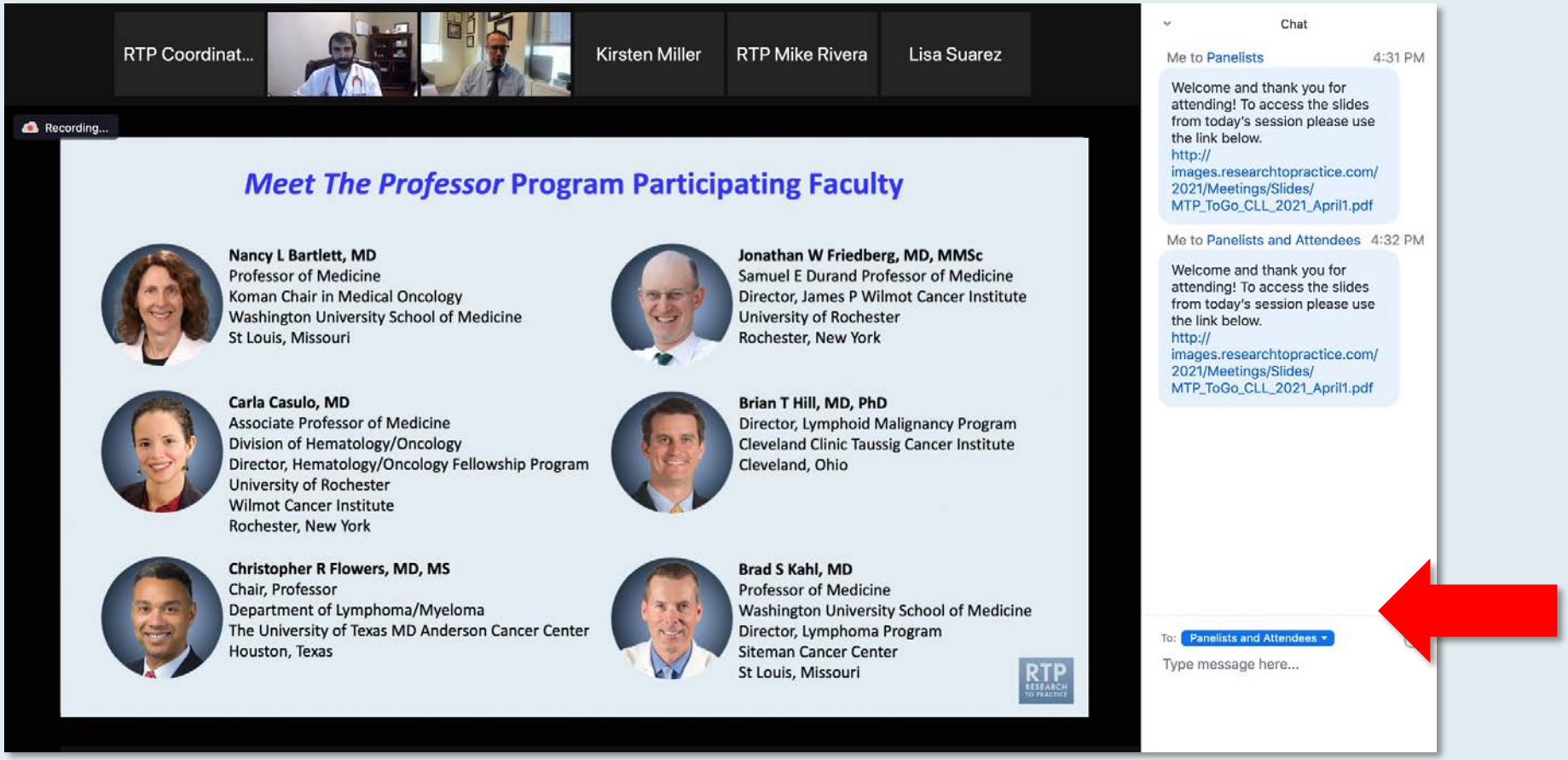


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

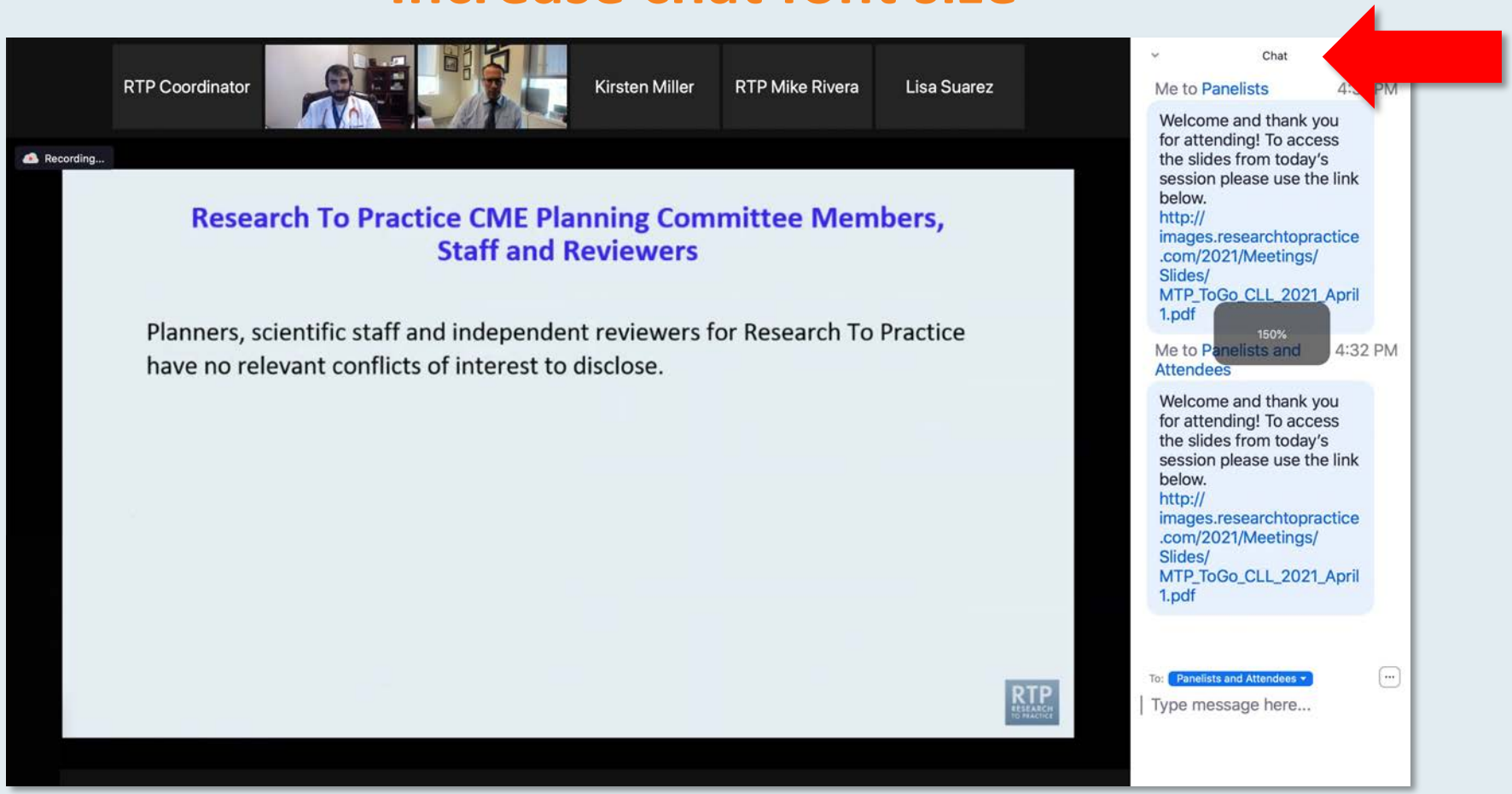


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

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

Current and Future Management of Follicular Lymphoma

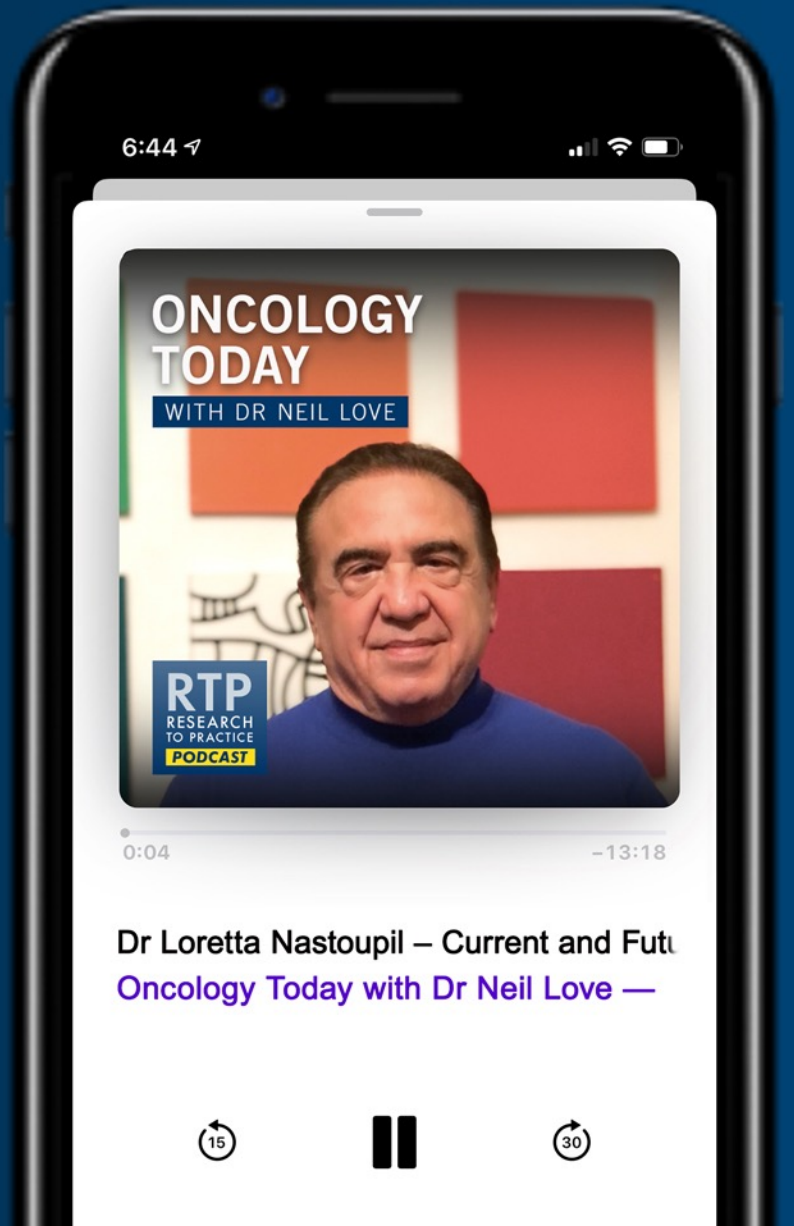
DR LORETTA NASTOUPIL

THE UNIVERSITY OF TEXAS
MD ANDERSON CANCER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Meet The Professor

Optimizing the Management of Small Cell Lung Cancer

Thursday, August 11, 2022
5:00 PM – 6:00 PM ET

Faculty

Jacob Sands, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Wednesday, August 17, 2022
5:00 PM – 6:00 PM ET

Faculty

John Strickler, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Ovarian Cancer

Thursday, August 25, 2022
5:00 PM – 6:00 PM ET

Faculty

Richard T Penson, MD, MRCP

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Current and Future Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Wednesday, August 31, 2022
5:00 PM – 6:00 PM ET

Faculty

Lecia V Sequist, MD, MPH

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

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

RTP
RESEARCH
TO PRACTICE

Data + Perspectives: Investigators Discuss the Current and Future Roles of Chimeric Antigen Receptor T-Cell Therapy and Bispecific Antibodies in the Care of Patients with Hematologic Cancers

A CE/NCPD-Accredited Virtual Event in Partnership with the 2022 Pan Pacific Lymphoma Conference

Tuesday, August 9, 2022

5:00 PM – 6:30 PM ET

Faculty

Ajai Chari, MD
Ian W Flinn, MD, PhD
Nikhil C Munshi, MD
Laurie H Sehn, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Ajai Chari, MD
Professor of Medicine (Hematology and Medical Oncology)
Icahn School of Medicine at Mount Sinai
Director, Clinical Research
Multiple Myeloma Program
Associate Medical Director
The Tisch Cancer Institute Clinical Trials Office
New York, New York

Ian W Flinn, MD, PhD
Director of Lymphoma Research Program
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee

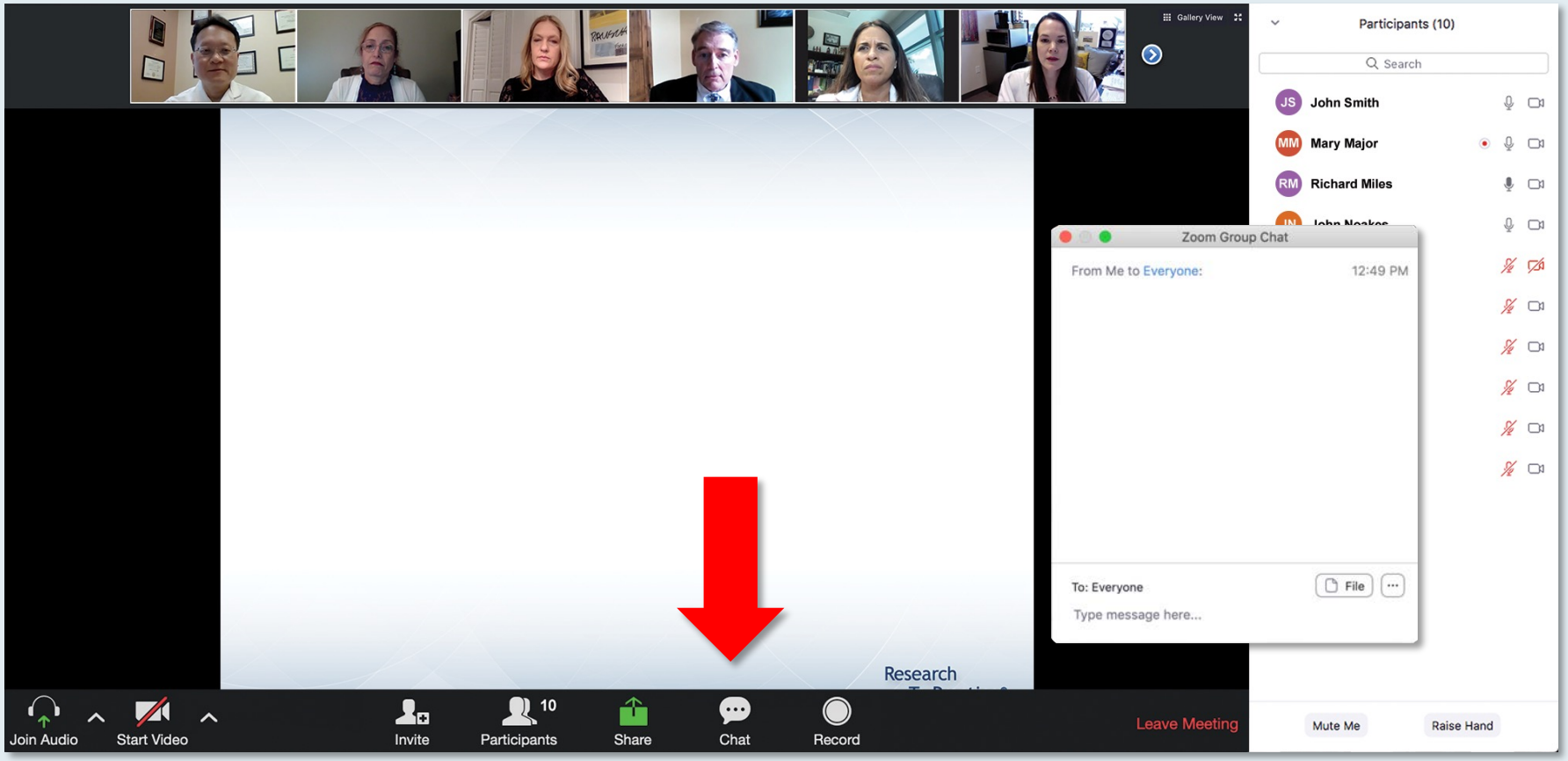
Nikhil C Munshi, MD
Kraft Family Chair
Director of Basic and Correlative Science
Jerome Lipper Multiple Myeloma Center
Professor of Medicine
Harvard Medical School
Dana-Farber Cancer Institute
Boston, Massachusetts

Laurie H Sehn, MD, MPH
Chair, Lymphoma Tumour Group
BC Cancer Centre for Lymphoid Cancer
Clinical Professor of Medicine
Division of Medical Oncology
University of British Columbia
Associate Editor, Blood
Vancouver, British Columbia, Canada

MODERATOR
Neil Love, MD
Research To Practice

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

Current and Future Management of Follicular Lymphoma

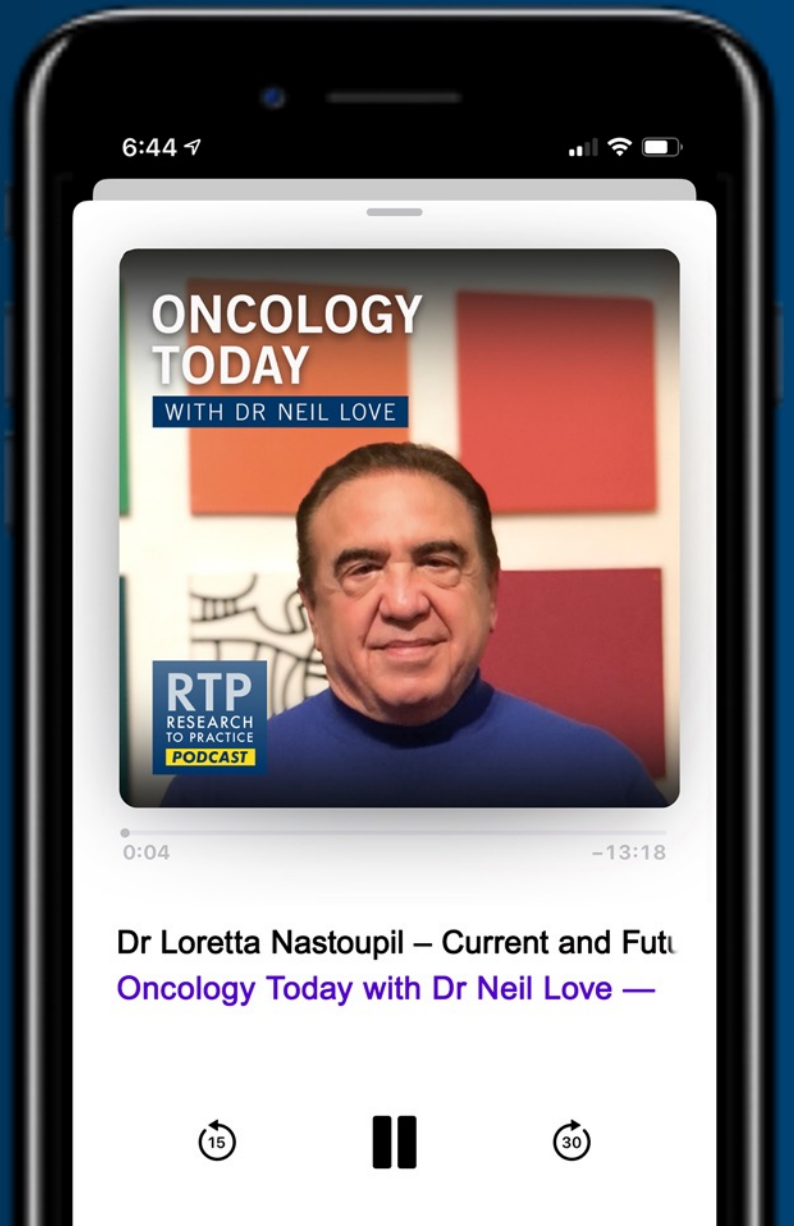
DR LORETTA NASTOUPIL

THE UNIVERSITY OF TEXAS
MD ANDERSON CANCER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Meet The Professor

Optimizing the Management of Small Cell Lung Cancer

Thursday, August 11, 2022
5:00 PM – 6:00 PM ET

Faculty

Jacob Sands, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Wednesday, August 17, 2022
5:00 PM – 6:00 PM ET

Faculty

John Strickler, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Ovarian Cancer

Thursday, August 25, 2022
5:00 PM – 6:00 PM ET

Faculty

Richard T Penson, MD, MRCP

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Current and Future Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Wednesday, August 31, 2022
5:00 PM – 6:00 PM ET

Faculty

Lecia V Sequist, MD, MPH

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Data + Perspectives: Investigators Discuss the Current and Future Roles of Chimeric Antigen Receptor T-Cell Therapy and Bispecific Antibodies in the Care of Patients with Hematologic Cancers

A CE/NCPD-Accredited Virtual Event in Partnership with the 2022 Pan Pacific Lymphoma Conference

Tuesday, August 9, 2022

5:00 PM – 6:30 PM ET

Faculty

Ajai Chari, MD
Ian W Flinn, MD, PhD
Nikhil C Munshi, MD
Laurie H Sehn, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Commercial Support

This activity is supported by educational grants from Genentech, a member of the Roche Group, and Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC.

The University of Nebraska Medical Center (UNMC) and Research To Practice (RTP) Planners, Staff and Reviewers

The below planning committee members have nothing to disclose: Neil Love, MD — RTP President and Planner, Atif Hussein, MD — RTP Reviewer, Renee Paulin, MSN, RN, CWOCN — UNMC Planner and Reviewer, Brenda Ram, CMP, CHCP — UNMC Planner, Michele Williams, DNP, AGPCNP-BC — RTP Reviewer and Kathryn Ault Ziel, PhD — RTP Staff and Planner.

RTP
RESEARCH
TO PRACTICE

Dr Chari — Disclosures

Advisory Committee	Amgen Inc, Celgene Corporation, Janssen Biotech Inc, Karyopharm Therapeutics, Sanofi Genzyme, Seagen Inc, Takeda Pharmaceuticals USA Inc
Consulting Agreements	Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, Janssen Biotech Inc, Karyopharm Therapeutics, Takeda Pharmaceuticals USA Inc
Contracted Research	Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Celgene Corporation, GlaxoSmithKline, Janssen Biotech Inc, Novartis, Oncoceutics Inc, Pharmacyclics LLC, an AbbVie Company, Seagen Inc, Takeda Pharmaceuticals USA Inc

Dr Flinn — Disclosures

Consulting Agreements (to Sarah Cannon Research Institute)	AbbVie Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Century Therapeutics, Genentech, a member of the Roche Group, Genmab, Hutchison MediPharma, Iksuda Therapeutics, InnoCare Pharma, Janssen Biotech Inc, Kite, A Gilead Company, MorphoSys, Myeloid Therapeutics, Novartis, Nurix Therapeutics Inc, Pharmacyclics LLC, an AbbVie Company, Roche Laboratories Inc, Secura Bio, Servier Pharmaceuticals LLC, Takeda Pharmaceuticals USA Inc, TG Therapeutics Inc, Verastem Inc, Vincerx Pharma, Xencor
Research Grants (to Sarah Cannon Research Institute)	2seventy bio, AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Agios Pharmaceuticals Inc, ArQule Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bio-Path Holdings Inc, Bristol-Myers Squibb Company, CALGB, Calibr, Celgene Corporation, City of Hope National Medical Center, Constellation Pharmaceuticals, CTI BioPharma Corp, Curis Inc, Epizyme Inc, Fate Therapeutics, FORMA Therapeutics, Forty Seven Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, IGM Biosciences Inc,Incyte Corporation, Infinity Pharmaceuticals Inc, InnoCare Pharma, Janssen Biotech Inc, Kite, A Gilead Company, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, MorphoSys, Myeloid Therapeutics, Novartis, Nurix Therapeutics Inc, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Portola Pharmaceuticals Inc, Rhizen Pharmaceuticals AG, Roche Laboratories Inc, Seagen Inc, Takeda Pharmaceuticals USA Inc, TCR2 Therapeutics, Tessa Therapeutics, TG Therapeutics Inc, Trillium Therapeutics Inc, Triphase Research and Development Corporation, Unum Therapeutics, Verastem Inc

RTP
RESEARCH
TO PRACTICE

Dr Munshi — Disclosures

Consulting Agreements	AbbVie Inc, Amgen Inc, Bristol-Myers Squibb Company, GlaxoSmithKline, Janssen Biotech Inc, Legend Biotech, Novartis, Oncopeptides, Pfizer Inc, Takeda Pharmaceuticals USA Inc
Stock Ownership	C4 Therapeutics

Dr Sehn — Disclosures

Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Incyte Corporation, Janssen Biotech Inc, Kite, A Gilead Company, Merck, Seagen Inc, Takeda Pharmaceuticals USA Inc, TG Therapeutics Inc
Contracted Research	Genentech, a member of the Roche Group, Teva Oncology

Agenda

PART 1: Case Presentations and Clinical Decision-Making

- Non-Hodgkin Lymphoma
- Multiple Myeloma

PART 2: Faculty Presentations

- CAR-T in Non-Hodgkin Lymphoma — Dr Flinn
- Bispecifics in Non-Hodgkin Lymphoma — Dr Sehn
- CAR-T in Multiple Myeloma — Dr Munshi
- Bispecifics in Multiple Myeloma— Dr Chari

Agenda

PART 1: Case Presentations and Clinical Decision-Making

- Non-Hodgkin Lymphoma
- Multiple Myeloma

PART 2: Faculty Presentations

- CAR-T in Non-Hodgkin Lymphoma — Dr Flinn
- Bispecifics in Non-Hodgkin Lymphoma — Dr Sehn
- CAR-T in Multiple Myeloma — Dr Munshi
- Bispecifics in Multiple Myeloma— Dr Chari

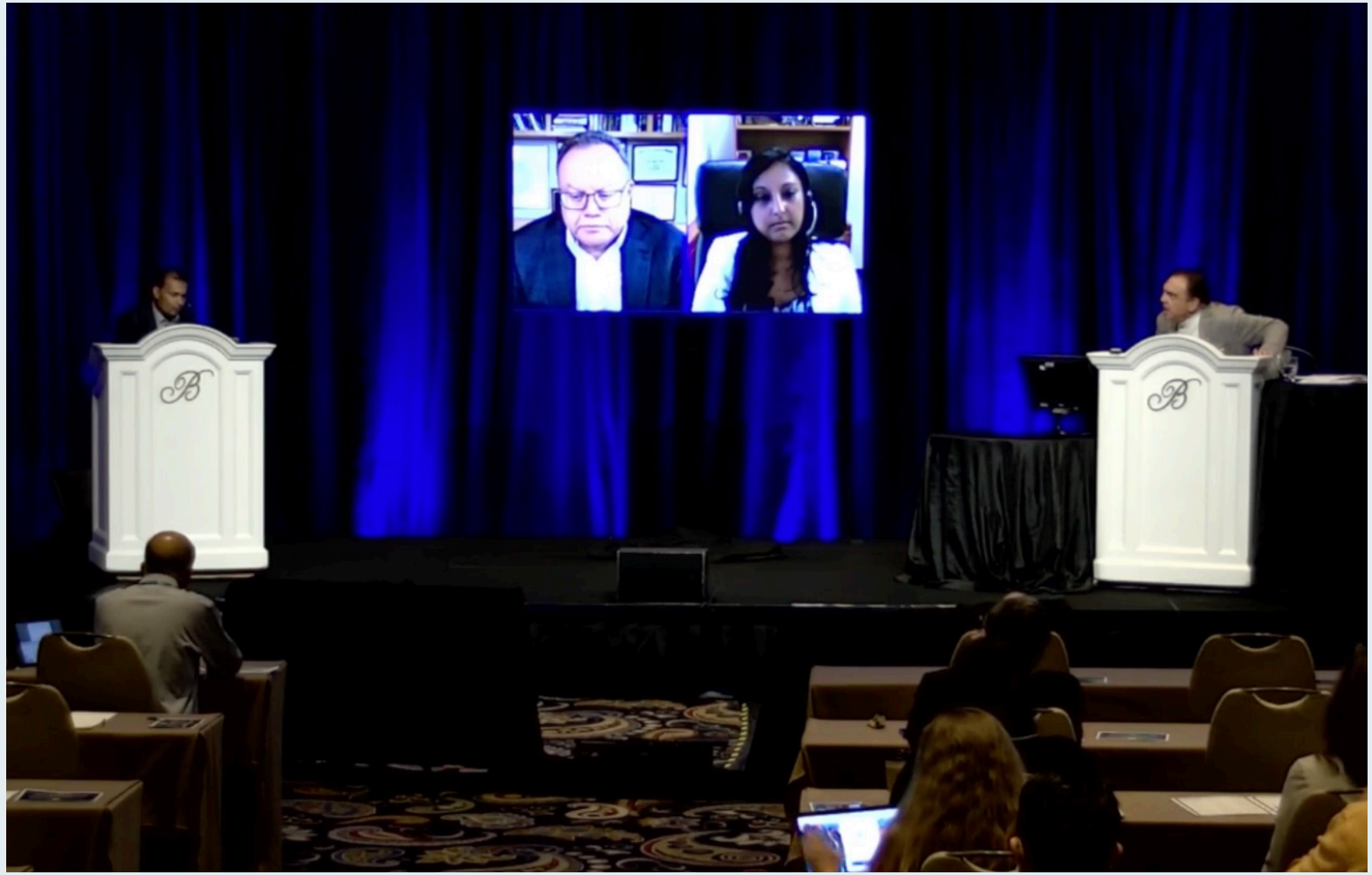
Recent Advances and Real-World Implications in Medical Oncology: A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network

A CME/MOC- and NCPD-Accredited Hybrid Event

Saturday, August 6, 2022
9:00 AM – 4:30 PM PT

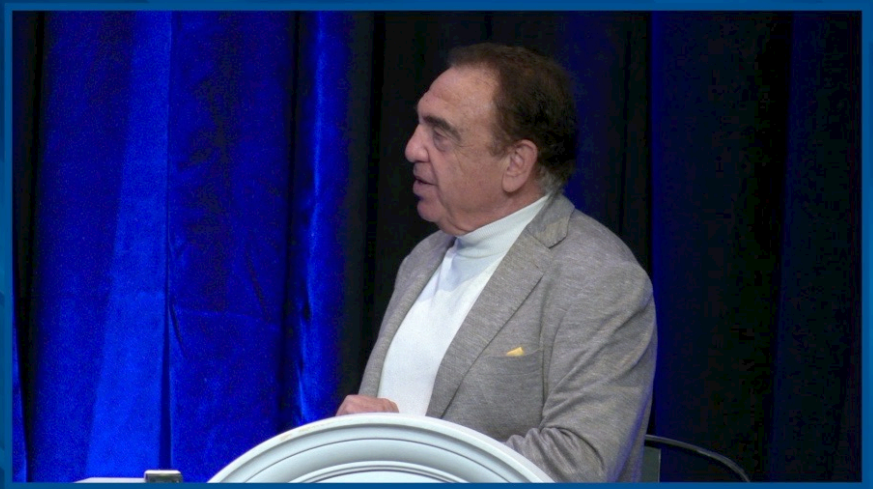
RTP
RESEARCH
TO PRACTICE

Recent Advances and Clinical Algorithms in General Medical Oncology: A Hybrid Live Event Held in Partnership with the American Oncology Network August 6, 2022



RTP RESEARCH TO PRACTICE

Recent Advances and Clinical Algorithms in General Medical Oncology: A Hybrid Live Event Held in Partnership with the American Oncology Network August 6, 2022



Krina Patel, MD

Rafael Fonseca, MD

Recent Advances and Clinical Algorithms in General Medical Oncology: A Hybrid Live Event Held in Partnership with the American Oncology Network August 6, 2022

RTP
RESEARCH
TO PRACTICE

Case Presentation – Dr Flinn: A 71-year-old man with DLBCL arising from follicular lymphoma

- 71 yo man is diagnosed with stage IIIA follicular lymphoma 6 years ago
- Observed until 1 year ago when he was hospitalized for nausea and vomiting
- EGD performed which revealed gastric ulcer, biopsy DLBCL
- PET/CT revealed marked hyper metabolic infiltrating mass in mesentery and retroperitoneum with extension to external iliac and inguinal regions
- RCHOP X 6 with post treatment PET Deauville 3
- Started on maintenance rituximab

Case Presentation – Dr Flinn: A 71-year-old man with DLBCL arising from follicular lymphoma (continued)

- CT scans prior to second dose of rituximab reveals PD
- Biopsy reveal double hit lymphoma
- Started on Pola-R
- After 2 cycles of Pola R PT scan Reveals PD with largest mass 67 X 62 mm
- Course complicated by GI bleed from duodenal mass with ulceration
- Received Axi-cel as an outpatient
- Developed Grade 1 CRS
- Day 90 PET CR

Discussion Question

In general, what is your preferred second-line therapy for an otherwise healthy 65-year-old patient with DLBCL who experiences disease relapse after R-CHOP?

- CAR T-cell therapy
- Autologous stem cell transplant
- Pola-BR (polatuzumab vedotin with bendamustine/rituximab)
- Tafasitamab/lenalidomide
- Selinexor
- Loncastuximab tesirine
- Other

RTP RESEARCH TO PRACTICE

Discussion Question

A patient with DLBCL experiences relapse after receiving R-CHOP and requires bridging therapy because of symptoms, which results in a complete response. What would likely be your next treatment?

- CAR T-cell therapy
- Autologous stem cell transplant
- I'm not sure

Discussion Question

For an otherwise healthy 70-year-old man with DLBCL that relapsed after R-CHOP to whom you plan to administer CAR T-cell therapy, do you have a preference among the following products?

- Axicabtagene ciloleucel
- Lisocabtagene maraleucel
- Tisagenlecleucel
- No preference

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Sehn: A 59-year-old man with non-GCB subtype DLBCL

- **59 yo male**
- **Presented with bulky abdominal lymphadenopathy and night sweats in June 2019**
- **Core biopsy of retroperitoneal mass: DLBCL non-GCB subtype, no *MYC* rearrangement, bone marrow biopsy negative**
- **Treated with R-CHOP x 6 for bulky stage 2B disease and achieved a CR**
- **Developed evidence of recurrence within 6 months and was treated with R-GDP x 2 cycles with plan for ASCT**
- **However, no response to salvage, so transplant not performed**
- **In March 2020, he received CAR T-cell therapy with axi-cel, with PR observed 3 months post, but developed evidence of progressive disease 6 months post CAR-T**

Case Presentation – Dr Sehn: A 59-year-old man with non-GCB subtype DLBCL (continued)

- **In October 2020, he was treated with mosunetuzumab monotherapy on phase I/II trial**
- **Received 8 cycles per protocol, achieving a CR, followed by observation**
- **No relevant toxicity, but acutely developed grade 2 CRS with rigors and respiratory distress requiring tocilizumab in cycle 1 (day 8 dose)**
- **Remains well, but concern for slow progression, mosunetuzumab retreatment being considered**

Discussion Question

Do you believe that general medical oncologists in a community-based setting will be using bispecific antibodies (for multiple myeloma or lymphoma) in their outpatient clinics within the next 2 years?

- Yes
- No
- I'm not sure

RTP RESEARCH TO PRACTICE

Discussion Question

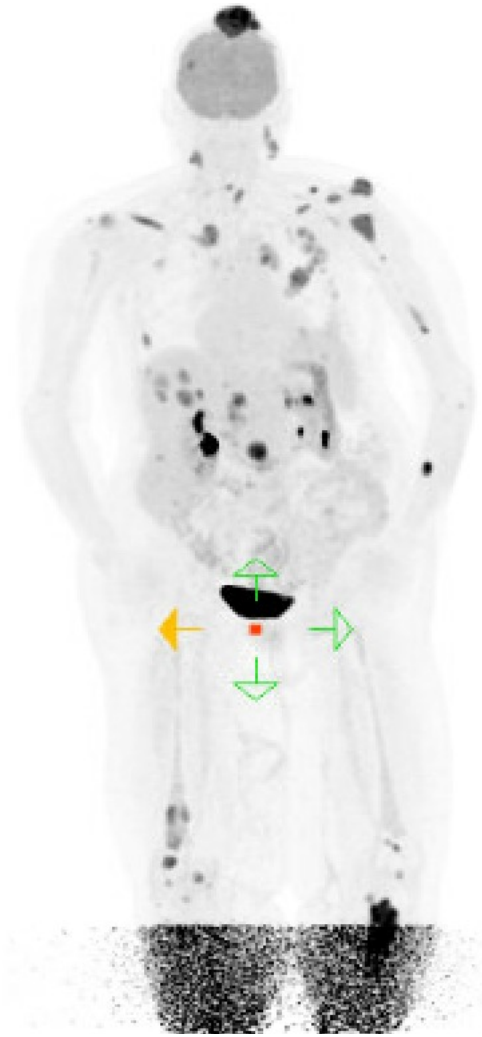
What are the targets of the novel bispecific antibodies glofitamab, epcoritamab and mosunetuzumab in patients with lymphoma?

- CD20 x CD3
- CD20 x CD8
- CD19 x CD3
- CD78 x CD3
- I'm not sure

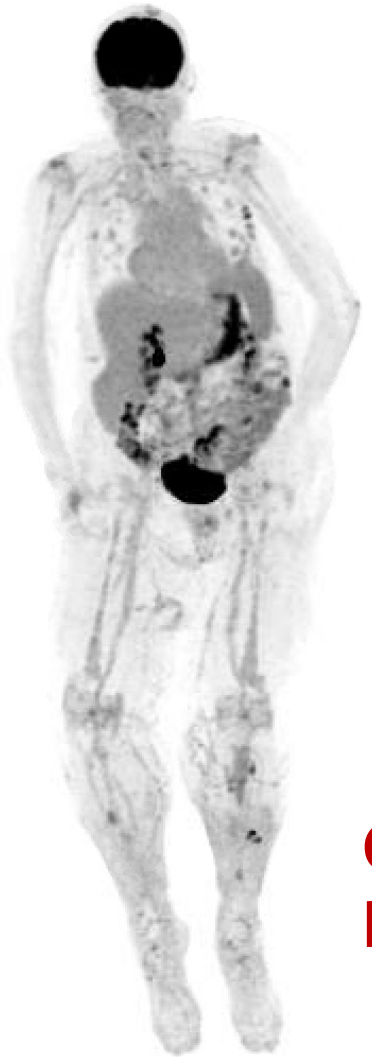
Case Presentation – Dr Munshi: CAR T therapy during the Pandemic

- 65 year old lady with IgG kappa multiple myeloma, BM plasma cells 45% with ISS stage I with a 1q amplification and 13q deletion diagnosed in 2016.
- Induction therapy with KRD. Excellent response but developed PE and on Rivaroxaban
- 09/2016 – HDT and ASCT – Maintenance with weekly Bortezomib + Lenalidomide
- 01/2018 – Progression on PET/CT – Started on DaraPD
- 04/2018 A localized head mass – Changed to DaraPVD
- 06/2018 – Progression on PET/CT – KCD
- 10/2018 – Anti-BCMA CAR T cell therapy

10/2018



03/2019



- Cytokine release syndrome Day +1 with fevers and fluid-responsive hypotension (grade 2 CRS) on day +2,
- Resolved with a single dose of tocilizumab.
- She was treated with empiric ceftazidime for neutropenic fever

COVID Pandemic

Patient gets COVID-19

	10/2018	11/2018	12/2019	2/2020	3/2020	05/2020	7/2020
Kappa FLC (mg/L)	436.7	1.9	40.2	72.9	125.2	----	5,368.9

Discussion Question

For an otherwise healthy 60-year-old patient with penta-drug-refractory myeloma to whom you plan to administer CAR T-cell therapy, do you have a preference between the following products?

- Ciltacabtagene autoleucel
- Idecabtagene vicleucel
- No preference

RTP RESEARCH TO PRACTICE

Discussion Question

A patient history of which of the following conditions would cause you to prefer idecabtagene vicleucel over ciltacabtagene autoleucel?

- Neurologic disease
- Cardiovascular disease
- Renal failure
- Diabetes
- Other
- None

Case Presentation – Dr Chari: Anti-BCMA Bispecific in Triple Class and Penta Drug Refractory Patient

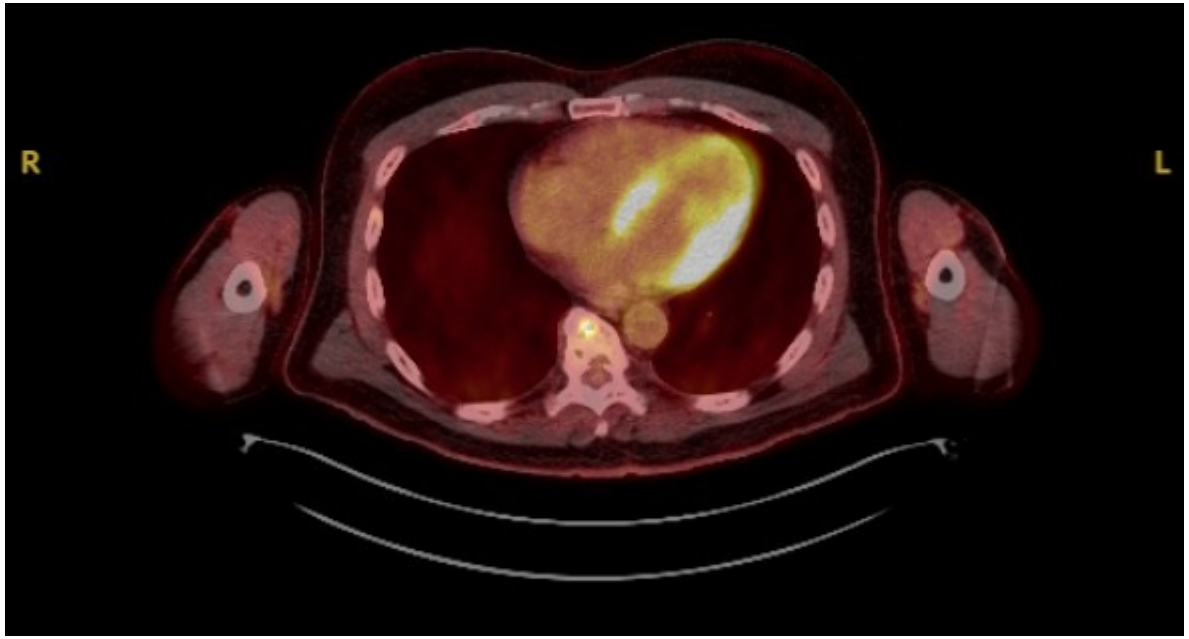
IgG lambda MM 3/3/16) DS3. RISS: II FISH t(11;14)

63 yo M Presented with R hip pain with anemia and lytic lesions, had further work up showing m-spike 6.56 g/dl; free lambda 924, IgG 8.2 g/dl. BMBx 3/6/16 > 90% of PC. B2M: 2.04, alb: 3.41, LDH: 196 on 7/5/17 FISH t(11;14) on 6/22/17). Bone surv 7/26/17: lucencies proximal humeri, L proximal femur & pelvis.

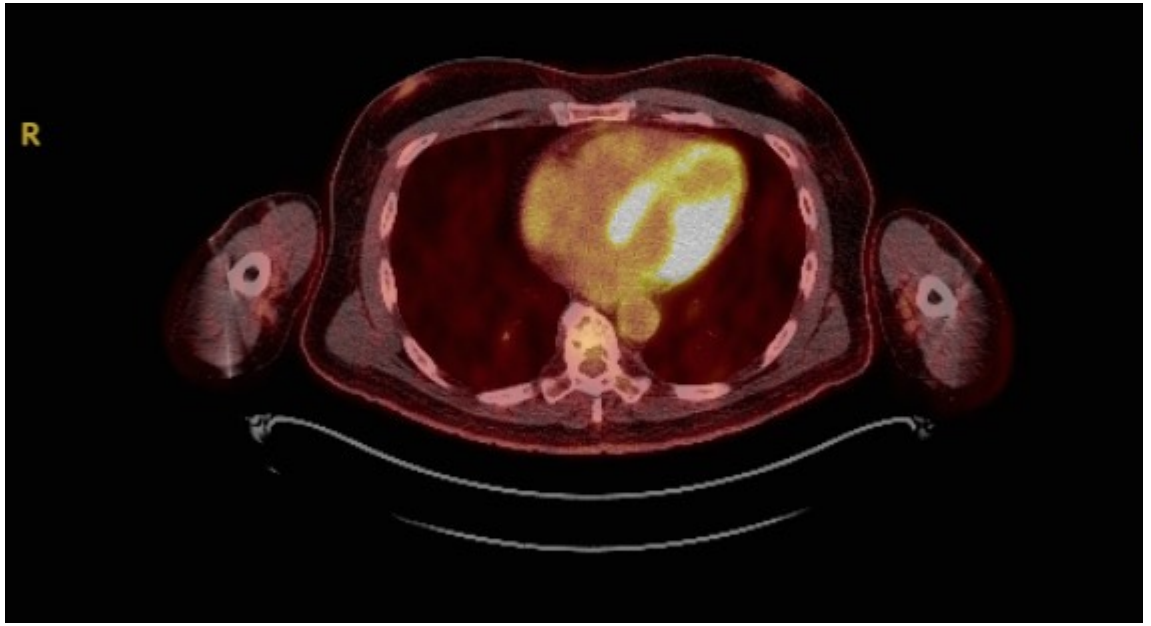
1. C1D1 VCD 3/22/16 * 10 cycles with PR (mspike 6.3 to nadir 2.1 g) then VRD 1/'18 with 7 cycles with PR to 0.9 then PD to 1.4 and FLC 255 6/2/17.
2. Melphalan 200 mg/m2 ASCT 8/23/17 with PR then rising FLC (PD). BM Bx 1/29/18 10-12% PC., nl cyto, FISH t(11;14) dup 1q. High risk GEP (52.8), CD2, t(11;14)
3. Clinical trial: IsaCar C1D1 2/20/18 x 10 cycles, PD by PET. OFF STUDY, EOT 12/11/18.
4. C1 PCD 2/8/19; Dara/pom started 5/17/19 - pom d/c'd 8/'19 d/t neutropenia. PD.
5. Clinical trial: Novel ADC C1D1 11/14/19 x 2 cycles with PD with cauda equina syndrome s/p XRT 12/27-31/19 2000 cGy
6. C1 Dar Vel Dex 1/14/20 + venetoclax 2/10/20, COVID+ and changed to Ixa/Venetoclax/dex 3/20/20
7. **BCMA Bispecific** Priming dose 1 12/11/20 Switched to biweekly dosing at C7. Intermittent GCSF requirement for 6 mos then off. Also c/b Grade 4 pericardial effusion s/p Pericardiocentesis, IV abx.

Case Presentation – Dr Chari: Anti-BCMA Bispecific in Triple Class and Penta Drug Refractory Patient (Continued)

PETCT Nov 2020

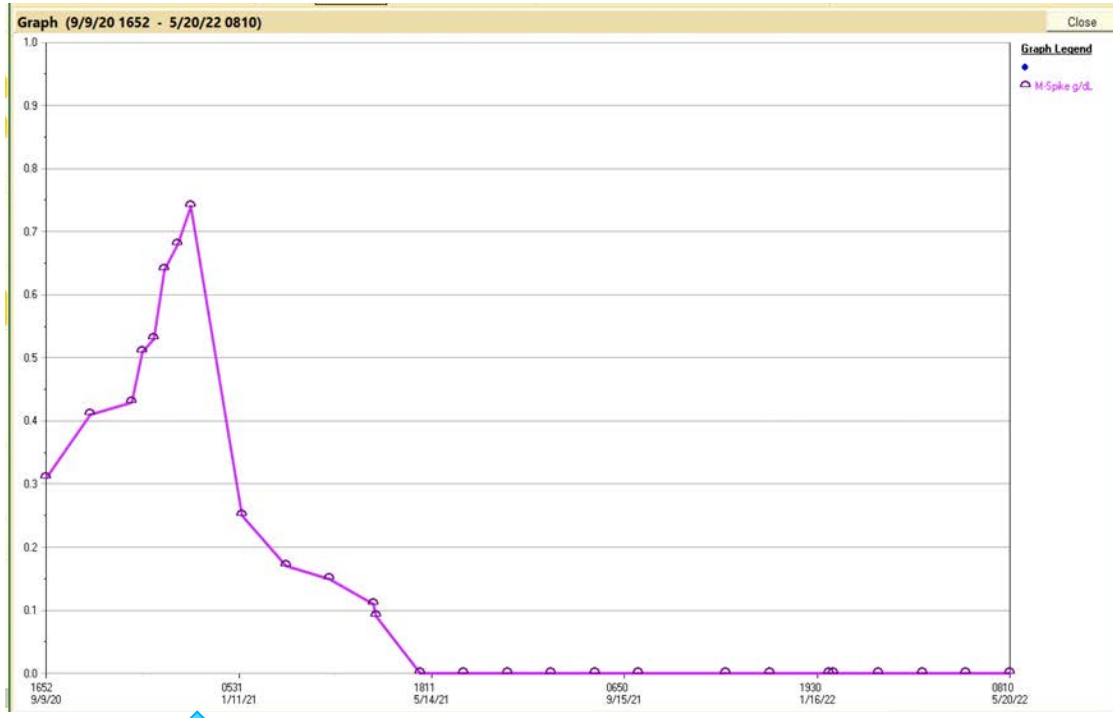


PETCT May 2022

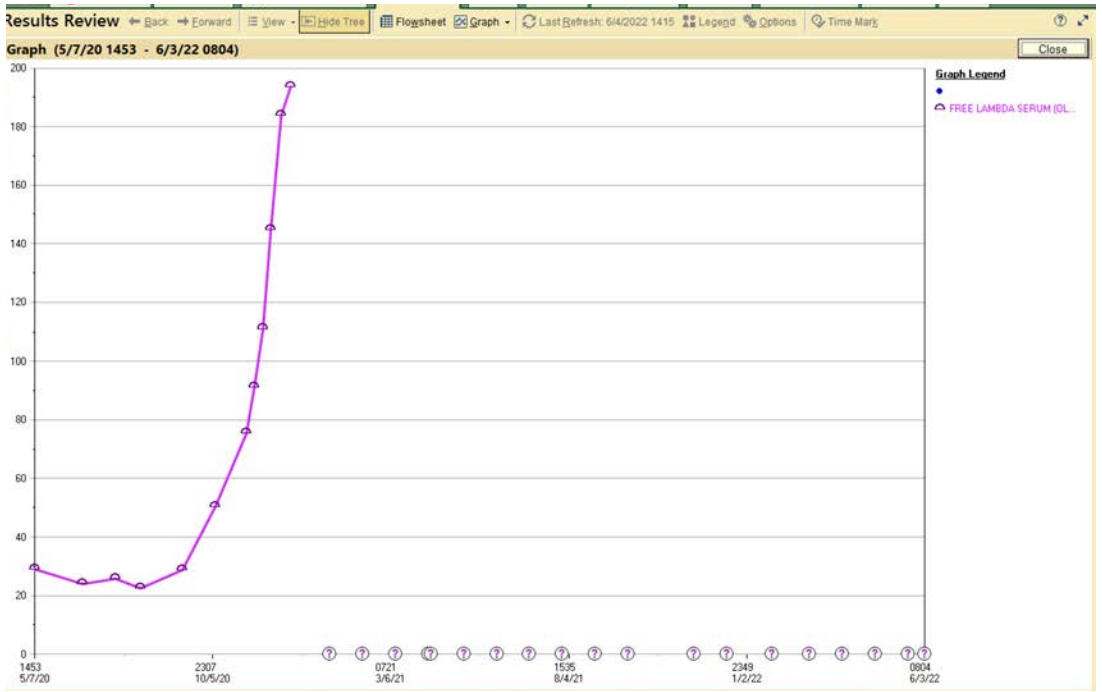


Case Presentation – Dr Chari: Anti-BCMA Bispecific in Triple Class and Penta Drug Refractory Patient (Continued)

Anti BCMA bispecific MRD negative stringent complete remission



M spike 0.74 mg/dl prior to teclistamab



Free lambda 193 mg/L prior to teclistamab

	12/2/2020 17:45	2/10/2021 18:15
% MINIMAL RESIDUAL DISEASE (MRD)	0.0074	0.0000
NON-AGGREGATE EVENTS	5330246	7737988
ABNORMAL PC EVENTS	397	0

In MRD neg sCR 1.5 years+

Discussion Question

The bispecific antibodies talquetamab, teclistamab and cevostamab have which of the following targets in common?

- BCMA
- CD3
- FcRH5
- GPRC5
- I'm not sure

Discussion Question

Does any evidence indicate that the use of bispecific antibodies for myeloma interferes with the ability to mount a response to vaccines?

- Yes, bispecific agents cause a significant detriment to vaccine response
- No, bispecific agents do not interfere with vaccine response
- No data on this subject are available
- I'm not sure

RTP RESEARCH TO PRACTICE

Discussion Question

Regulatory and reimbursement issues aside, what would be your likely third-line therapy for a patient with follicular lymphoma who received bendamustine/rituximab followed by R^2 (lenalidomide/rituximab)?

- Bispecific antibody
- PI3K inhibitor
- CAR T-cell therapy
- EZH2 inhibitor (only with EZH2 mutation)
- EZH2 inhibitor (independent of EZH2 status)
- Other

Agenda

PART 1: Case Presentations and Clinical Decision-Making

- Non-Hodgkin Lymphoma
- Multiple Myeloma

PART 2: Faculty Presentations

- CAR-T in Non-Hodgkin Lymphoma — Dr Flinn
- Bispecifics in Non-Hodgkin Lymphoma — Dr Sehn
- CAR-T in Multiple Myeloma — Dr Munshi
- Bispecifics in Multiple Myeloma— Dr Chari

Agenda

PART 1: Case Presentations and Clinical Decision-Making

- Non-Hodgkin Lymphoma
- Multiple Myeloma

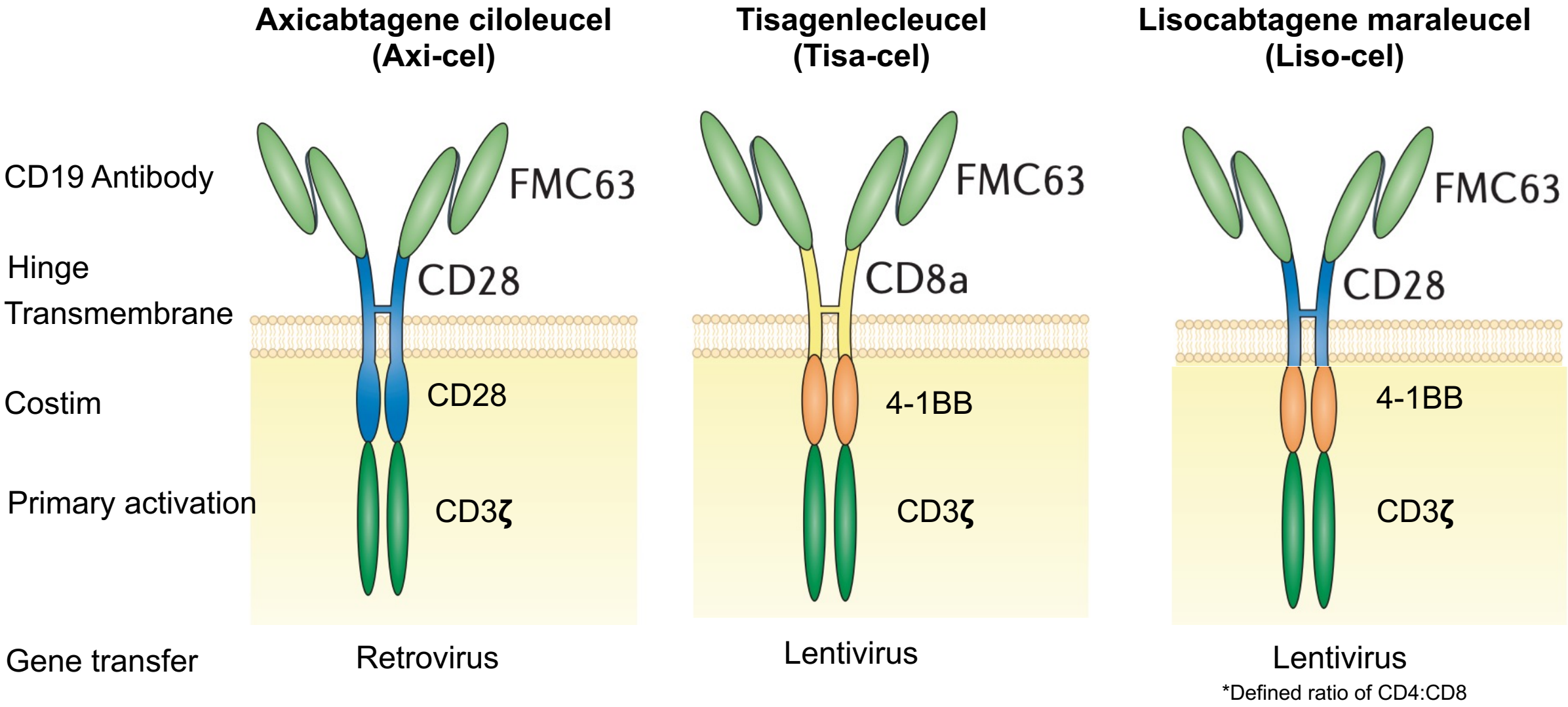
PART 2: Faculty Presentations

- CAR-T in Non-Hodgkin Lymphoma — Dr Flinn
- Bispecifics in Non-Hodgkin Lymphoma — Dr Sehn
- CAR-T in Multiple Myeloma — Dr Munshi
- Bispecifics in Multiple Myeloma— Dr Chari

Current Role of CAR T-Cell Therapy in Patients with Aggressive and Indolent Lymphomas

Ian W. Flinn, M.D., Ph.D.
Sarah Cannon Research Institute and Tennessee Oncology

CD19-Directed CAR T Cells in the Clinic: LBCL



Adapted from van der Stegen SJ, Hamieh M, Sadelain M. *Nat Rev Drug Discov*. 2015 Jul; 14(7): 499–509.

CAR T-Cell Therapy in 3L DLBCL: Overview of Pivotal Trials

	ZUMA-1[1-3]		JULIET[4]	TRANSCEND NHL 001[5]
CAR T-cell agent	Axicabtagene ciloleucel		Tisagenlecleucel	Lisocabtagene maraleucel
Study phase	2		2	1
Patient population	Adults with refractory DLBCL		Adults with R/R DLBCL	Adults with R/R DLBCL
Patients pheresed/treated, n	111/101		165/111	344/269[b]
Bridging therapy, %	None allowed		92	59
ORR, % (IRC)	74		52	73
CR, % (IRC)	54		40	53
Median OS, %	25.8[a]		12	21.1
Median PFS, months	5.8		NR	6.8
CRS		With steroid:		
Median onset	2 days	5 days	3 days	5 days
All grade CRS	94%	80%	58%	42%
Grade 3-4 CRS	13%	0%	22%	2%
ICANS (neurologic toxicity)		With steroid:		
Median onset	4 days	6 days	6 days	9 days
All grade ICANS	67% to 80%	58%	21%	30%
Grade 3-4 ICANS	31%	13%	12%	10%

[a] With ≥4 years of follow-up. [b] 256 included in the efficacy evaluable set.
ORR, objective response rate.

1. Locke FL, et al. *Lancet Oncol*. 2019;20(1):31-42. 2. Jacobson C, et al. ASH 2020. Abstract 1187. 3. Oluwole O, et al. *Br J Haematol*. 2021;194(4):690-700. 4. Schuster SJ, et al. *N Engl J Med*. 2019;380(1):45-56. 5. Abramson JS, et al. *Lancet*. 2020;396(10254):839-852.

ZUMA-7 Study Schema and Endpoints: Axi-Cel Versus SOC as Second-Line Therapy in Patients With R/R LBCL

R/R LBCL
N=359
77 sites

Key Eligibility:
- Aged ≥18 y
- LBCL[1]
- R/R ≤12 mo of 1L therapy[a]
- Intended to proceed to HDT-ASCT

Stratification:
- Response to 1L therapy
- Second-line age-adjusted IPI (sAAIPI)

Optional Steroid-Only Bridging (No Chemotherapy)

1:1 Randomization

Axi-Cel (n=180)
Conditioning Chemotherapy + Axi-cel[b]

SOC (n=179)
Cycle 1 | Cycle 2 | Cycle 3 (Optional)
Investigator-Selected Platinum-Based Chemoimmunotherapy[c]

Initial Disease Assessment (Day 50)

Responders (CR or PR)
Proceed to HDT-ASCT

Nonresponders
Additional Treatment Off Protocol[d]

Day 100 Assessment

Day 150 Assessment

LTFU Assessment

Primary Endpoint
- Event-free survival[e] (EFS) by blinded central review

Key Secondary Endpoints
- ORR
- OS

Secondary Endpoints
- PFS
- Safety
- PROs

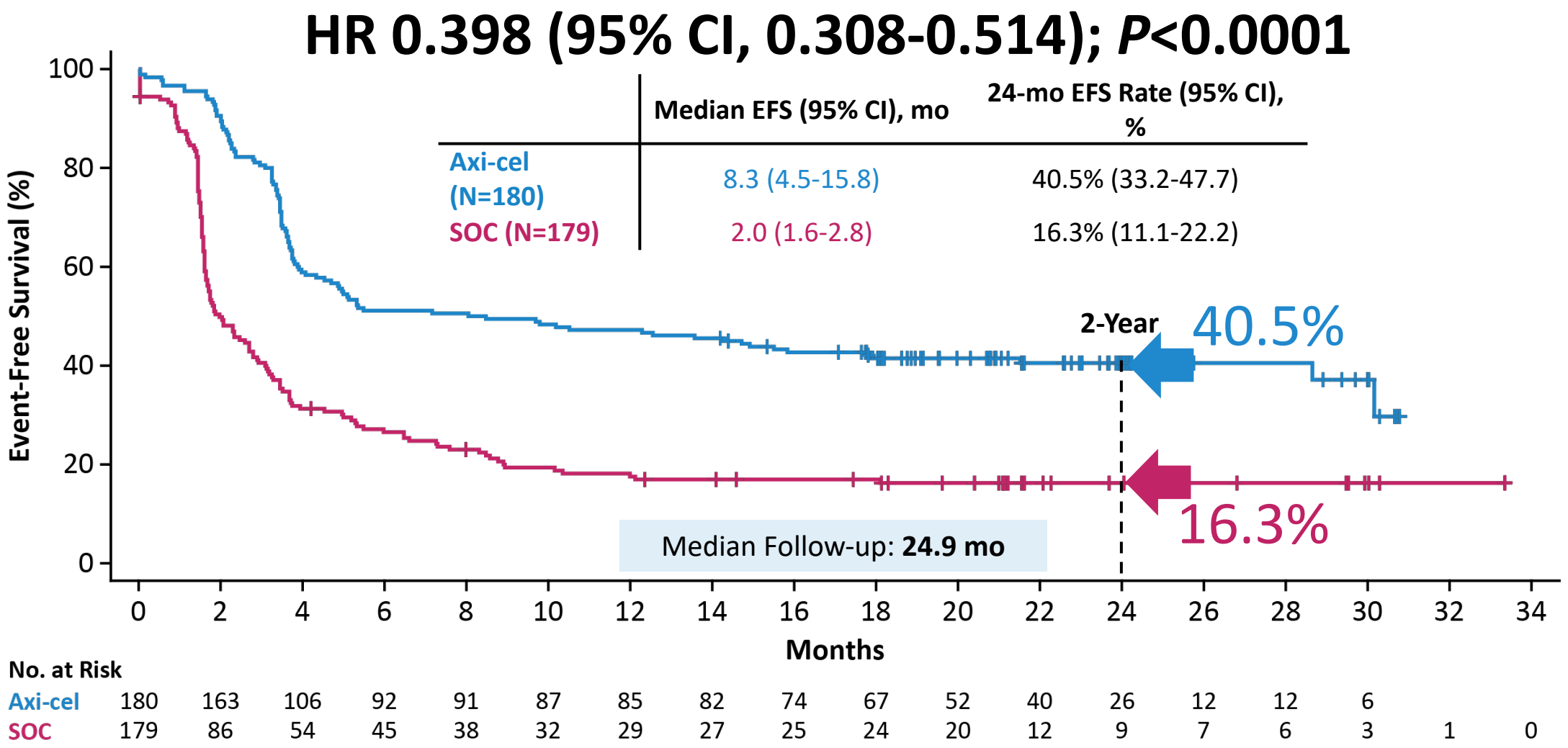
No Protocol-Specified Crossover

[a] Refractory disease was defined as no CR to 1L therapy; relapsed disease was defined as CR followed by biopsy-proven disease relapse ≤12 months from completion of 1L therapy. [b] Axi-cel patients underwent leukapheresis followed by conditioning chemotherapy with cyclophosphamide (500 mg/m^2/day) and fludarabine (30 mg/m^2/day) 5, 4, and 3 days before receiving a single axi-cel infusion (target intravenous dose, 2×10^6 CAR T cells/kg). [c] Protocol-defined SOC regimens included R-GDP, R-DHAP, R-ICE, or R-ESHAP. [d] 56% of patients received subsequent cellular immunotherapy. [e] EFS was defined as time from randomization to the earliest date of disease progression per Lugano Classification,[2] commencement of new lymphoma therapy, or death from any cause.

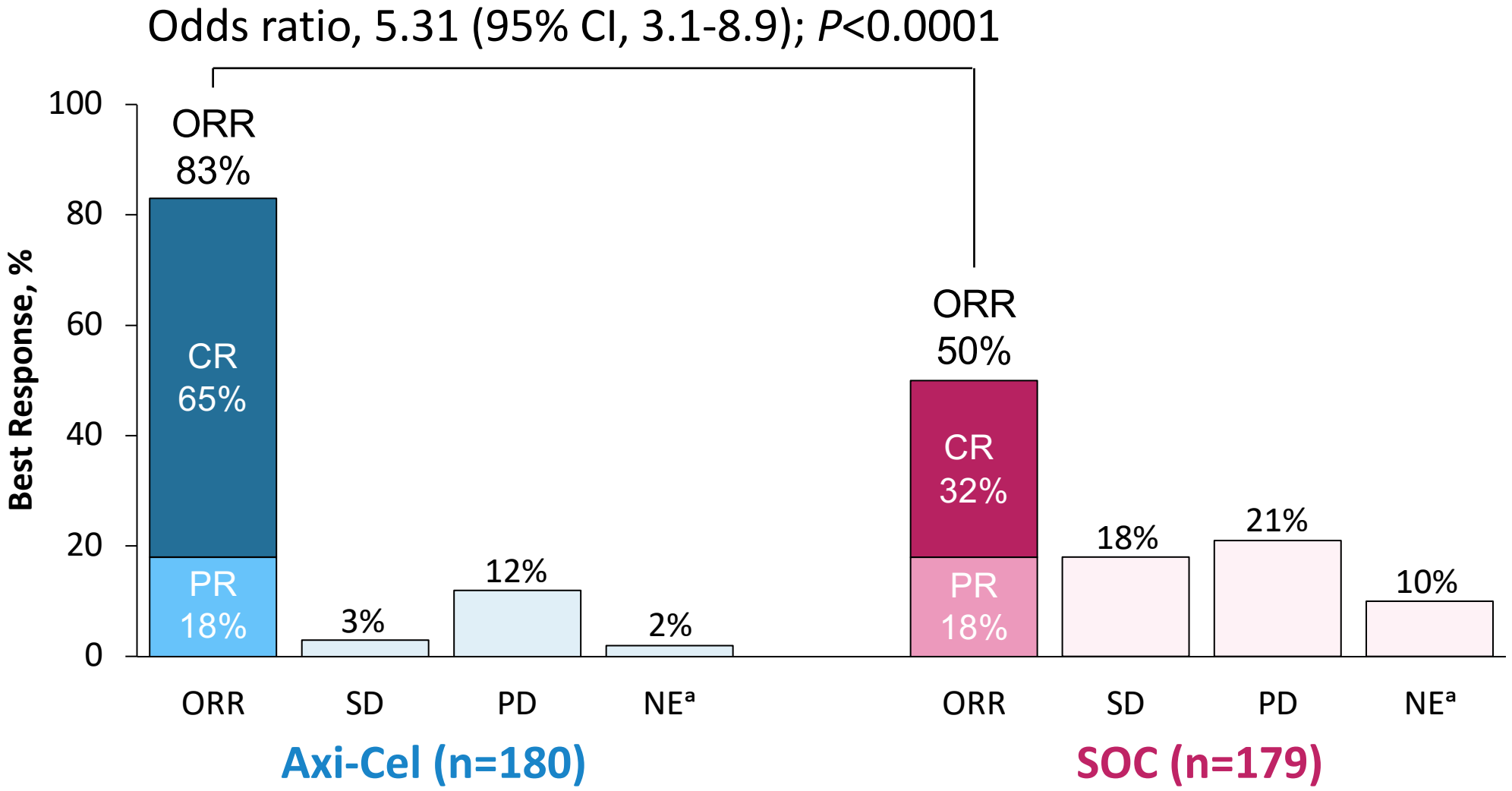
1. Swerdlow SH, et al. *Blood.* 2016;127:2375-2390. 2. Cheson BD, et al. *J Clin Oncol.* 2014;32:3059-3068.

Locke N Engl J Med 2022;386(7):640-654.

Primary EFS Endpoint: Axi-Cel Is Superior to SOC

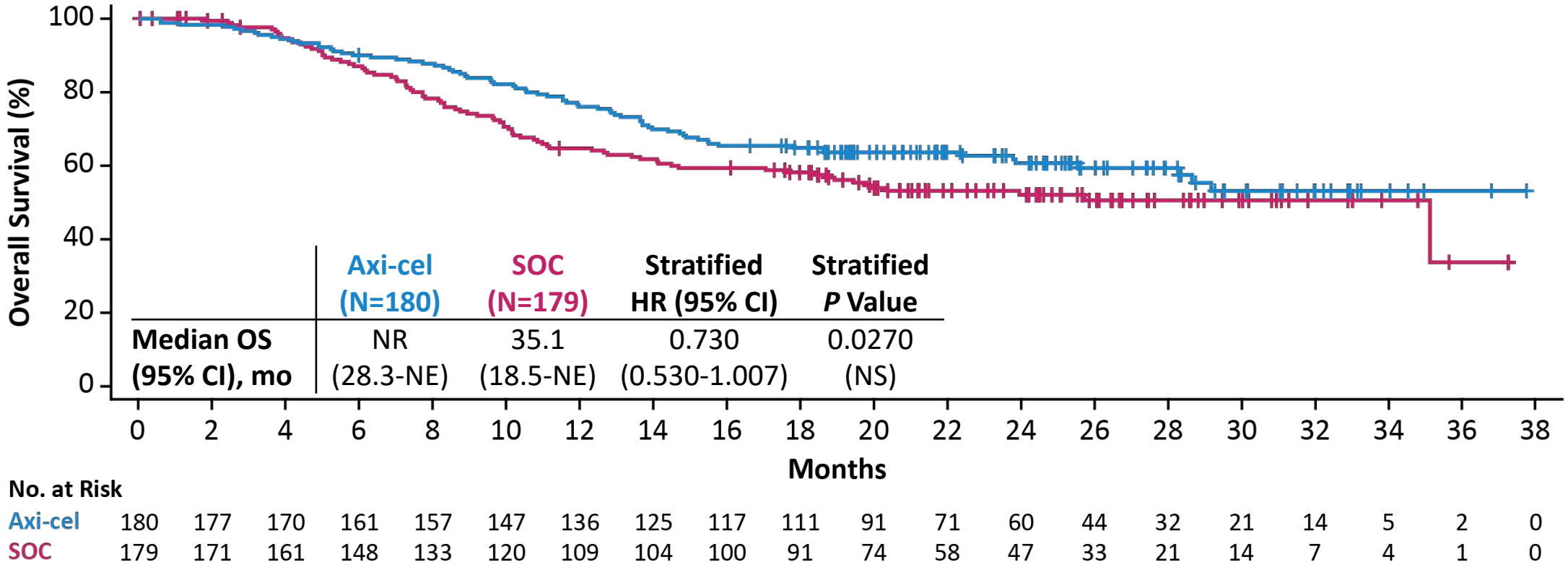


ORR Was Significantly Higher in Axi-Cel Versus SOC Patients



[a] Not evaluable (NE): In the axi-cel arm, response assessments were not done for 4 patients. In the SOC arm, there were 4 patients with undefined disease and 14 who did not have response assessments done.

Median OS, Evaluated as an Interim Analysis, Was Not Reached for Axi-Cel Versus 35.1 Months for SOC



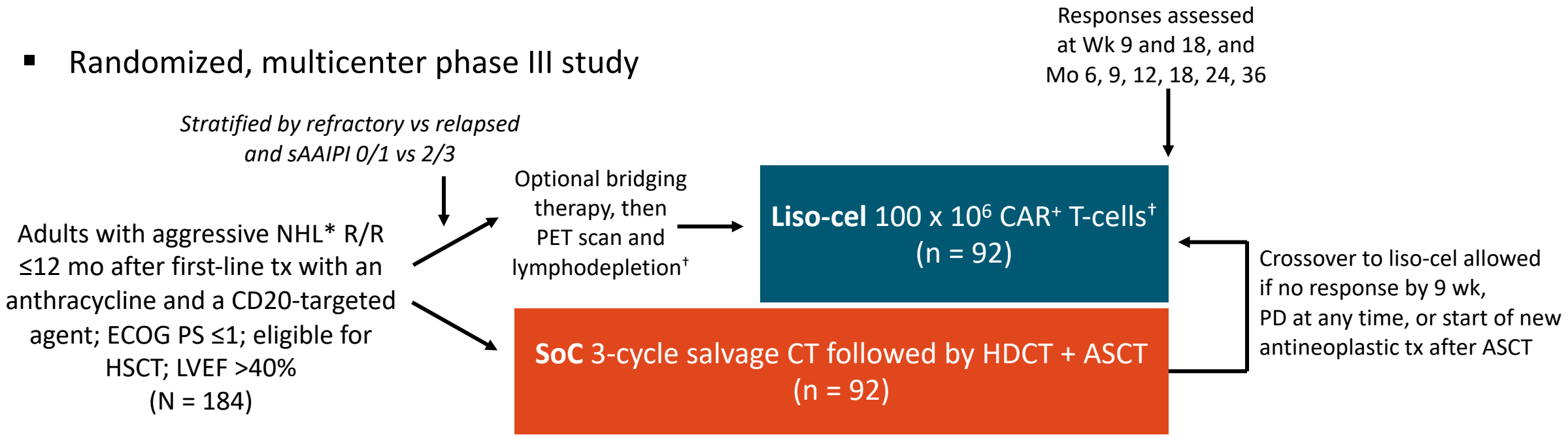
	Axi-cel (N=180)	SOC (N=179)	Stratified HR (95% CI)	Stratified *P* Value
Median OS (95% CI), mo	NR (28.3-NE)	35.1 (18.5-NE)	0.730 (0.530-1.007)	0.0270 (NS)

- 56% of SOC patients received subsequent cellular immunotherapy (off protocol)
- Preplanned sensitivity analysis[a] suggests an OS benefit, likely confounded by SOC treatment switching

[a] Analysis utilized the validated and commonly used Rank Preserving Structural Failure Time model, which preserves randomization as described by Robins and Tsiatis *(Commun Stat Theory Methods.* 1991;2609-2631) and revealed the difference in treatment effect if SOC patients did not receive subsequent cellular immunotherapy. Stratified hazard ratio was 0.580 (95% CI, 0.416-0.809).

TRANSFORM: Study Design

- Randomized, multicenter phase III study

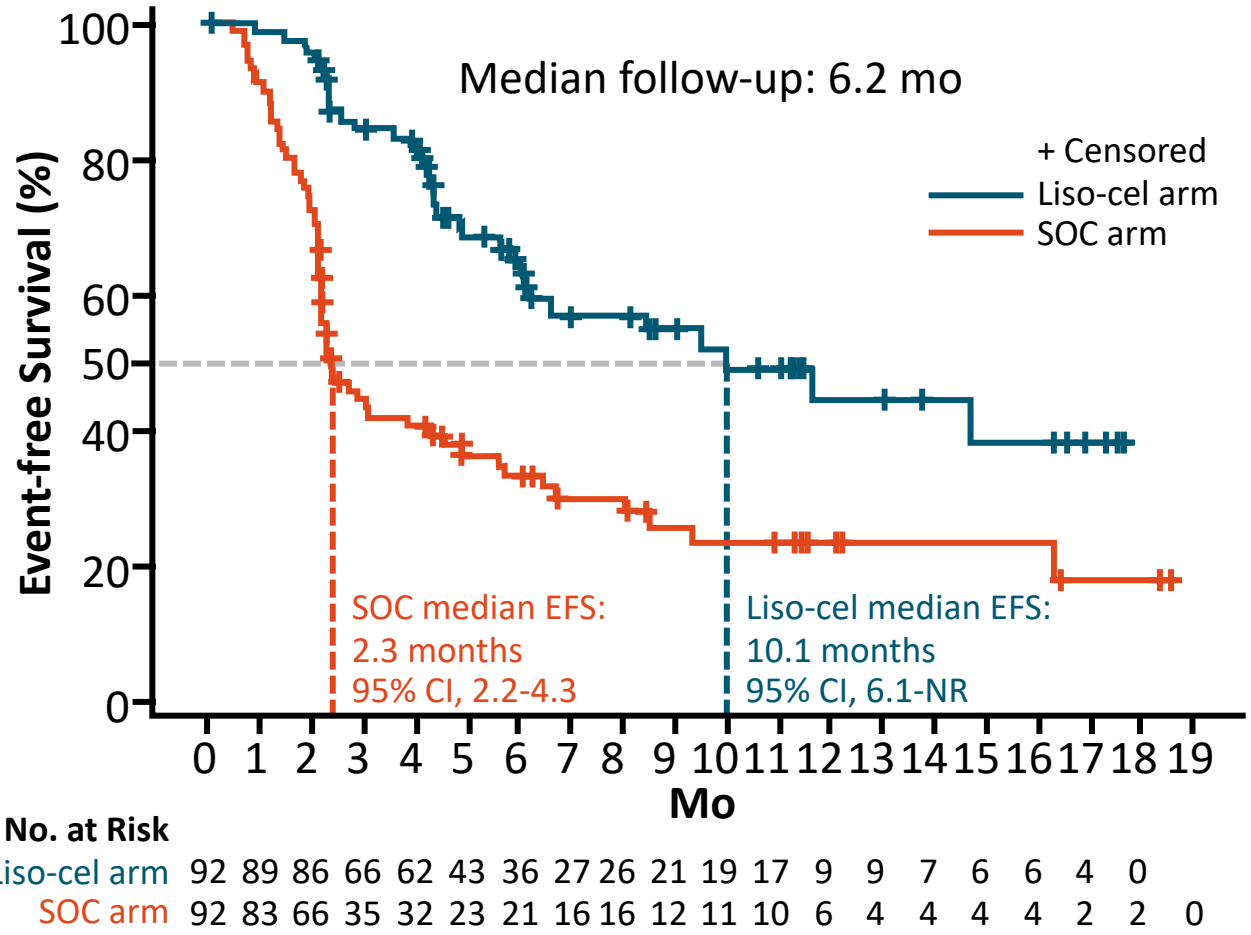


*DLBCL NOS, HGBCL (double/triple hit) with DLBCL histology, FL3B, PMBCL, THRBCL.
†Fludarabine 30 mg/m^2 + cyclophosphamide 300 mg/m^2 x 3 days.

- Primary endpoint: EFS per IRC
- Key secondary endpoints: CR, PFS, OS; other secondary endpoints: DoR, ORR, PFS on next line of tx, safety, PROs
- Exploratory endpoints: cellular kinetics, B-cell aplasia

Kamdar. ASH 2021. Abstr 91. NCT03575351. Kamdar M et al. Lancet 2022;399(10343):2294-308.

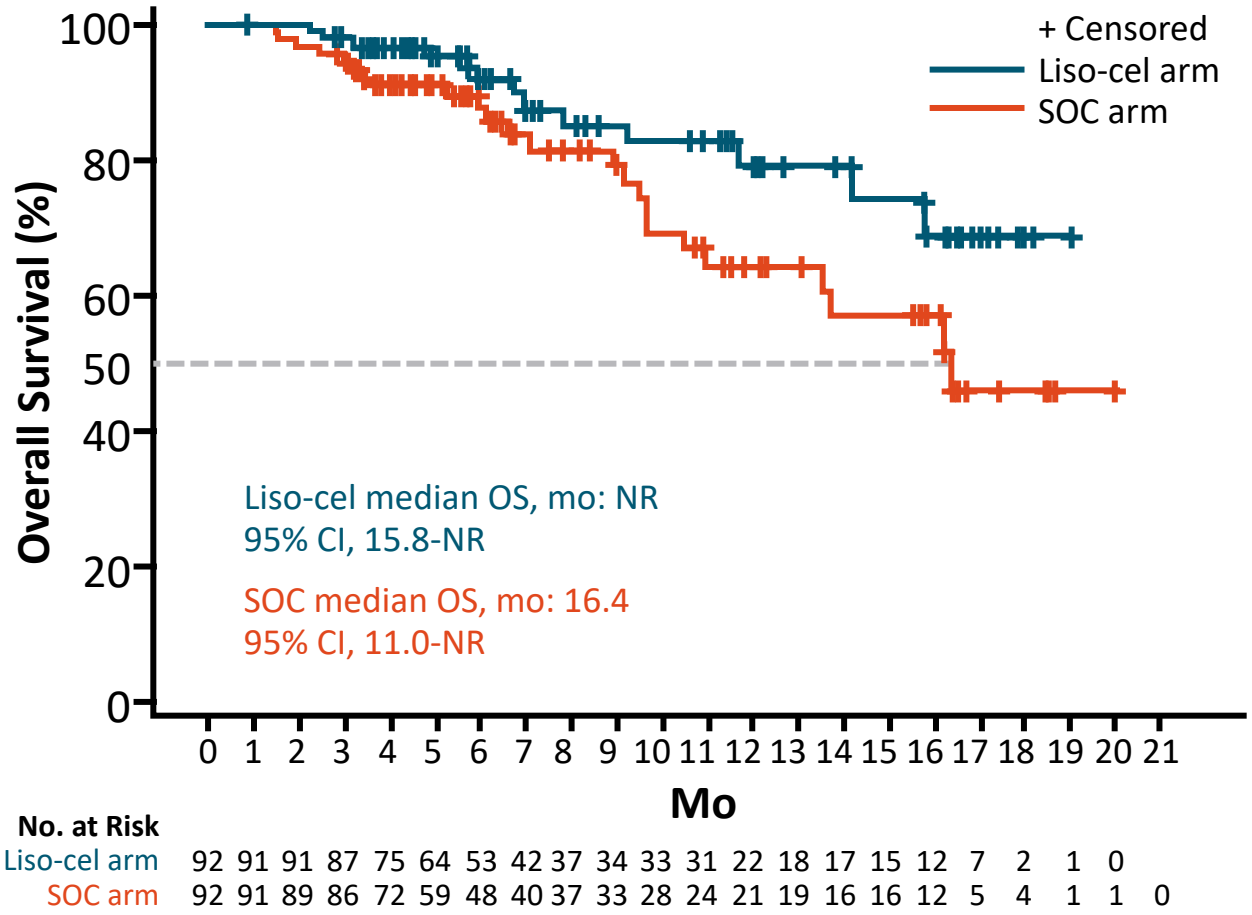
TRANSFORM: EFS per IRC (Primary Endpoint)



Outcome, n (%)	Liso-Cel (N = 92)	SoC (n = 92)
Patients with events, n	35	63
Stratified HR (95% CI)	0.349 (0.229-0.530) *P* <.0001	
6-month EFS rate, % (SE)	63.3 (5.77)	33.4 (5.30)
▪ 2-sided 95% CI	52.0-74.7	23.0-43.8
12-month EFS rate, % (SE)	44.5 (7.72)	23.7 (5.28)
▪ 2-sided 95% CI	29.4-59.6	13.4-34.1

Kamdar. ASH 2021. Abstr 91. Reproduced with permission ; Kamdar M et al. Lancet 2022;399(10343):2294-308.

TRANSFORM: OS per IRC (ITT)



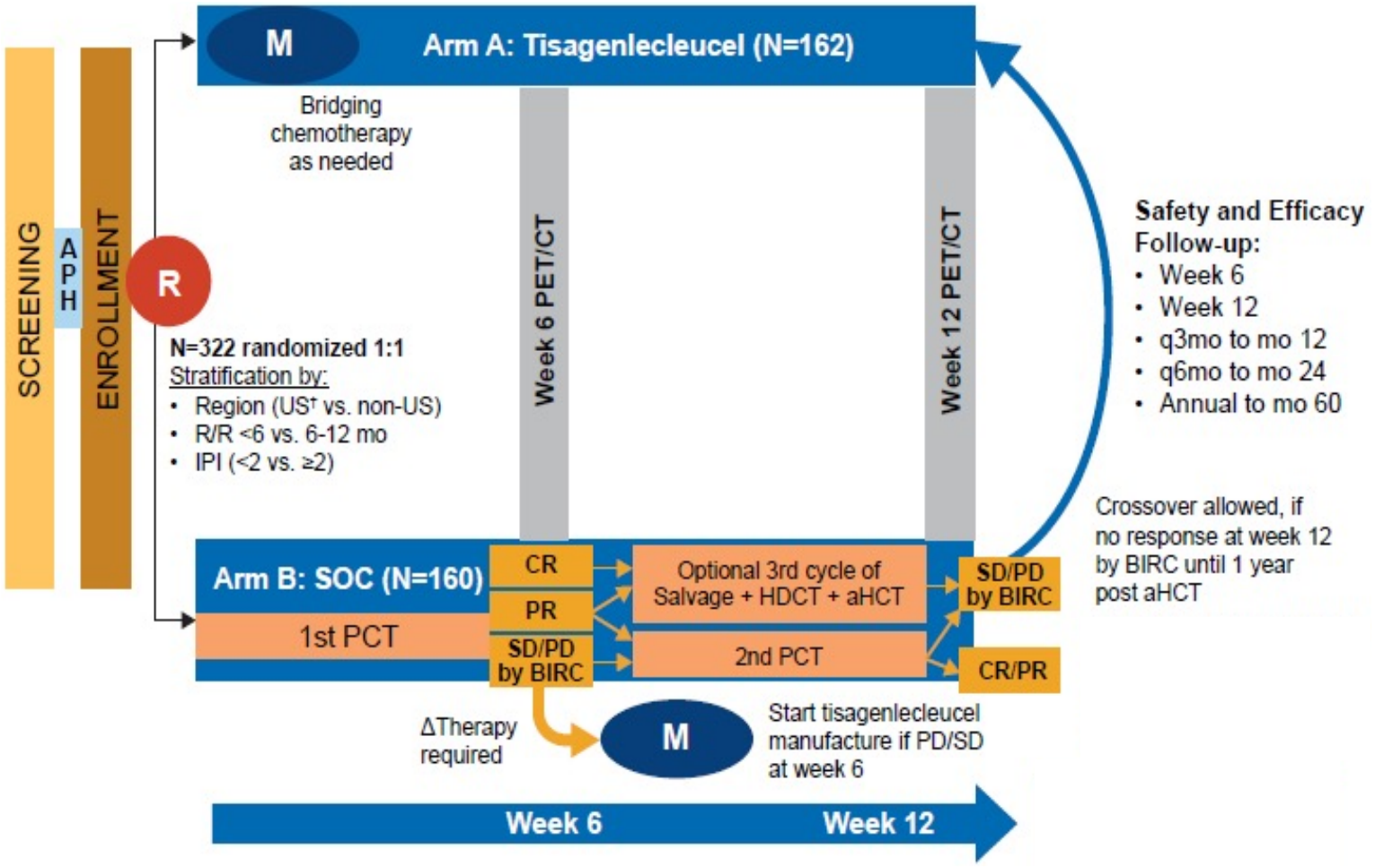
Outcome, n (%)	Liso-Cel (n = 92)	SoC (n = 92)
Patients with events, n	13	24
Stratified HR (95% CI)	0.509 (0.258-1.004) *P* = .0257	
Median OS, mo (95% CI)	NR (15.8-NR)	16.4* (11.0-NR)
6-mo OS rate, % (SE) ▪ 2-sided 95% CI	91.8 (3.29) 85.4-98.2	89.4 (3.36) 82.9-96.0
12-month OS rate, % (SE) ▪ 2-sided 95% CI	79.1 (6.13) 67.1-91.1	64.2 (6.99) 50.5-77.9

*Patients who crossed over to receive liso-cel continued to be followed for OS in SoC arm.

Kamdar. ASH 2021. Abstr 91. Reproduced with permission. Kamdar M et al. Lancet 2022;399(10343):2294-308. .

BELINDA Study Design

Key eligibility criteria:
- ≥18 years-old
- Histologically-confirmed aNHL r/r within 12 mo of first-line treatment
- aHCT eligible
- ECOG PS 0-1



Data cutoff: May 6, 2021

Primary Endpoint: *EFS*
EFS Event:
- **SD/PD by BIRC at/after week 12 ± 1 week**
- **Death at any time**

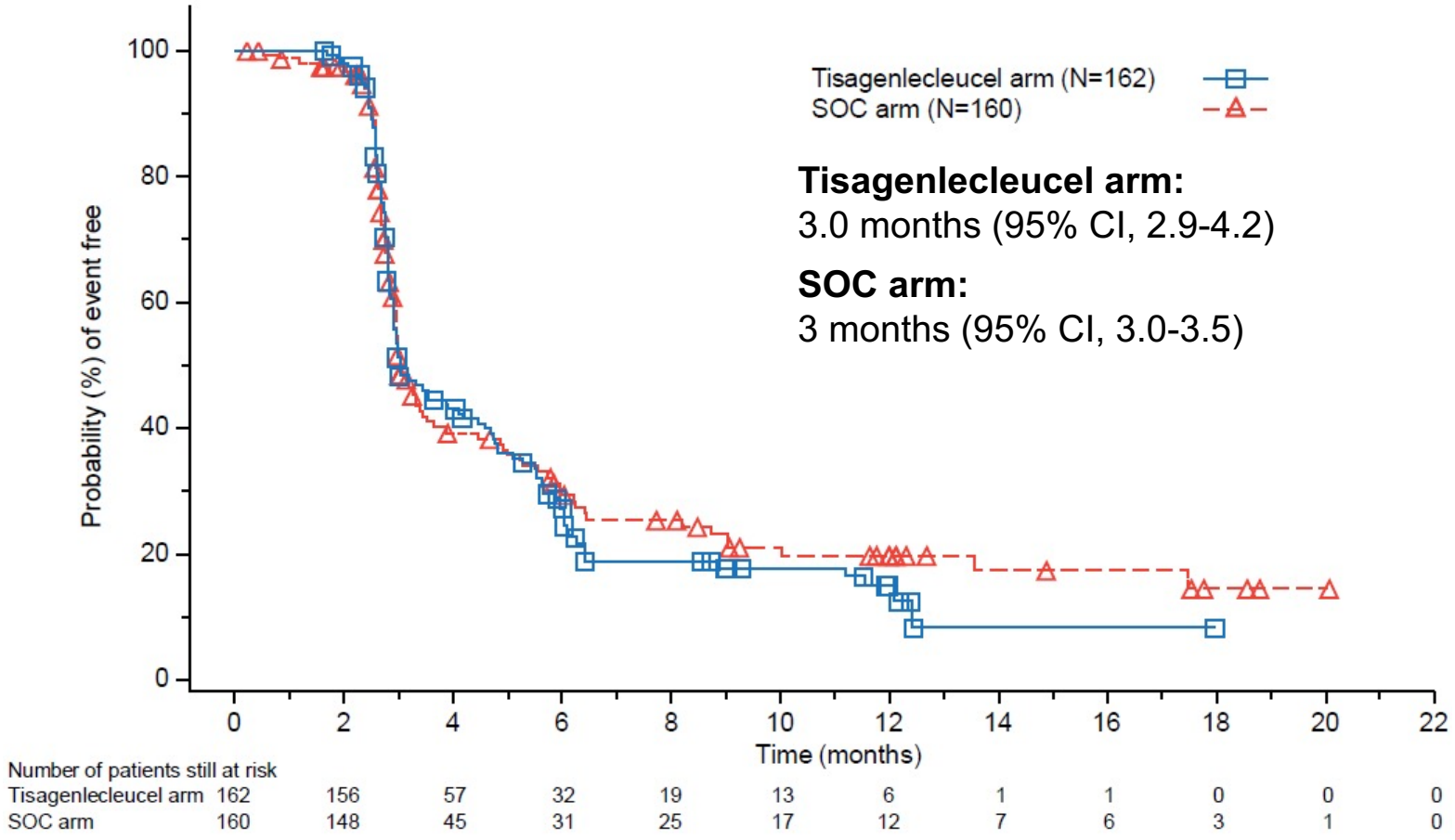
Secondary Endpoints:
- OS
- ORR: Best overall response at/after week 12
- Safety

aNHL, aggressive non-Hodgkin lymphoma; APH, leukapheresis; aHCT, autologous hematopoietic cell transplantation; BIRC, blinded independent review committee; CR, complete response; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; HDCT, high-dose chemotherapy; IPI, International Prognostic Index; M, manufacturing; ORR, overall response rate; OS, overall survival; PCT, platinum-based immunochemotherapy; PD, progressive disease; PET, positron emission tomography; PR, partial response; q3mo, every 3 months; q6mo, every 6 months; R, randomization; SD, stable disease; SOC, standard of care; US, United States.

Bishop MR et al. N Engl J Med 2022;386:629-39

No Difference in EFS Between Treatment Arms

EFS per BIRC in Tisagenlecleucel and SOC Arms



Tisagenlecleucel arm:
3.0 months (95% CI, 2.9-4.2)

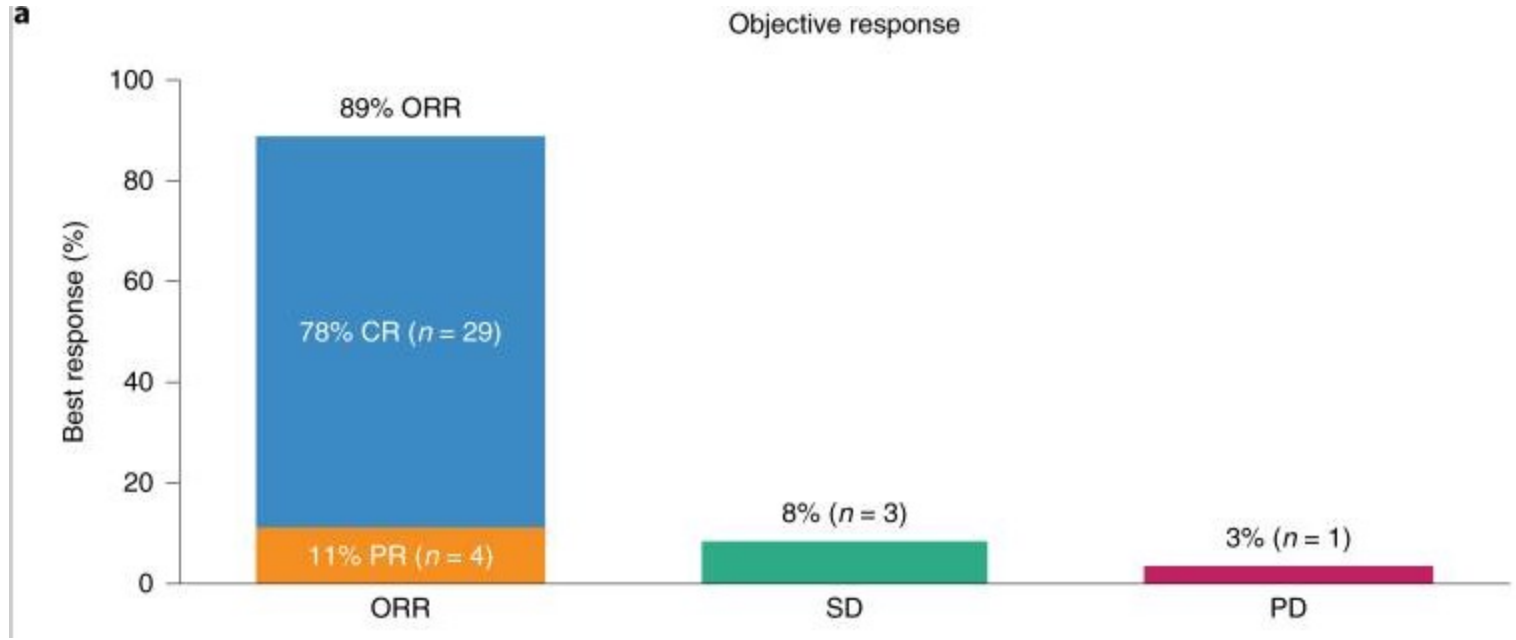
SOC arm:
3 months (95% CI, 3.0-3.5)

- Median EFS* was not significantly different between treatment arms
  - Stratified unadjusted HR: 1.07 (95% CI, 0.82-1.40; stratified log-rank P=0.69, 1-sided)
  - Stratified adjusted HR: 0.95 (95% CI, 0.72-1.25)

*EFS events defined as PD/SD after day 71 or death at any time (EFS at a given timepoint represents the estimated proportion of responders at this timepoint among all randomized patients)
BIRC, blinded independent review committee; CI, confidence interval; EFS, event-free survival; HR, hazard ratio; OS, overall survival; PD, progressive disease; SD, stable disease; SOC, standard of care.

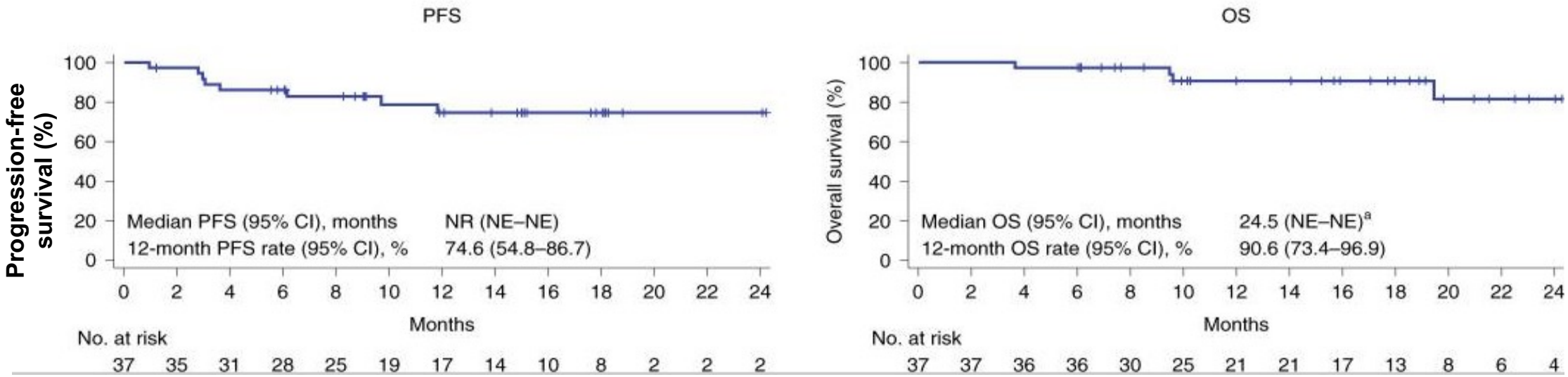
Bishop MR et al. N Engl J Med 2022;386:629-39

ZUMA-12: High Risk Patients who are PET+ after 2 cycles of Chemo: Response Rates



Neelapu SS, Dickinson M, Munoz J, Ulrickson ML, Thieblemont C, Oluwole OO, Herrera AF, Ujjani CS, Lin Y, Riedell PA, Kekre N, de Vos S, Lui C, Milletti F, Dong J, Xu H, Chavez JC. Axicabtagene ciloleucel as first-line therapy in high-risk large B-cell lymphoma: the phase 2 ZUMA-12 trial. Nat Med. 2022 Apr;28(4):735-742. doi: 10.1038/s41591-022-01731-4. Epub 2022 Mar 21. PMID: 35314842; PMCID: PMC9018426.

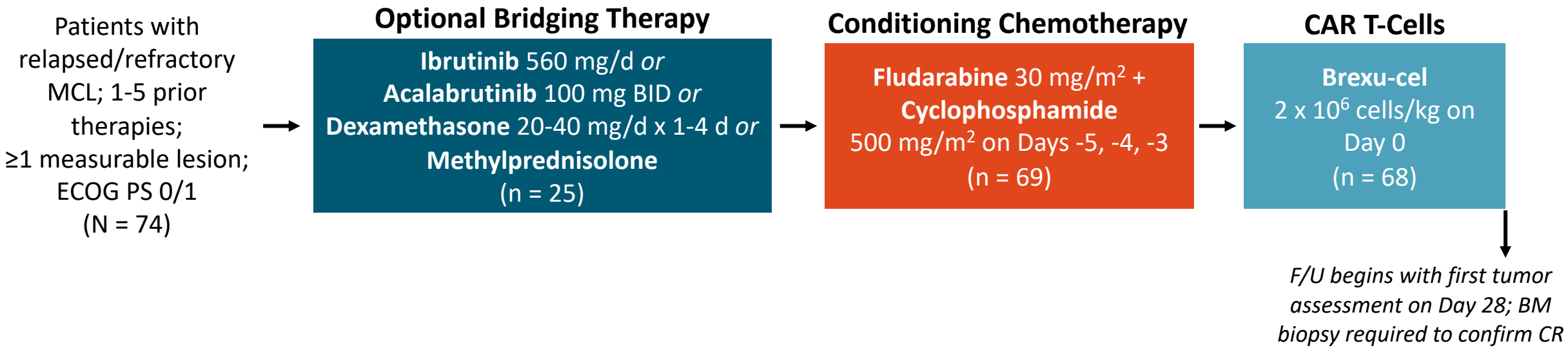
ZUMA-12: High Risk Patients who are PET+ after 2 cycles of Chemo: PFS and OS



Neelapu SS, Dickinson M, Munoz J, Ulrickson ML, Thieblemont C, Oluwole OO, Herrera AF, Ujjani CS, Lin Y, Riedell PA, Kekre N, de Vos S, Lui C, Milletti F, Dong J, Xu H, Chavez JC. Axicabtagene ciloleucel as first-line therapy in high-risk large B-cell lymphoma: the phase 2 ZUMA-12 trial. Nat Med. 2022 Apr;28(4):735-742. doi: 10.1038/s41591-022-01731-4. Epub 2022 Mar 21. PMID: 35314842; PMCID: PMC9018426.

ZUMA-2: Brexucabtagene Autoleucel in R/R MCL

- International, open-label phase II trial



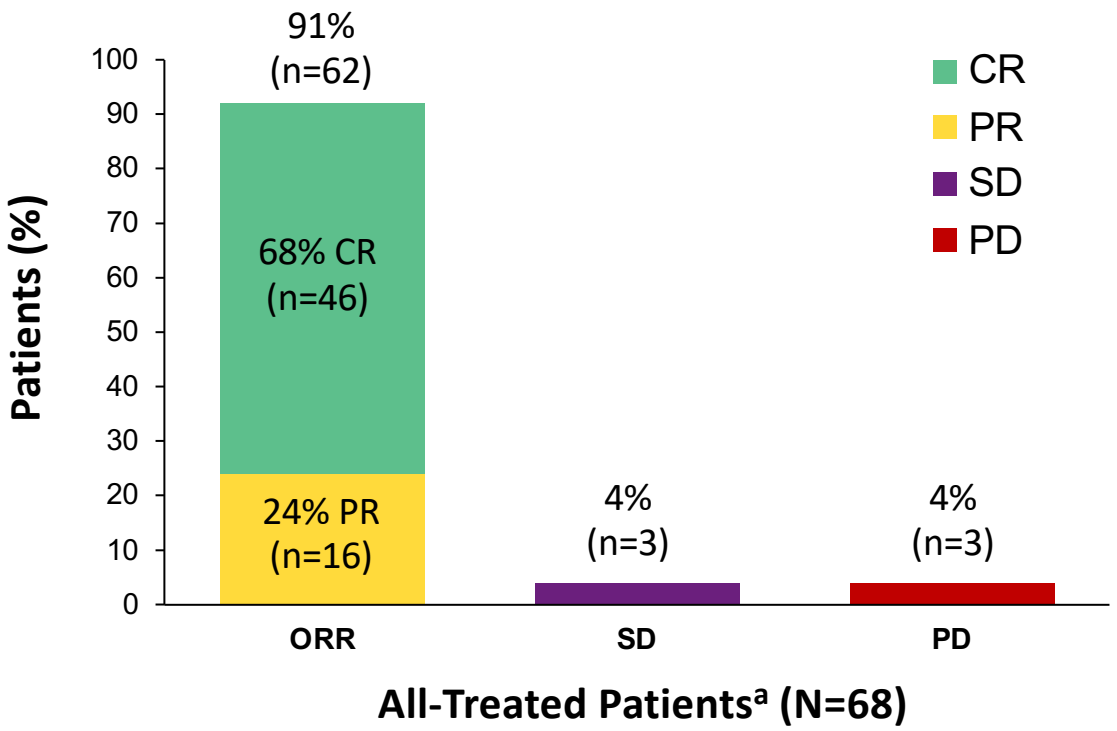
- **Primary endpoint:** ORR (IRRC assessed per Lugano classification)
- **Secondary endpoints:** DoR, PFS, OS, safety, ORR (investigator assessed), QoL (EQ-5D), CAR T-cell levels in blood, cytokines in serum

- Brexu-cel was successfully manufactured in 96% of patients and administered to 92% of patients
- Median time from leukapheresis to brexu-cel delivery was 16 days

Wang. NEJM. 2020;382:1331. Wang. ASH 2019. Abstr 759.

ZUMA-2: RESULTS

Figure 2. ORR by IRRC Assessment in All-Treated Patients (N=68; Median Follow-up, 35.6 Months)



Assessed by an IRRC according to the Lugano Classification.[10]
[a] Since the previous report,[9] IRRC review determined that 1 patient who was previously reported as best response of PR had no disease at baseline; this patient is reported as PD in the current report.
CR, complete response; IRRC, Independent Radiology Review Committee; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

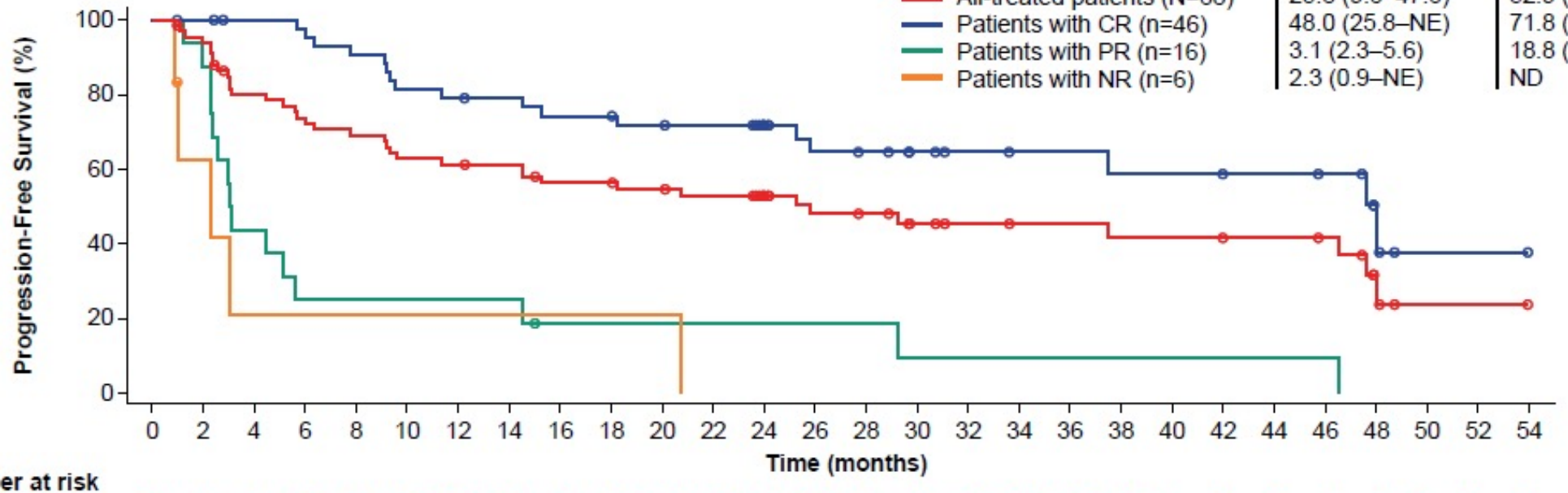
- After 35.6 months median follow-up (range, 25.9-56.3), the ORR (CR + partial response [PR]) was 91% (95% CI, 81.8-96.7), with a 68% CR rate (95% CI, 55.2-78.5; **Figure 2**)
- In the ITT population, ORR was 84% (95% CI, 73.4-91.3), with a 62% CR rate (95% CI, 50.1-73.2)

ZUMA-2: RESULTS

Figure 3. DOR, PFS, OS, and Subgroup Analysis of Ongoing Response in All-Treated Patients (N=68) (continued)

PFS

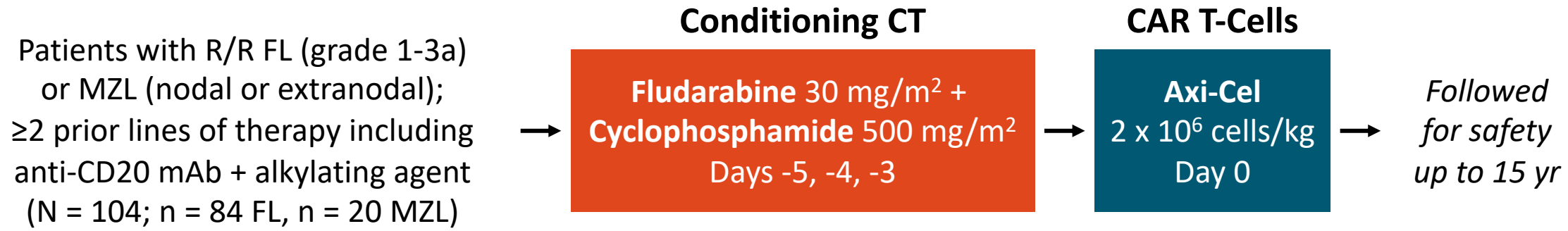
	Median PFS (95% CI), months	24-month PFS Rate (95% CI), %
All-treated patients (N=68)	25.8 (9.6–47.6)	52.9 (39.9–64.3)
Patients with CR (n=46)	48.0 (25.8–NE)	71.8 (55.7–82.9)
Patients with PR (n=16)	3.1 (2.3–5.6)	18.8 (4.6–40.2)
Patients with NR (n=6)	2.3 (0.9–NE)	ND



Number at risk																												
All-treated patients	68	62	51	47	44	40	39	38	34	34	32	30	24	20	19	15	13	12	12	11	11	10	10	9	4	1	1	0
Patients with CR	46	45	43	42	39	35	34	33	31	31	29	28	22	18	17	14	12	11	11	10	10	9	9	8	4	1	1	0
Patients with PR	16	14	7	4	4	4	4	4	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	0	0	0	0
Patients with NR	6	3	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

ZUMA-5: Axicabtagene Ciloleucel in FL and MZL

- Multicenter, single-arm phase II trial



Patients with SD but no relapse >1 yr from completion of last therapy ineligible. Single-agent anti-CD20 mAb not counted as line of therapy for eligibility. Median time to delivery of axi-cel: 17 days following leukapheresis.

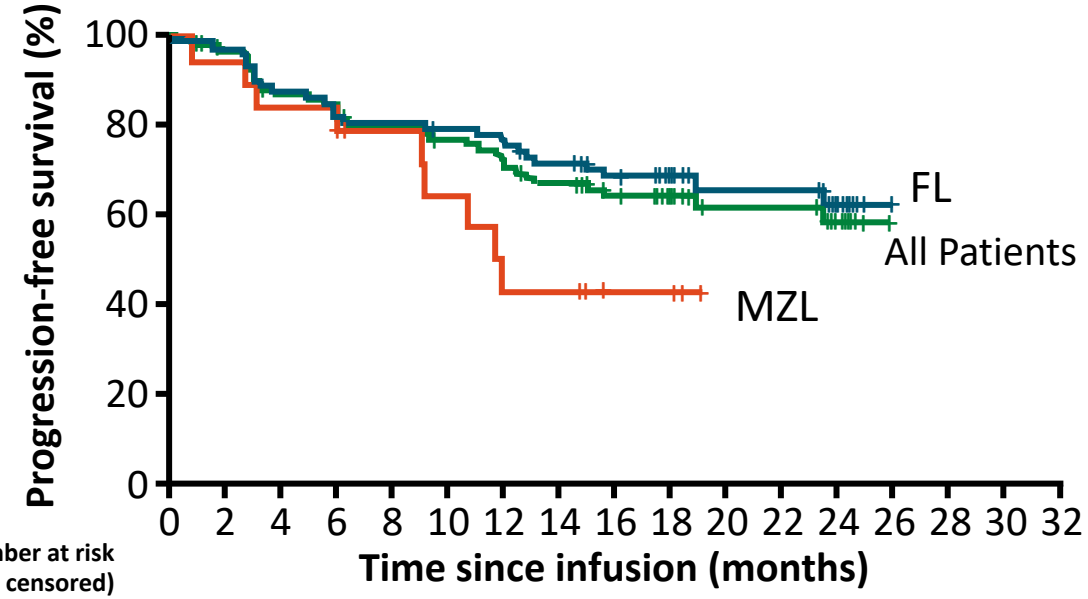
- Primary endpoint: 94% ORR (FL) and 85% ORR (MZL) after 17.5 mo follow-up
- Key secondary endpoints: CR rate (IRRC assessed), ORR (investigator assessed), DoR, PFS, OS, AEs, CAR T-cell and cytokine levels

Jacobson. Lancet 2022;23:91.

ZUMA-5: PFS and OS

PFS

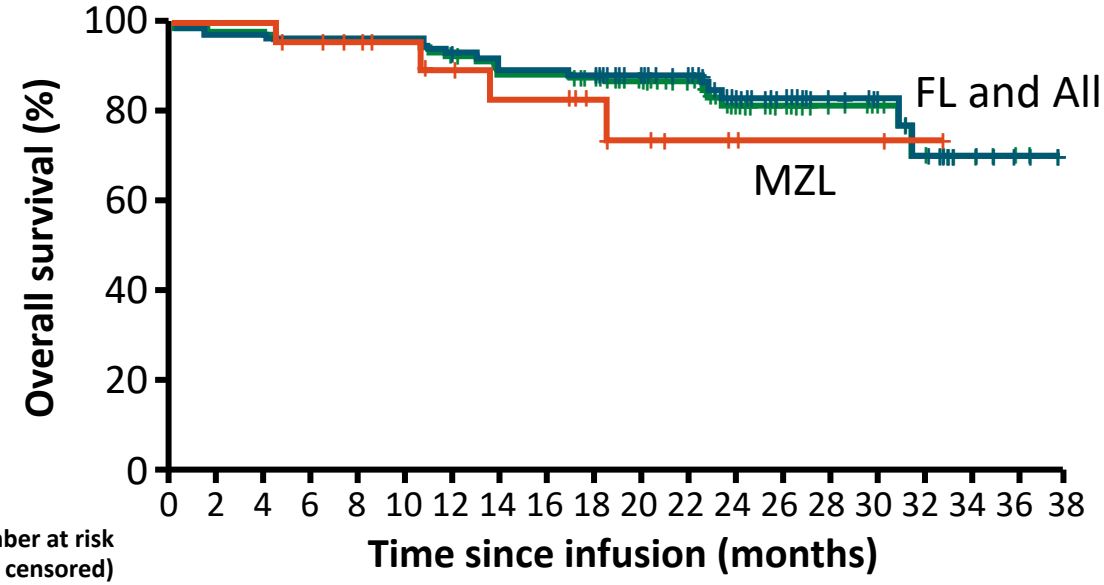
	Patients with follicular lymphoma (n = 86)	Patients with marginal zone lymphoma (n = 23)	All patients (n = 109)
Median progression-free survival (95% CI), months	NR (23.5 NE)	12.0 (9.1 NE)	NR (23.5 NE)



Number at risk (number censored)																	
Patients with follicular lymphoma	86 (0)	82 (2)	73 (3)	68 (4)	64 (6)	61 (8)	59 (8)	54 (9)	49 (12)	40 (21)	24 (36)	24 (36)	12 (47)	0 (59)			
Patients with marginal zone lymphoma	23 (0)	19 (3)	16 (4)	15 (5)	11 (8)	9 (8)	7 (8)	6 (8)	3 (11)	3 (11)	0 (14)						
All patients	109 (0)	101 (5)	89 (7)	83 (9)	75 (14)	70 (14)	56 (16)	50 (17)	52 (23)	43 (32)	24 (50)	24 (50)	12 (61)	0 (73)			

OS

	Patients with follicular lymphoma (n = 86)	Patients with marginal zone lymphoma (n = 23)	All patients (n = 109)
Median overall survival (95% CI), months	NR (31.6 NE)	NR (18.7 NE)	NR (NE-NE)



Number at risk (number censored)																			
Patients with follicular lymphoma	86 (0)	84 (0)	84 (0)	83 (0)	83 (0)	80 (0)	77 (1)	76 (1)	75 (1)	64 (12)	56 (20)	39 (34)	27 (46)	19 (54)	15 (58)	11 (60)	5 (66)	2 (69)	0 (71)
Patients with marginal zone lymphoma	23 (0)	23 (0)	23 (0)	21 (1)	19 (3)	14 (7)	12 (8)	12 (8)	9 (11)	4 (15)	4 (15)	3 (16)	2 (17)	2 (17)	2 (17)	1 (18)	0 (19)		
All patients	109 (0)	107 (0)	107 (0)	104 (1)	102 (3)	94 (7)	88 (9)	88 (9)	84 (12)	60 (35)	60 (35)	42 (50)	29 (63)	21 (71)	17 (75)	12 (78)	5 (85)	2 (88)	0 (90)

Jacobson. Lancet 2022;23:91.

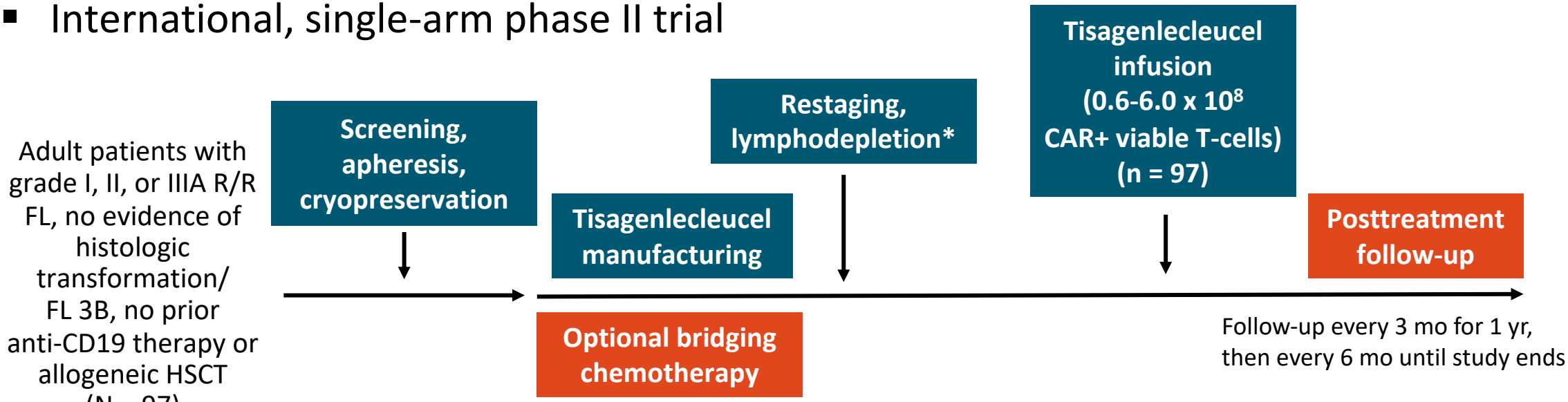
ZUMA-5: Safety Results

- Most common grade ≥3 AEs were neutropenia (33%), decreased neutrophil count (27%), and anemia (25%)
- Grade ≥3 events occurred in 85% of patients with FL and 96% with MZL
- CRS occurred in 78% of patients with FL and 100% with MZL (grade ≥3 in 6% FL, 8% MZL)
  - All CRS events resolved except 1 event
- NE occurred in 56% of patients with FL and 71% with MZL (grade ≥3 in 15% FL, 38% MZL)
  - Median duration of NE was 14 days in FL and 10 days in MZL

Jacobson. Lancet 2022;23:91.

ELARA: Tisagenlecleucel in R/R FL

- International, single-arm phase II trial



*Lymphodepleting therapy: fludarabine 25 mg/m^2/day IV for 3 days + cyclophosphamide 250 mg/m^2/day IV for 3 days or bendamustine 90 mg/m^2/day IV for 2 days.

- **Primary endpoint:** CRR by IRC
- **Secondary endpoints:** ORR, DoR, PFS, OS, safety, cellular kinetics

Schuster. ASCO 2021. Abstr 7508. Fowler. Nat Med. 2022; 28:325.

ELARA: Efficacy of Tisagenlecleucel in R/R FL

Response, %	Evaluable Patients (n = 94)
Investigator assessed	
▪ CRR	72.3
▪ ORR	90.4
IRC-assessed	
▪ CR	69.1
▪ PR	17
▪ ORR (CR + PR)	86.2
Survival	**Evaluable Patients (n = 94)**
12-mo PFS, % (95% CI)	67 (56-76)

*Including age, sex, no. prior lines of therapy, use of PI3K inhibitors, prior HSCT, disease status to last line of therapy, POD24 from first-line anti-CD20 mAb-containing therapy.

- Median follow-up for efficacy was 16.6 mo (interquartile range 13.8-20.2)
- Median DoR, PFS, and OS were not reached
- CRR consistent across all subgroups examined*
- 48.3% (15/31) of patients achieving PR converted to CR
  - 11 occurred between Mo 3 and 6

Fowler. Nat Med. 2022; 28:325.

ELARA: Safety of Tisagenlecleucel in R/R FL

AEs, n (%)	Patients (N = 97)	
Any AE, n (%)	96 (99.0)	
Grade 3/4 AE, n (%)	76 (78.4)	
Death, n (%)	7 (7.2)	
▪ Due to study indication	5 (5.1)	
▪ Due to CRS	1 (1)	
▪ Due to general disorders	1 (1)	
▪ Within 30 days post infusion	0	
AEs of Special Interest,* %	**All grades**	**Grade ≥3**
▪ CRS	48.5	0
▪ Neurological events	37.1	3.1
▪ Infections	18.6	5.2
▪ Hypogammaglobulinemia	9.3	0
▪ Neutropenia	33	32
▪ Febrile neutropenia	10.3	10.3
▪ Anemia	24.7	13.4
▪ Thrombocytopenia	16.5	9.3

* 8 wk post infusion

- Tocilizumab and corticosteroids required for AE management in 34% and 6.4% of patients, respectively
- Median onset of CRS: 4.0 (IQR 2-7) days
- Median onset of serious neurological events: 9 days (IQR: 35)
- Within 8 weeks, ICANS in 4.1%

Fowler. Nat Med. 2022; 28:325.

Agenda

PART 1: Case Presentations and Clinical Decision-Making

- Non-Hodgkin Lymphoma
- Multiple Myeloma

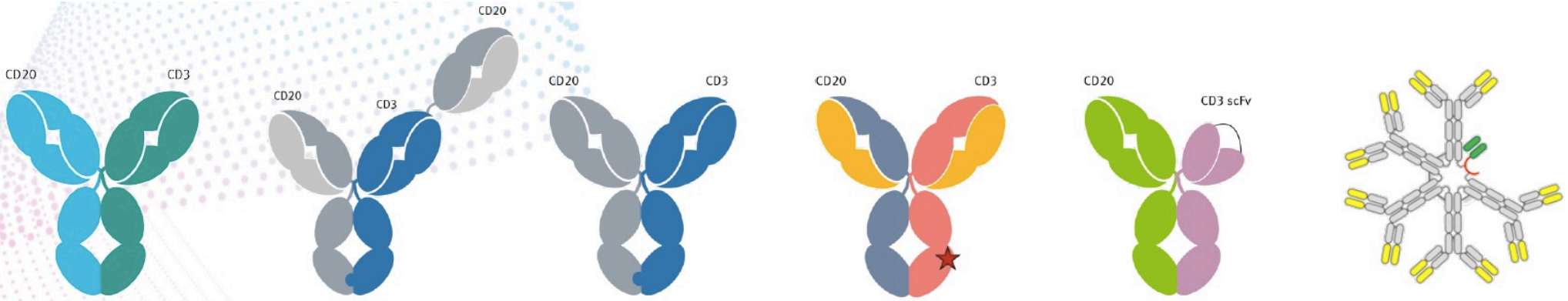
PART 2: Faculty Presentations

- CAR-T in Non-Hodgkin Lymphoma — Dr Flinn
- Bispecifics in Non-Hodgkin Lymphoma — Dr Sehn
- CAR-T in Multiple Myeloma — Dr Munshi
- Bispecifics in Multiple Myeloma— Dr Chari

Available Data with and Potential Clinical Use of Bispecific Antibodies in Patients with Lymphoma

Laurie H Sehn, MD, MPH
Chair, Lymphoma Tumour Group
BC Cancer Centre for Lymphoid Cancer
Clinical Professor of Medicine
Division of Medical Oncology
University of British Columbia
Associate Editor, *Blood*
Vancouver, British Columbia, Canada

An Overview of CD3 X CD20 Bispecific Antibodies



Name of bispecific	Epcoritamab	Glofitamab	Mosunetuzumab	Odronextamab	Plamotamab	IGM-2323
Bispecific format	DuoBody IgG1	Fab-Fc x Fab-Fab-Fc Knob-into-hole (HC) XmAb (LC-HC)	Knob-into-hole (HC) IgG1	FcΔAdp IgG4	XmAb Fab-Fc x scFv-Fc	Proprietary IgM platform
CD3 Ab clone	huCACAO (SP34-der.) (CD3ε)	(SP34-der.) (CD3ε)	UCHT1v9 (CD3δε)	REG1250 (CD3δε)	α-CD3_H1.30 (SP34-der.) (CD3ε)	Not reported
CD20 Ab clone	7D8 (OFA epitope)	Obinutuzumab (Ritux epitope)	2H7 (Ritux epitope)	3B9-10 (OFA epitope)	C2B8_H1_L1 (Rituximab > Ritux epitope)	Not reported
Inert format	L234F,L235E,D265A (No FcγR,C1q binding)	IgG1-P329G-LALA (No FcγR binding)	N297G (No FcγR binding)	Modified IgG4 (No FcγRIII binding)	G236R, L328R (No FcγR binding)	IgM + modified J chain (10 CD-20 and 2 CD-3 binding domains)

Mosunetuzumab Monotherapy in Patients with Relapsed/Refractory (R/R) FL after ≥2 Prior Lines of Therapy: Pivotal Results from a Phase I/II Study

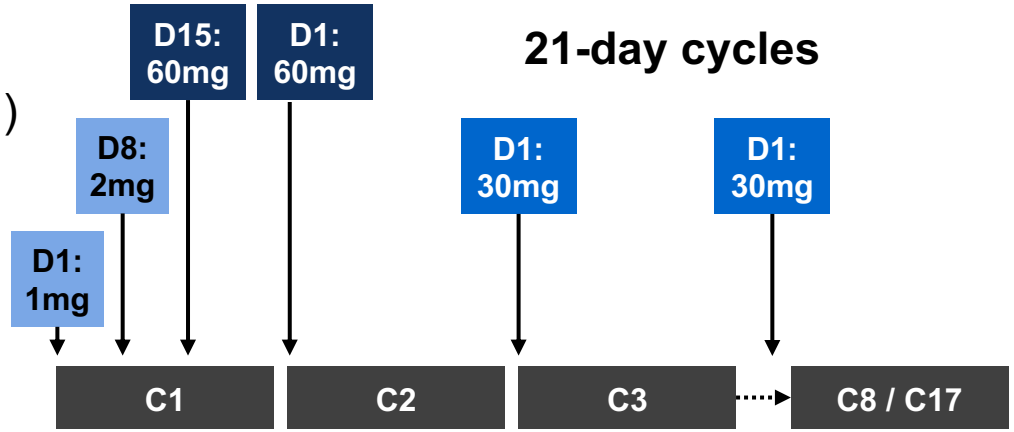
- Single-arm, pivotal Phase II expansion in patients with R/R FL and ≥2 prior therapies

Key inclusion criteria

- FL (Grade 1–3a)
- ECOG PS 0–1
- ≥2 prior regimens, including
  - ≥1 anti-CD20 Ab
  - ≥1 alkylating agent

Mosunetuzumab administration

- Q3W intravenous administration
- C1 step-up dosing (CRS mitigation)
- **Fixed-duration treatment**
  - 8 cycles if CR after C8
  - 17 cycles if PR/SD after C8
- **No mandatory hospitalization**



Endpoints

- Primary: CR (best response) rate by IRF* – assessed vs 14% historical control CR rate[1]
- Secondary: ORR, DoR, PFS, safety and tolerability

Budde LE et al. Lancet Oncol 2022;23(8):1055-65. Budde LE et al. ASH 2021;Abstract 127.

Baseline characteristics

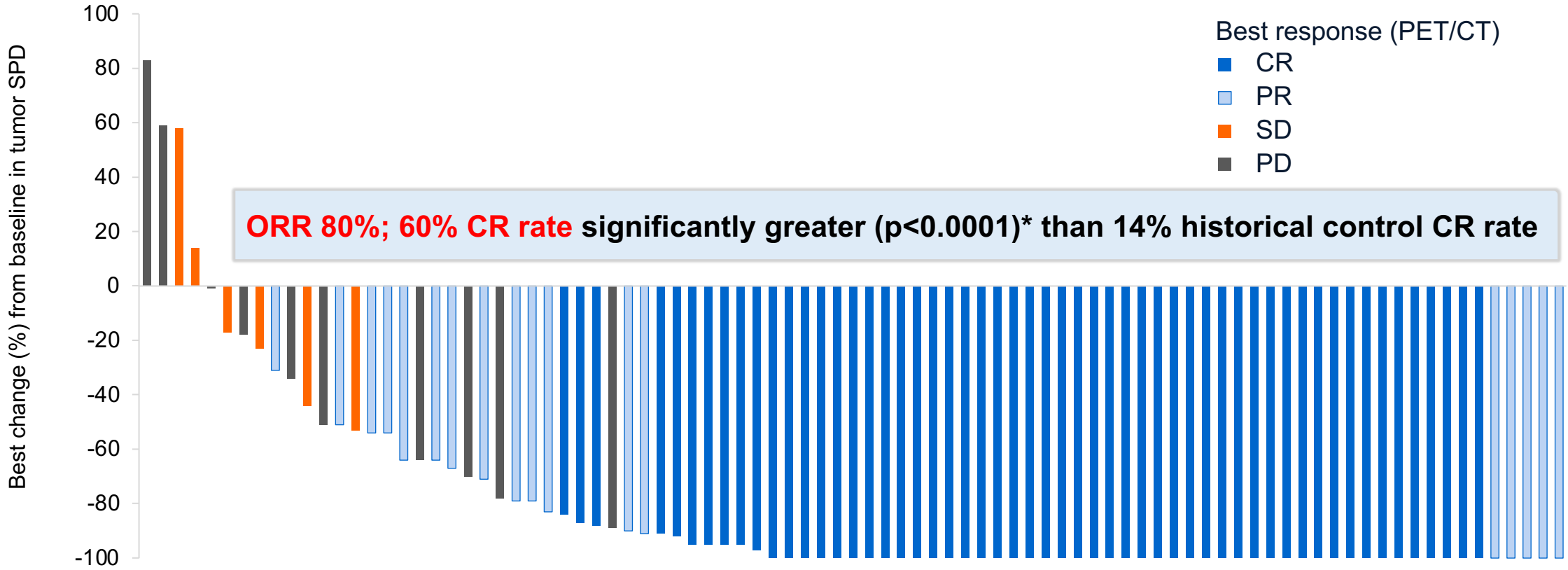
		N=90
Median age, years (range)		60 (29–90)
Male		55 (61.1%)
ECOG PS	0 1	53 (58.9%) 37 (41.1%)
Ann Arbor stage	I–II III–IV	21 (23.3%) 69 (76.7%)

		N=90
Median number of prior lines, n (range)		3 (2–10)
Prior systemic therapy	Anti-CD20 therapy Alkylator therapy PI3K inhibitor IMiD CAR-T	90 (100%) 90 (100%) 17 (18.9%) 13 (14.4%) 3 (3.3%)
Prior ASCT		19 (21.1%)
Refractory to last prior therapy		62 (68.9%)
Refractory to any prior aCD20 therapy		71 (78.9%)
Refractory to any prior aCD20 therapy and alkylator therapy (double refractory)		48 (53.3%)
POD24		47 (52.2%)

Budde LE et al. Lancet Oncol 2022;23(8):1055-65.
Budde LE et al. ASH 2021;Abstract 127.

Anti-tumor efficacy

Best percentage change from baseline in tumor SPD*

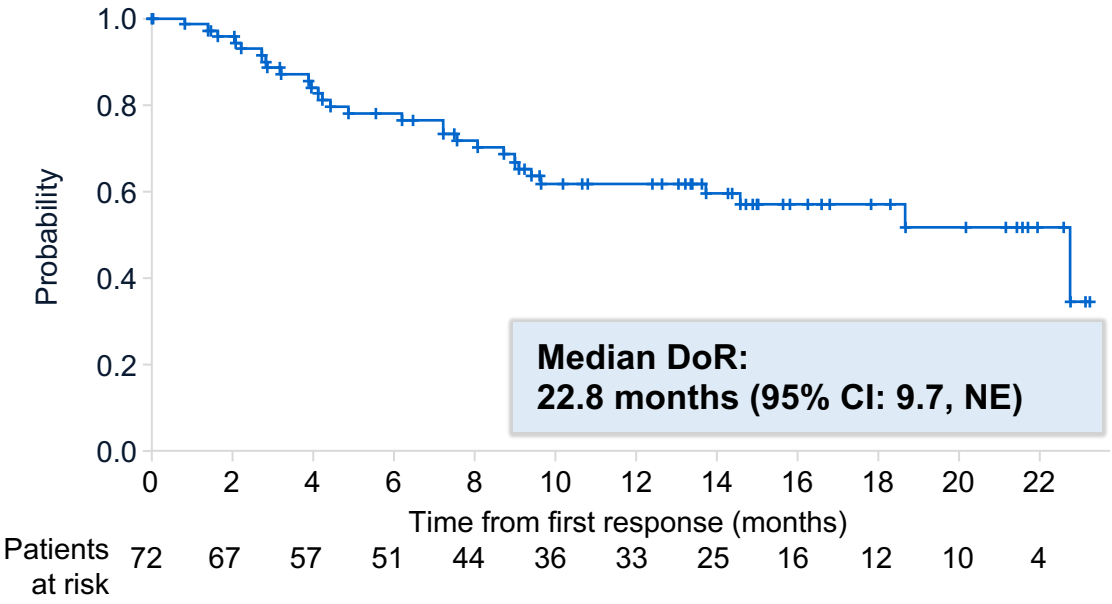


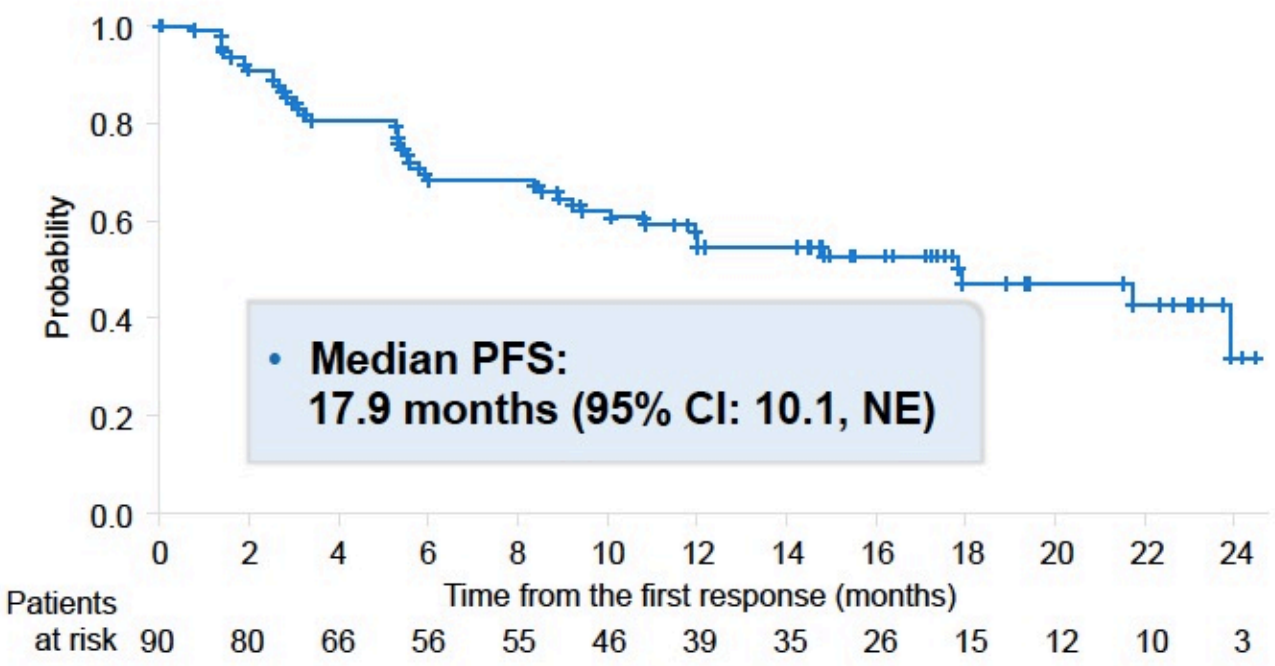
*in all patients with a baseline and ≥1 post-baseline SPD available; PD, progressive disease; SPD, sum of product diameters

Budde LE et al. Lancet Oncol 2022;23(8):1055-65. Budde LE et al. ASH 2021;Abstract 127.

Duration of Response and PFS (median follow-up: 18.3 m)

Duration of response in responders





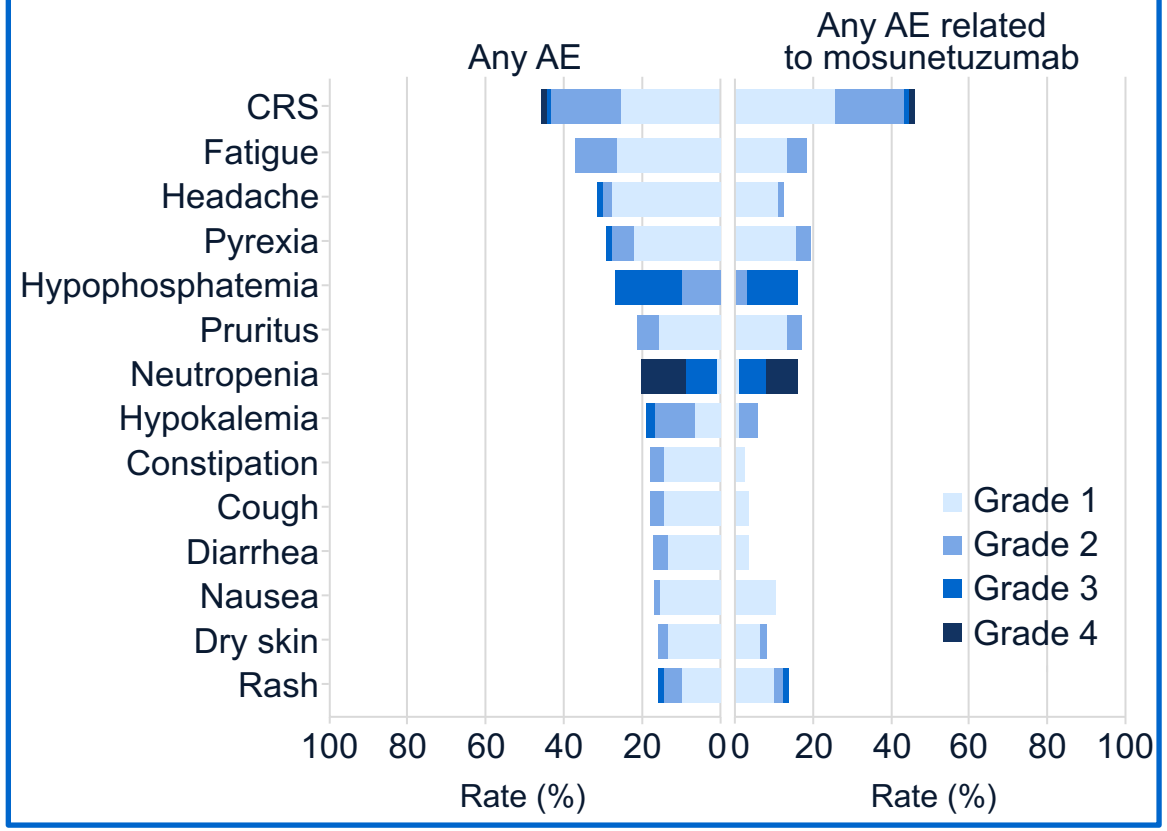
Median time to first response, mo (range)	1.4 (1.1, 8.9)

Budde LE et al. Lancet Oncol 2022;23(8):1055-65. Budde LE et al. ASH 2021;Abstract 127.

Safety Profile

N (%)	N=90
AE Mosunetuzumab related*	90 (100%) 83 (92.2%)
Grade 3–4 AE Mosunetuzumab related*	63 (70.0%) 46 (51.1%)
Serious AE Mosunetuzumab related*	42 (46.7%) 30 (33.3%)
Grade 5 (fatal) AE Mosunetuzumab related*	2 (2.2%)† 0
AE leading to discontinuation of treatment Mosunetuzumab related*	4 (4.4%)‡ 2 (2.2%)‡

AEs (≥15%) by Gr and relationship with mosunetuzumab



ICANS 4.4%: all grade 1-2 (confusion, attention or cognitive disorder), all resolved

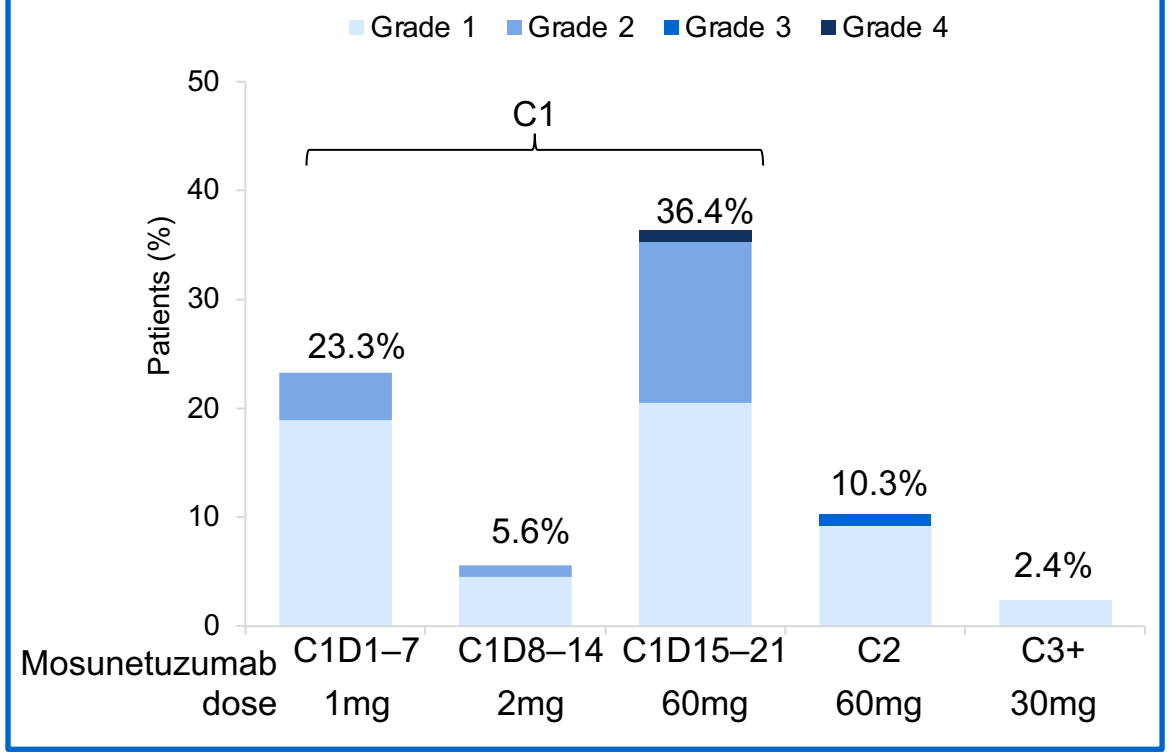
Budde LE et al. Lancet Oncol 2022;23(8):1055-65. Budde LE et al. ASH 2021;Abstract 127.

Budde LE et al. Lancet Oncol 2022;23(8):1055-65. Budde LE et al. ASH 2021;Abstract 127.

Cytokine release syndrome

N (%)	N=90
CRS (any grade) Grade 1 Grade 2 Grade 3 Grade 4	40 (44.4%) 23 (25.6%) 15 (16.7%) 1 (1.1%) 1 (1.1%)†
Median time to CRS onset, hours (range) C1D1 C1D15	 5.2 (1.2–23.7) 26.6 (0.1–390.9)
Median CRS duration, days (range)	3 (1–29)
Corticosteroids for CRS management	10 (11.1%)
Tocilizumab for CRS management	7 (7.8%)

CRS by Cycle and Grade



- **CRS was predominately low grade and in Cycle 1. All events resolved.**

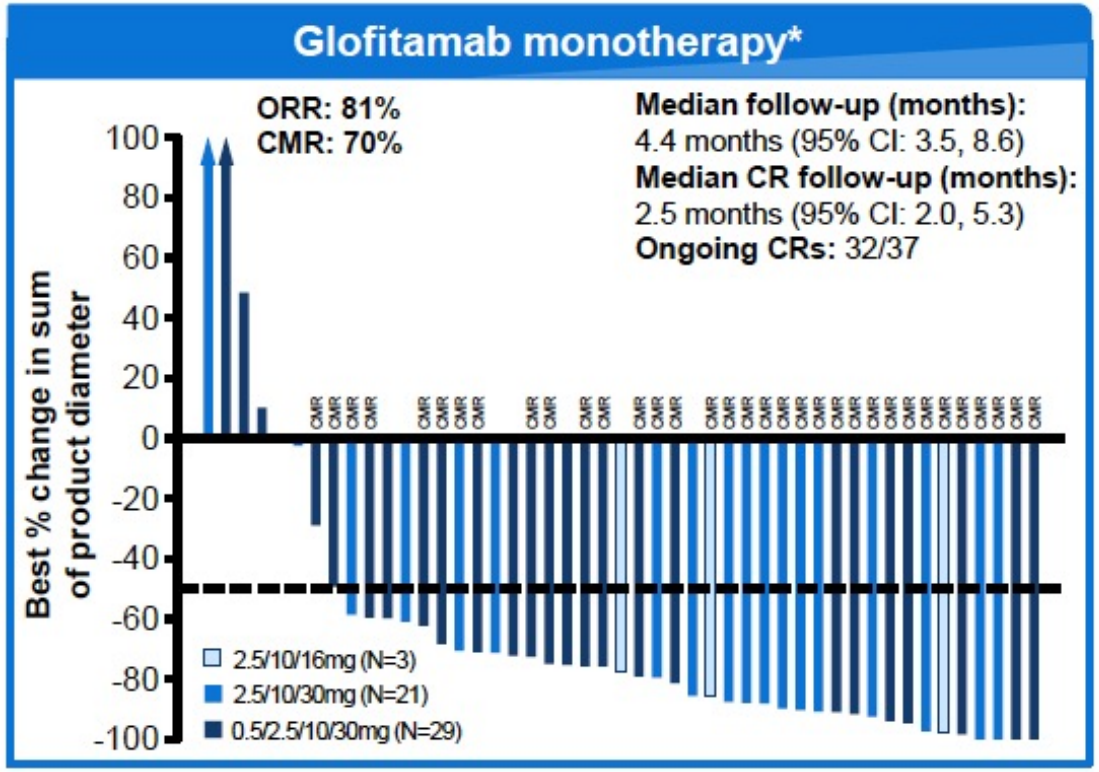
Glofitamab as Monotherapy and in Combination with Obinutuzumab Induces High Complete Response Rates in Patients with Multiple Relapsed or Refractory (R/R) Follicular Lymphoma (FL)

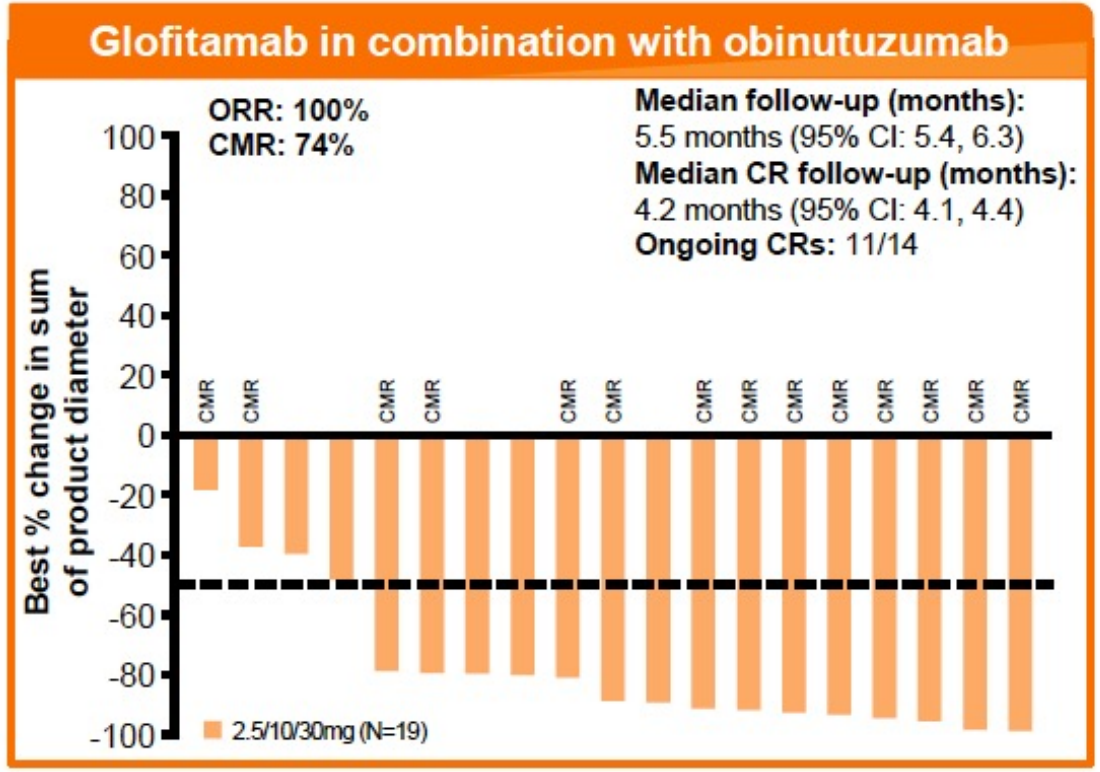
Franck Morschhauser,[1] Carmelo Carlo-Stella,[2] Michael Dickinson,[3] Tycel Phillips,[4] Roch Houot,[5] Fritz Offner,[6] Corinne Haioun,[7] Paolo Corradini,[8] Martin Hutchings,[9] Anna Sureda,[10] Joaquin Martinez-Lopez,[11] Tomasz Wróbel,[12] Shang-Ju Wu,[13] Linda Lundberg,[14] Estefania Mulvihill,[14] David Perez-Callejo,[14] James Relf,[15] Anesh Panchal,[15] Kathryn Humphrey,[15] Emmanuel Bachy[16]

[1]CHU Lille, Service des Maladies du Sang, F-59000 Lille, France; [2]Humanitas University and Humanitas Research Hospital, Milan, Italy; [3]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and The University of Melbourne, Melbourne, Australia; [4]University of Michigan Medical School, Ann Arbor, Michigan, USA; [5]CHU de Rennes, Université de Rennes, INSERM U1236, EFS, Rennes, France; [6]Universitair Ziekenhuis Gent, Ghent, Belgium; [7]Hôpital Henri Mondor, AP-HP, Créteil, France; [8]University of Milan; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [9]Rigshospitalet, Copenhagen, Denmark; [10]Institut Català d'Oncologia Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain; [11]Hospital Universitario 12 de Octubre (H12O), Centro Nacional de Investigaciones Oncológicas (CNIO)-H12O and Universidad Complutense de Madrid, Madrid, Spain; [12]Wrocław Medical University, Wrocław, Poland; [13]National Taiwan University Hospital, Taipei, Taiwan; [14]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [15]Roche Products Ltd, Welwyn Garden City, United Kingdom; [16]Hospices Civils de Lyon and Université Claude Bernard, Pierre-Bénite, France.

Accepted as an Oral Presentation at the 63rd ASH Annual Meeting and Exposition

Phase I/II Study of Glofitamab as Monotherapy or in Combination with Obinutuzumab for R/R FL





- **Deep responses observed across glofitamab dosing regimens; most complete responses were ongoing**

- Myelosuppression was more common with the combination
- CRS rates were high and comparable, and cases were mainly low grade

Morschhauser F et al. ASH 2021;Abstract 128.

Glofitamab Pivotal Phase II Trial

Pivotal Phase II expansion in patients with R/R DLBCL and ≥2 prior therapies (NP30179)

Key inclusion criteria

- DLBCL NOS, HGBCL, transformed FL or PMBCL
- ECOG PS 0–1
- ≥2 prior therapies, including:
  - anti-CD20 antibody
  - anthracycline

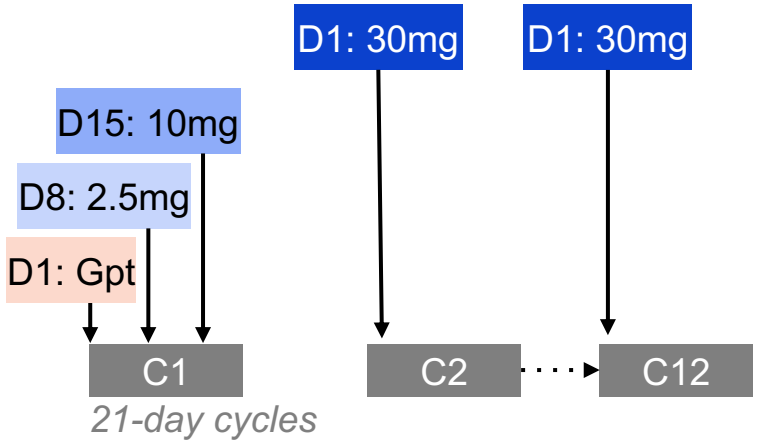
Glofitamab IV administration

Fixed-duration treatment

- max. 12 cycles

CRS mitigation:

- obinutuzumab pretreatment (1 x 1000mg)
- C1 step-up dosing
- monitoring after first dose (2.5mg)



Endpoints

- **Primary: CR (best response) rate by IRC**
- **Key secondary:** ORR rate,† DoR, DoCR,† PFS, and OS

Dickinson M et al. ASCO 2022;Abstract 7500.

Glofitamab Pivotal Phase II Trial: Baseline Characteristics

n (%)*		N=154†
Median age, years (range)		66.0 (21–90)
Male		100 (64.9)
ECOG PS‡	0	69 (44.8)
	1	84 (54.5)
Ann Arbor stage	I	10 (6.5)
	II	25 (16.2)
	III	31 (20.1)
	IV	85 (55.2)
NHL subtype	DLBCL	110 (71.4)
	trFL	27 (17.5)
	HGBCL	11 (7.1)
	PMBCL	6 (3.9)
Bulky disease	>6cm	64 (41.6)
	>10cm	18 (11.7)

n (%)*	N=154
Median no. of prior lines, n (range)	3 (2–7)
2 prior lines	62 (40.3)
≥3 prior lines	92 (59.7)
Prior anti-CD20 Ab	154 (100.0)
Prior anthracycline	149 (96.8)
Prior CAR-T	51 (33.1)
Prior ASCT	28 (18.2)
Refractory to any prior therapy	139 (90.3)
Refractory to last prior therapy	132 (85.7)
Primary refractory	90 (58.4)
Refractory to prior CAR-T	46 (29.9)
Refractory to any prior anti-CD20	128 (83.1)

- **Heavily pre-treated, highly refractory population**

Dickinson M et al. ASCO 2022;Abstract 7500.

Response rates – primary endpoint met

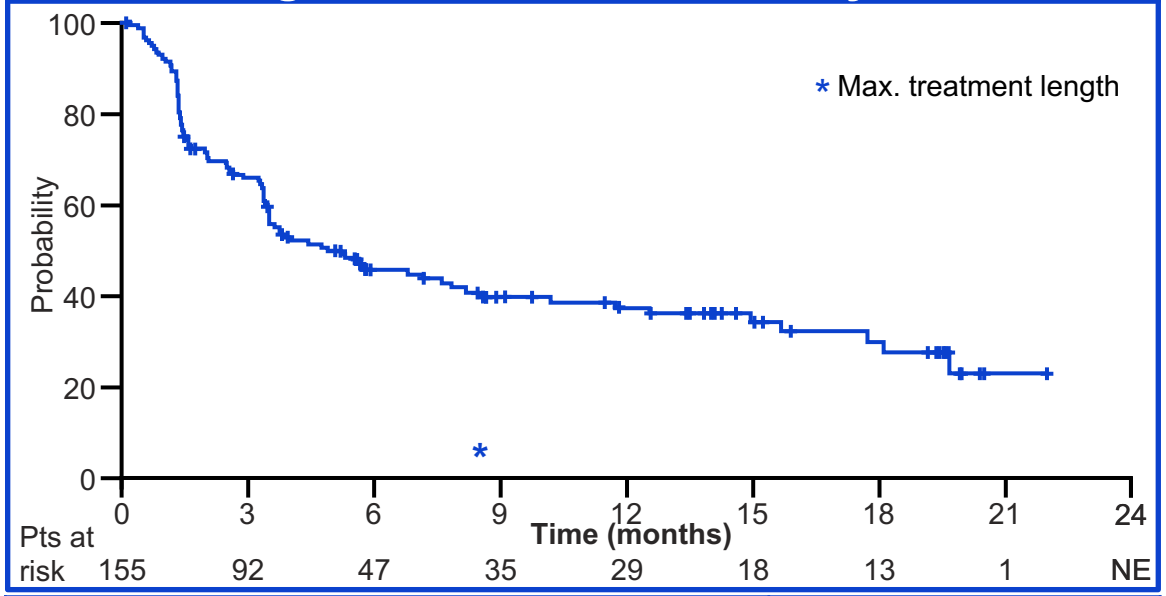
Efficacy endpoint[1]	Glofitamab 2.5/10/30mg (n=155)
CR rate*	**61 (39.4%)** [95% CI: 31.6%, 47.5%]
ORR*	**80 (51.6%)** [95% CI: 43.5%, 59.7%]

- Responses were achieved early: median time to first CR was 42 days (95% CI: 42, 44)

Dickinson M et al. ASCO 2022;Abstract 7500.

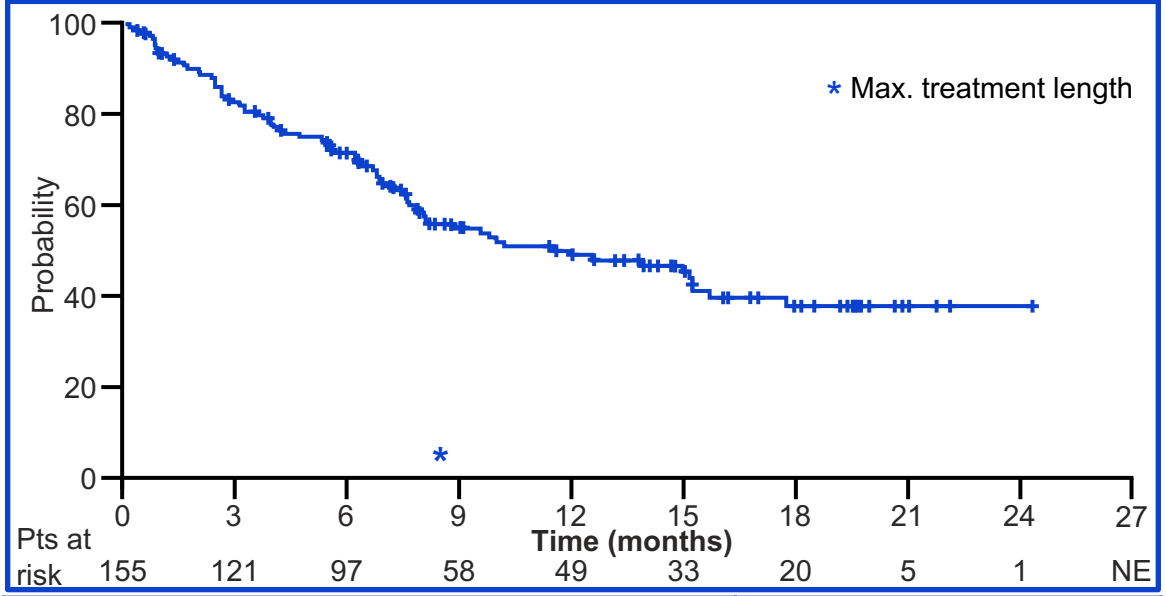
Time-to-event endpoints

Progression-free survival by IRC



	N=155
Median PFS follow-up, mo (range)	12.6 (0–22)
Median PFS, months (95% CI)†	4.9 (3.4, 8.1)
6-month event-free rate, % (95% CI)	45.5 (37.2, 53.8)
12-month event-free rate, % (95% CI)	37.1 (28.5, 45.8)

Overall survival*



	N=155
Median OS, months (95% CI)†	11.5 (7.9, 15.7)
12-month OS rate, % (95% CI)	49.8 (41.1, 58.5)

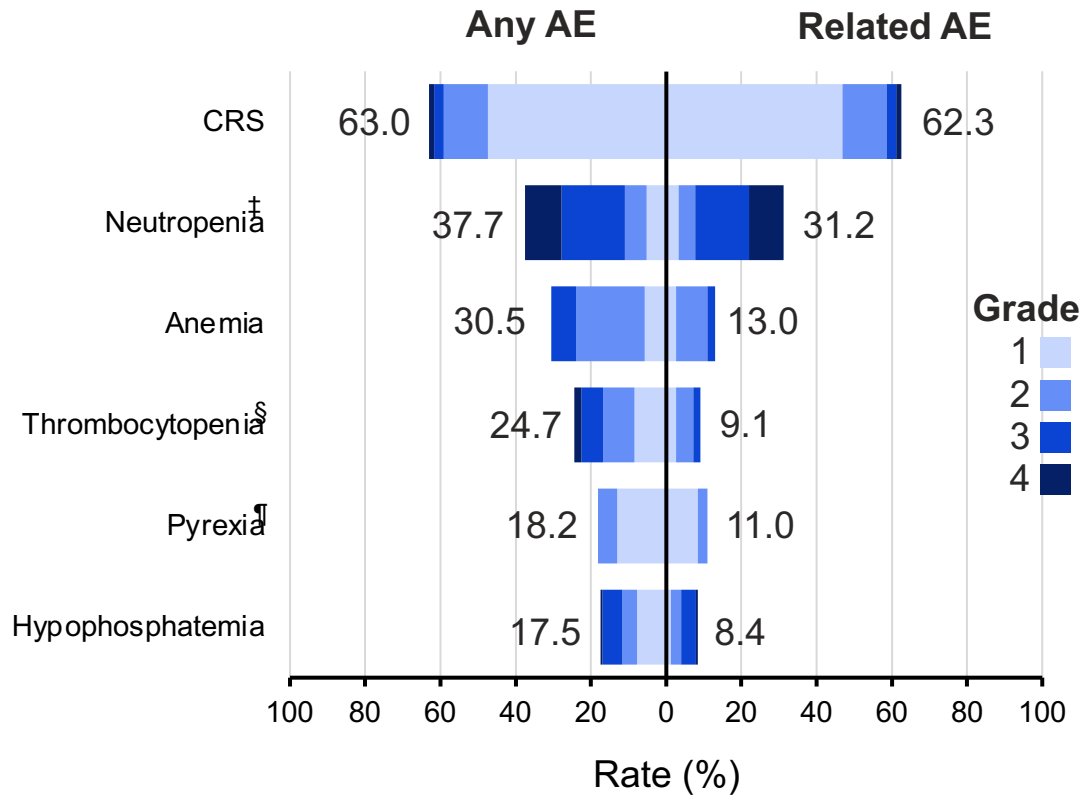
Median DOR 18.4 m (13.7,NE)

Dickinson M et al. ASCO 2022;Abstract 7500.

Glofitamab safety profile

n (%)*	N=154
Median no. of cycles received (range)	5 (1–13)
Median relative dose intensity, % (range)	100 (94–100)
AE	152 (98.7)
Related AE	140 (90.9)
Grade 3–4 AE	87 (56.5)
Related AE	64 (41.6)
Serious AE	73 (47.4)
Related AE	46 (29.9)
Grade 5 (fatal AE)	8 (5.2)†
Related AE	0
AE leading to treatment discontinuation	14 (9.1)
Related AE	5 (3.2)

AEs (≥15%) by grade and relationship with glofitamab



Dickinson M et al. ASCO 2022;Abstract 7500.

Pivotal Phase 2 Trial of Subcutaneous Epcoritamab in R/R LBCL

Dose escalation

Dose expansion data cutoff: January 31, 2022
Median follow-up: 10.7 mo

B-NHL:

- ✓ No DLTs
- ✓ MTD not reached
- ✓ RP2D identified
- ✓ Manageable safety profile
- ✓ Encouraging antitumor activity

Key inclusion criteria:

- R/R CD20+ mature B-cell neoplasm
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- FDG PET–avid and measurable disease by CT/MRI
- Prior CAR T allowed

Step-up dosing[a]

Epcoritamab SC RP2D 48 mg
QW C1–3,
Q2W C4–9,
Q4W C10+

→

Treatment until PD[b,c] or unacceptable toxicity

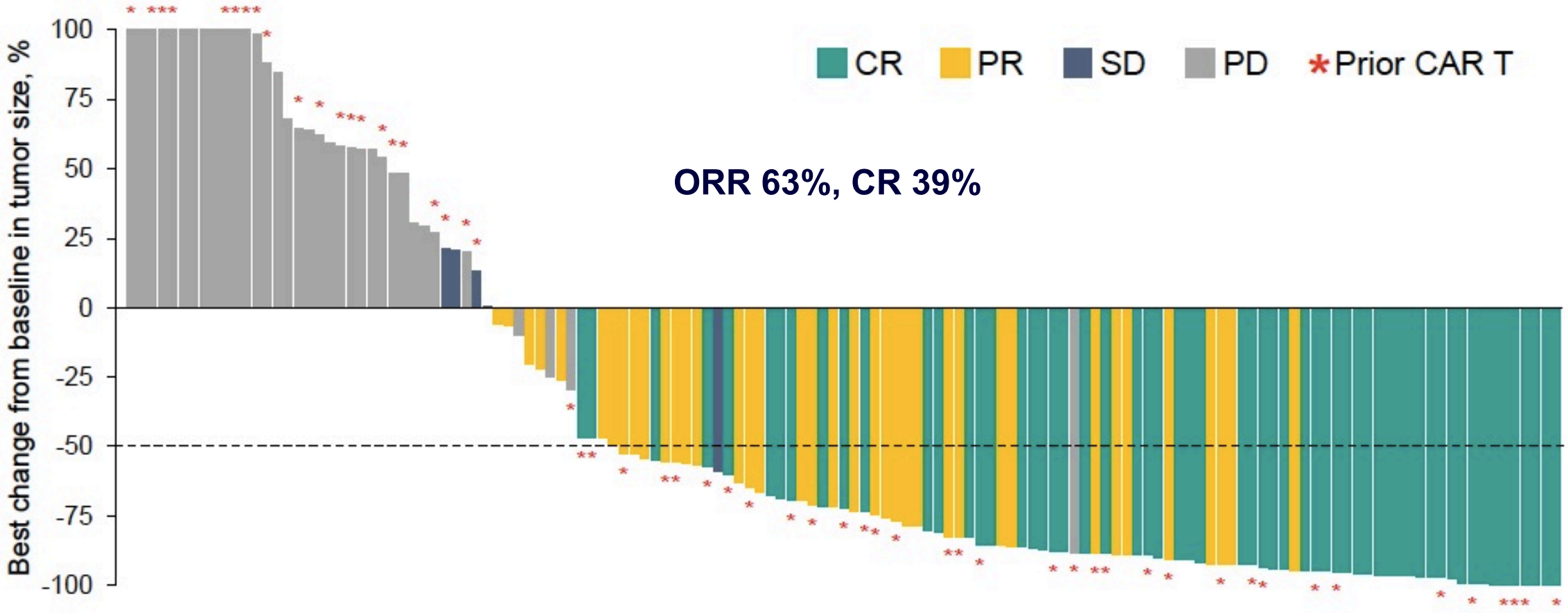
→

LBCL Cohort N=157
DLBCL, HGBCL, PMBCL, and FL Gr3B

- To ensure patient safety and better characterize CRS, inpatient monitoring was required at first full dose for 24 h in this part of the study
- **Primary endpoint:** ORR by independent review committee (IRC)
- **Key secondary endpoints:** DOR, TTR, PFS, OS, CR rate, and safety/tolerability

Thieblemont C et al. EHA 2022;Abstract LB2364.

Epcoritamab Induced Deep Responses in R/R LBCL

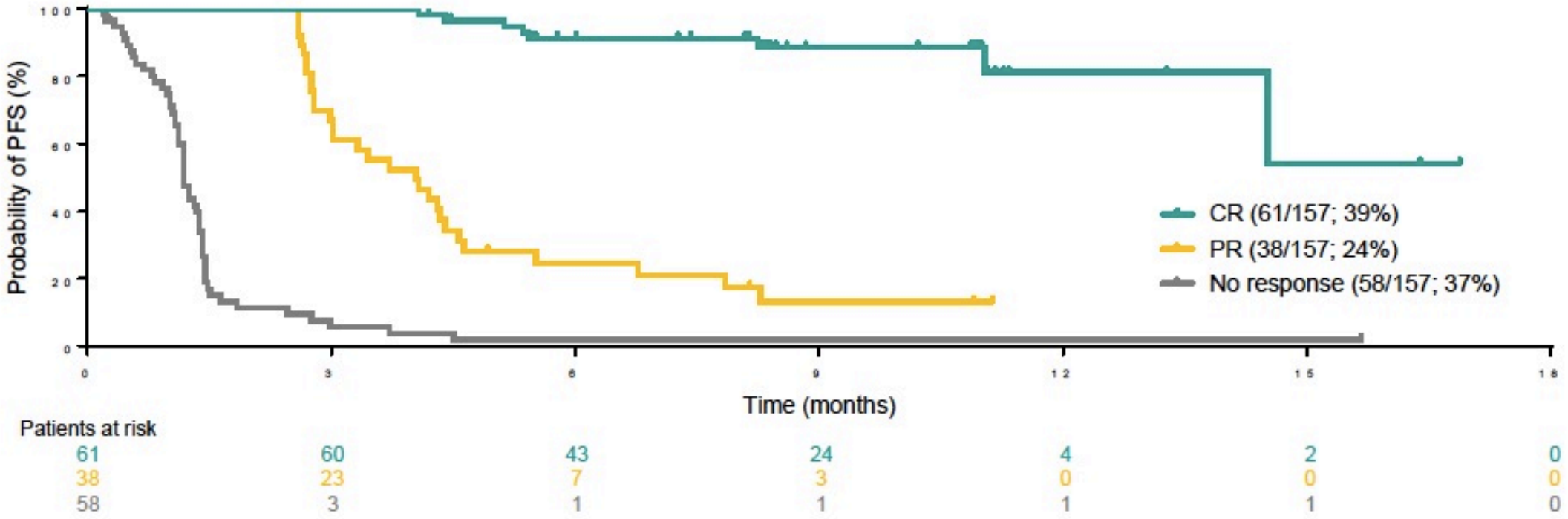


ORR 63%, CR 39%

Based on IRC assessment and Lugano criteria.

Thieblemont C et al. EHA 2022;Abstract LB2364.

PFS by Best Response per IRC



Kaplan–Meier Estimate	
Median PFS for complete responders	**Not reached**
Complete responders remaining in complete response at 9 mo	**89%**
Median PFS, mo (95% CI)	4.4 (3.0–7.9)
PFS at 6 mo, % (95% CI)	43.9 (35.7–51.7)

A correlation between depth of response and PFS was observed

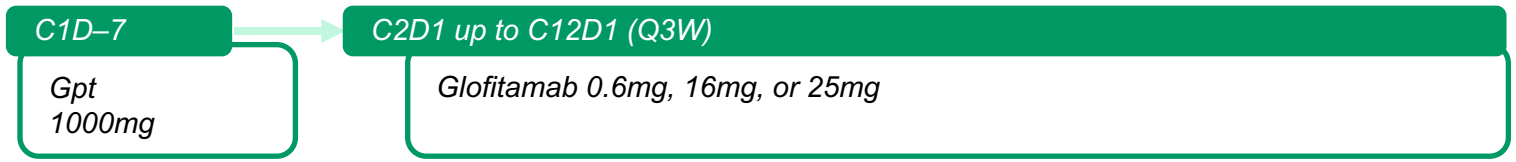
Thieblemont C et al. EHA 2022;Abstract LB2364.

Glofitamab in R/R Mantle Cell Lymphoma

Dose escalation (Phase I)

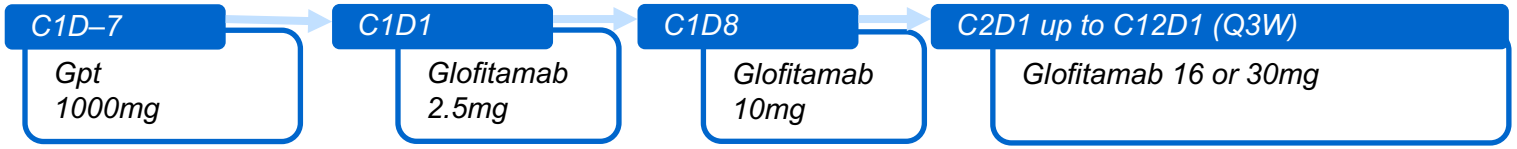
Glofitamab fixed dosing

Gpt 1000mg
Glofitamab
0.6, 16 or 25mg*:
n=3

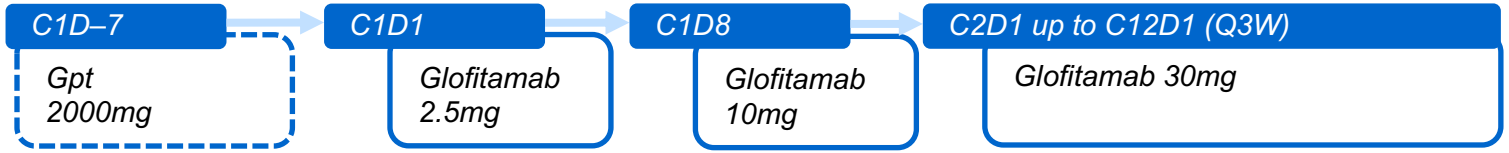


Glofitamab SUD

Gpt 1000mg
Glofitamab
2.5/10/16mg or
2.5/10/30mg†: n=7



Gpt 2000mg
Glofitamab
2.5/10/30mg: n=19



Population characteristics:

- *Age ≥18 years*
- *≥1 prior systemic therapy*
- *ECOG PS ≤1*

Phillips T et al. ASH 2021;Abstract 130.

Baseline characteristics

n (%) of patients unless stated		Glofitamab fixed dosing + 1000mg Gpt (n=3)	Glofitamab SUD + 1000mg Gpt (n=7)	Glofitamab SUD + 2000mg Gpt (n=19)	All patients (N=29*)
Median age, years (range)		81.0 (66–84)	69.0 (64–75)	66.0 (41–84)	69.0 (41–84)
Male		2 (66.7)	6 (85.7)	12 (63.2)	20 (69.0)
Ann Arbor stage III–IV at study entry		2 (66.7)	6 (85.7)	16 (84.2)	24 (82.8)
MCL IPI score ≥6 at study entry		3 (100)	3 (42.9)	12 (63.2)	18 (62.1)
Prior therapy	Median time since last therapy, months (range)	1.1 (1.0–8.5)	3.4 (1.2–53.2)	1.6 (0.1–107.5)	1.7 (0.1–107.5)
	Prior lines of therapy, median (range)	3 (2–5)	4 (3–5)	3 (1–6)	3 (1–6)
	BTKi	3 (100)	6 (85.7)	11 (57.9)	20 (69.0)
	Lenalidomide	0	1 (14.3)	3 (15.8)	4 (13.8)
	Chemotherapy	3 (100)	7 (100)	18 (94.7)	28 (96.6)
	Alkylator	0	6 (85.7)	7 (36.8)	13 (44.8)
	Anti-CD20 monoclonal antibody	3 (100)	6 (85.7)	14 (73.7)	23 (79.3)
Refractory status	Refractory to any prior therapy	3 (100)	7 (100)	16 (84.2)	26 (89.7)
	Refractory to prior anti-CD20 therapy	2 (66.7)	3 (42.9)	10 (52.6)	15 (51.7)
	Refractory to first-line therapy	2 (66.7)	2 (28.6)	11 (57.9)	15 (51.7)
	Refractory to last prior therapy	2 (66.7)	5 (71.4)	13 (68.4)	20 (69.0)

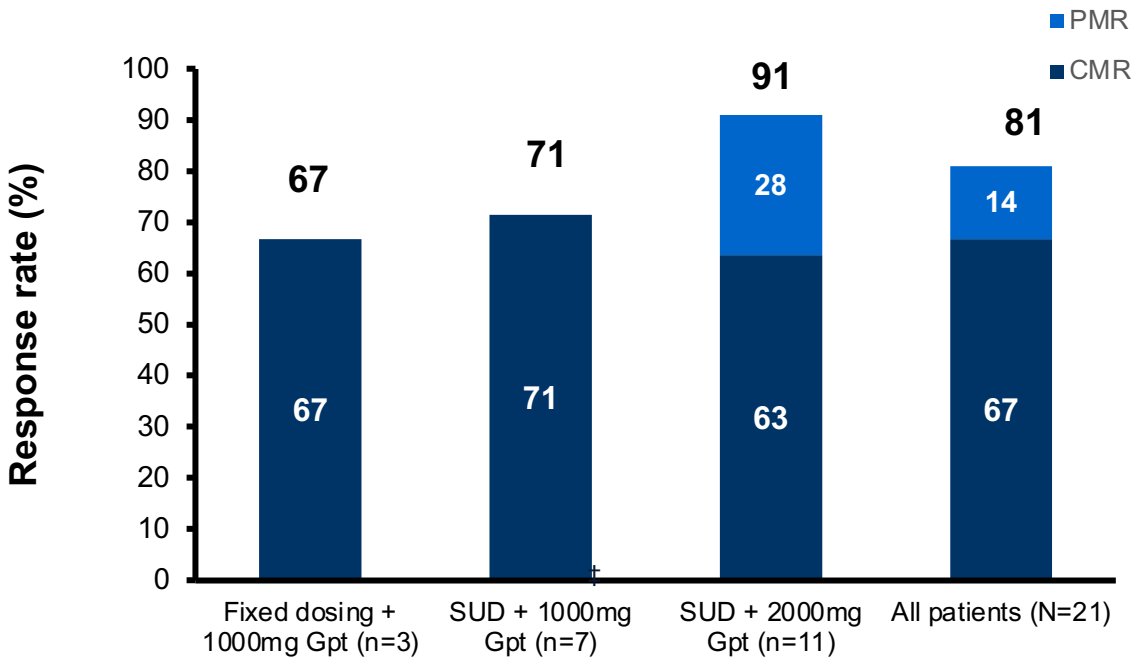
Most patients had received prior BTKi therapy

*Three patients were treated with glofitamab in combination with obinutuzumab (G-combo). IPI, International Prognostic Index.

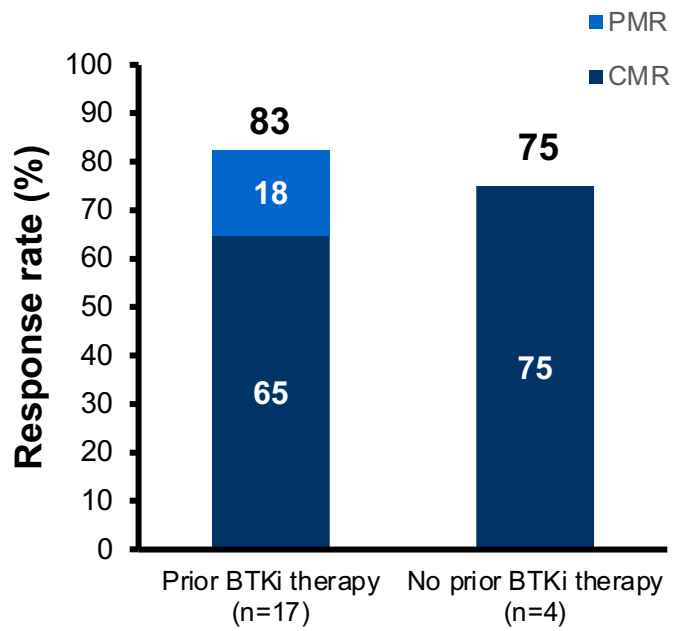
Phillips T et al. ASH 2021;Abstract 130.

Response rates

Response rates[1] by glofitamab regimen*



Response rates[1] by prior BTKi therapy*



Glofitamab resulted in high response rates in patients with R/R MCL

Median follow-up short, but long-term responses >24 months observed

7523

First-line treatment (Tx) with subcutaneous (SC) epcoritamab (epco) + R-CHOP in patients (pts) with high-risk diffuse large B-cell lymphoma (DLBCL): phase 1/2 data update

Lorenzo Falchi, MD,[1]* Fritz Offner, MD, PhD,[2] David Belada, MD, PhD,[3] Joshua Brody, MD,[4] Kim M. Linton, MBChB, PhD,[5] Yasmin Karimi, MD,[6] Raul Cordoba, MD, PhD,[7] Sylvia Snauwaert, MD, PhD,[8] Aqeel Abbas, MS,[9] Liwei Wang, PhD,[9] Jun Wu, MD, MS,[10] Brian Elliott, MD,[9] Michael Roost Clausen, MD, PhD[11]

[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Universitair Ziekenhuis Gent, Ghent, Belgium; [3]4th Department of Internal Medicine – Hematology, University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic; [4]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [5]The Christie NHS Foundation Trust and Manchester Cancer Research Centre, Manchester, UK; [6]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI, USA; [7]Fundacion Jimenez Diaz University Hospital, Health Research Institute IIS-FJD, Madrid, Spain; [8]Department of Hematology, AZ Sint-Jan Hospital, Bruges, Belgium; [9]Genmab, Princeton, NJ, USA; [10]AbbVie, North Chicago, IL, USA; [11]Vejle Hospital, Vejle, Denmark

*Email address for questions: falchil@mskcc.org

Objectives

- The EPCORE NHL-2 trial (phase 1/2; NCT04663347) is evaluating epcoritamab combined with different standard of care therapies in patients with B-cell NHL
- To present data from arm 1, which is investigating epcoritamab + R-CHOP in patients with previously untreated high-risk DLBCL

Conclusions

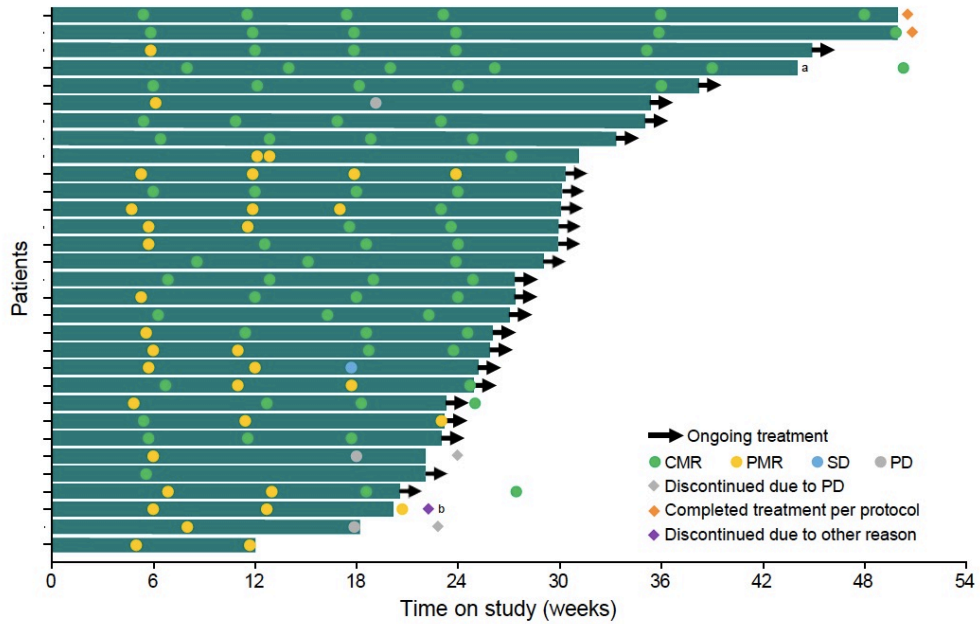
- Epcoritamab + R-CHOP showed encouraging responses:
  - ORR 100%, CMR 77%
- Epcoritamab + R-CHOP has a manageable safety profile; no new safety signals were detected
  - CRS was predictable and generally low grade
  - All CRS events resolved
- These updated data support further exploration of epcoritamab + R-CHOP in first-line DLBCL

Best Overall Responses

Response, n (%)[a]	Total n=31
Overall response	31 (100)
CMR	24 (77)
PMR	7 (23)
Stable disease	0
Progressive disease	0

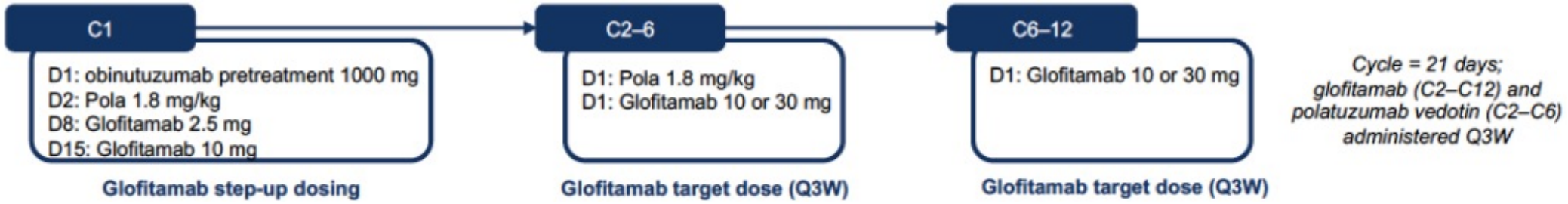
Data cutoff: March 25, 2022. [a]Based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and ≥1 postbaseline response evaluation and patients who died within 60 d of first dose.

Response Profile



Falchi L et al. ASCO 2022;Abstract 7523.

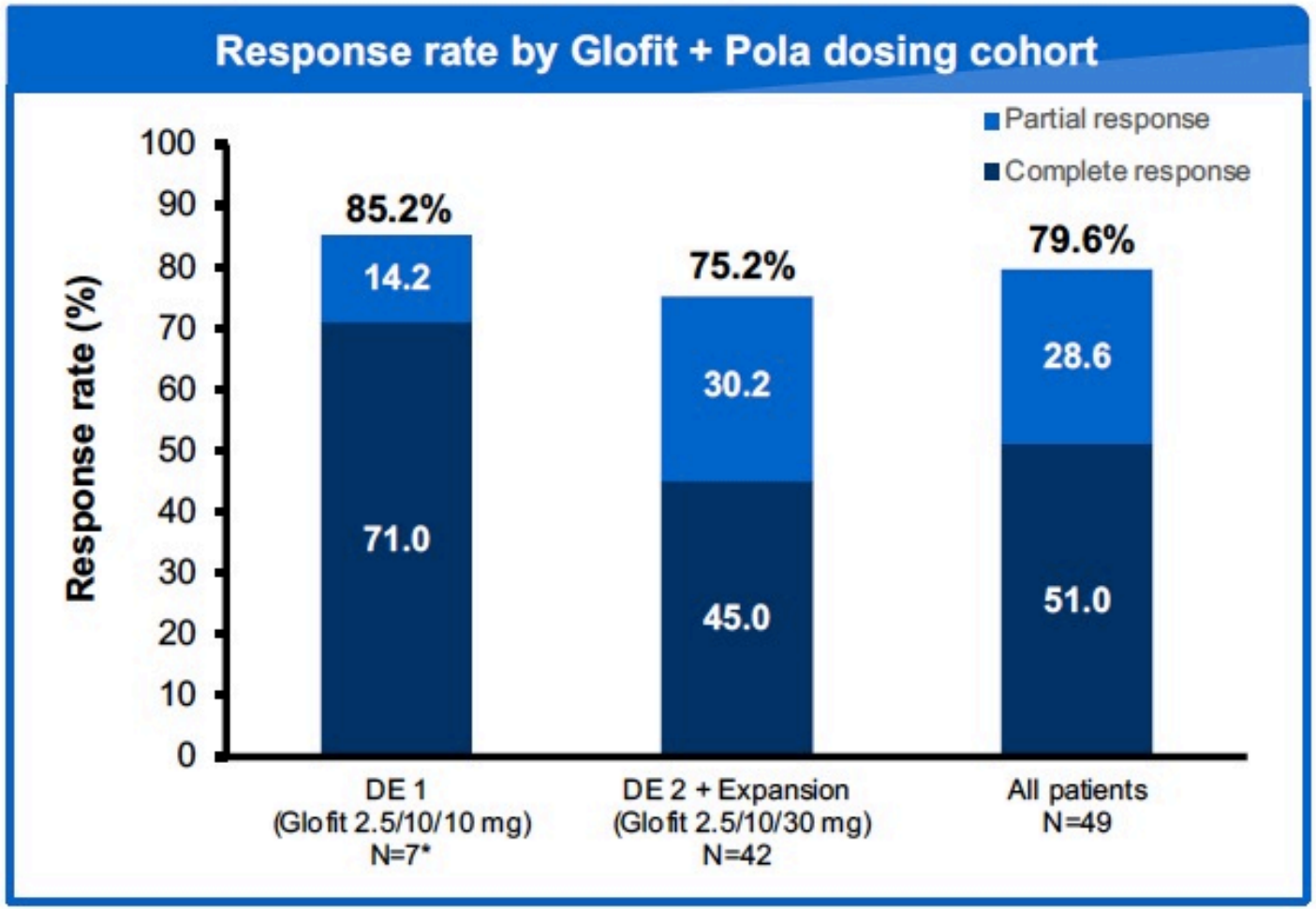
Glofitamab Plus Polatuzumab Vedotin in R/R DLBCL



N (%) of patients unless stated		DE 1 (2.5/10/10 mg) N=6	DE 2/Expansion (2.5/10/30 mg) N=53	All patients N=59
Median age, years (range)		65.5 (55–76)	63.8 (29–82)	59.0 (29–82)
Male gender		3 (50.0)	33 (62.2)	36 (61.0)
ECOG PS 0–1		6 (100.0)	49 (92.4)	55 (94.9)
Ann Arbor Stage III–IV at study entry		4 (66.7)	42 (79.2)	46(78.0)
NHL histology	DLBCL	5 (83.3)	31 (58.4)	36 (61.0)
	HGBCL	0	9 (16.9)	9 (15.3)
	trFL	1 (16.7)	13 (24.5)	14 (23.7)
Median prior lines of therapy, n (range)		3 (1–4)	2 (1–5)	2 (1–5)
Refractory status	Any prior therapy	3 (50.0)	45 (84.9)	48 (81.0)
	Most recent therapy line	3 (50.0)	38 (71.6)	41 (69.5)
	Any prior anti-CD20	3 (50.0)	42 (79.2)	45 (76.3)

Hutchings M et al. ASH 2021;Abstract 525.

Glofitamab Plus Pola in R/R DLBCL: Response Rates



- **49/59 patients were evaluable for interim response**
- **7/49 (14.3%) patients had PD as best response and discontinued study treatment**
- **Encouraging ORR and CR rates in patients with:**
  - trFL: ORR, 8/11 and CR, 7/11
  - HGBCL: ORR, 5/8 and CR, 4/8

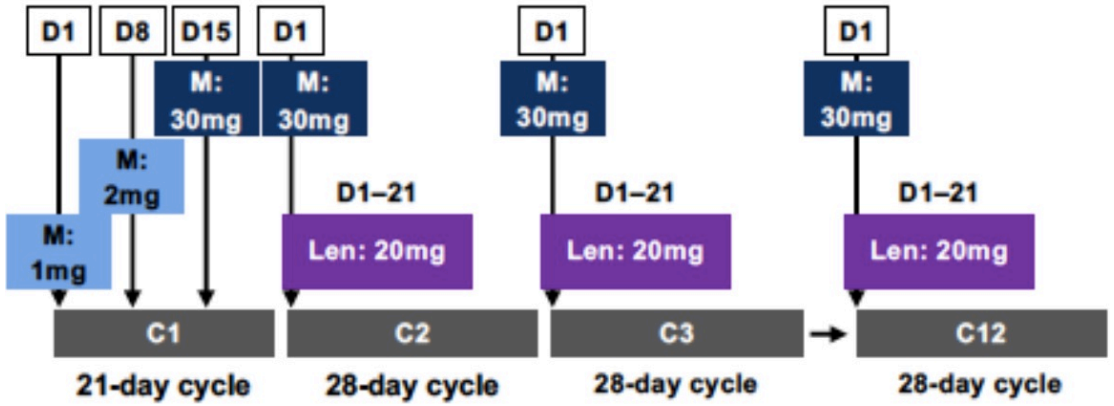
- **Glofit + Pola combination resulted in high response rates**

Hutchings M et al. ASH 2021;Abstract 525.

Mosunetuzumab + Lenalidomide in R/R FL

Key inclusion criteria

- CD20+ FL Grade 1–3a
- R/R to ≥1 prior chemo-immunotherapy regimen including an aCD20 antibody; prior lenalidomide allowed
- ECOG PS 0–2

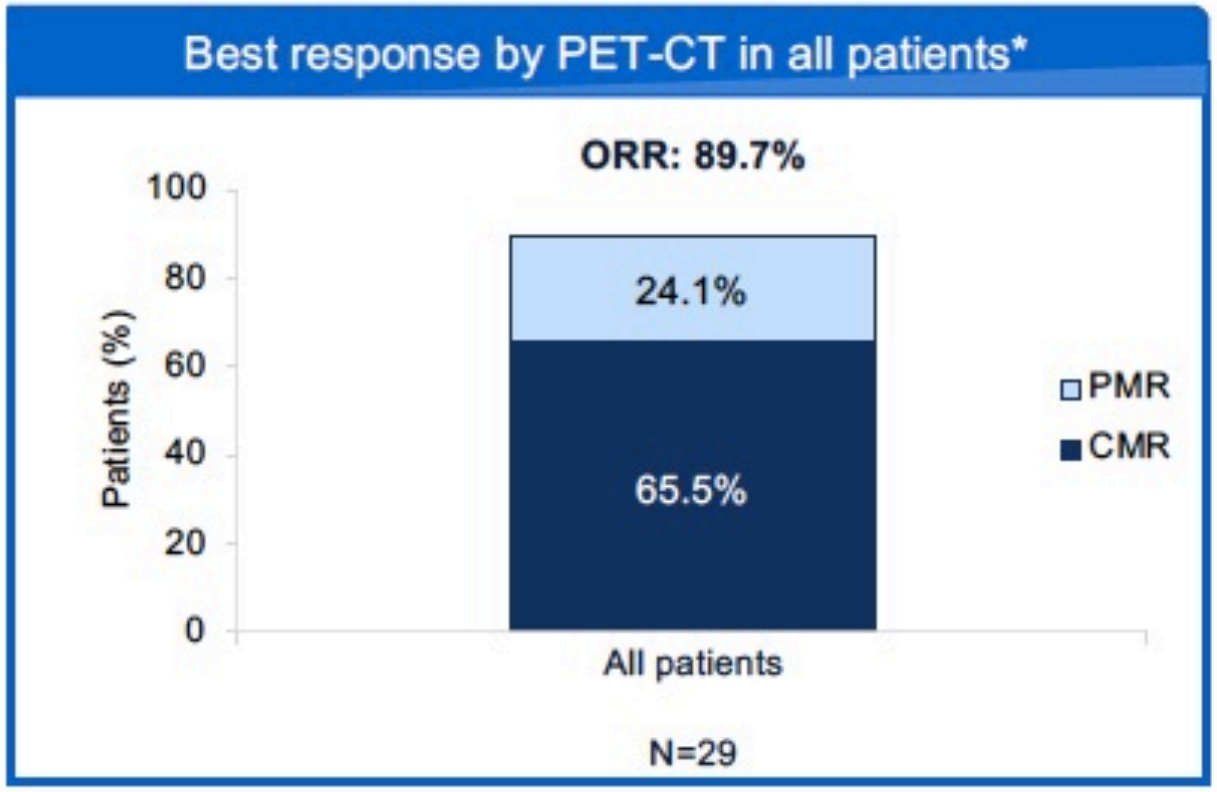


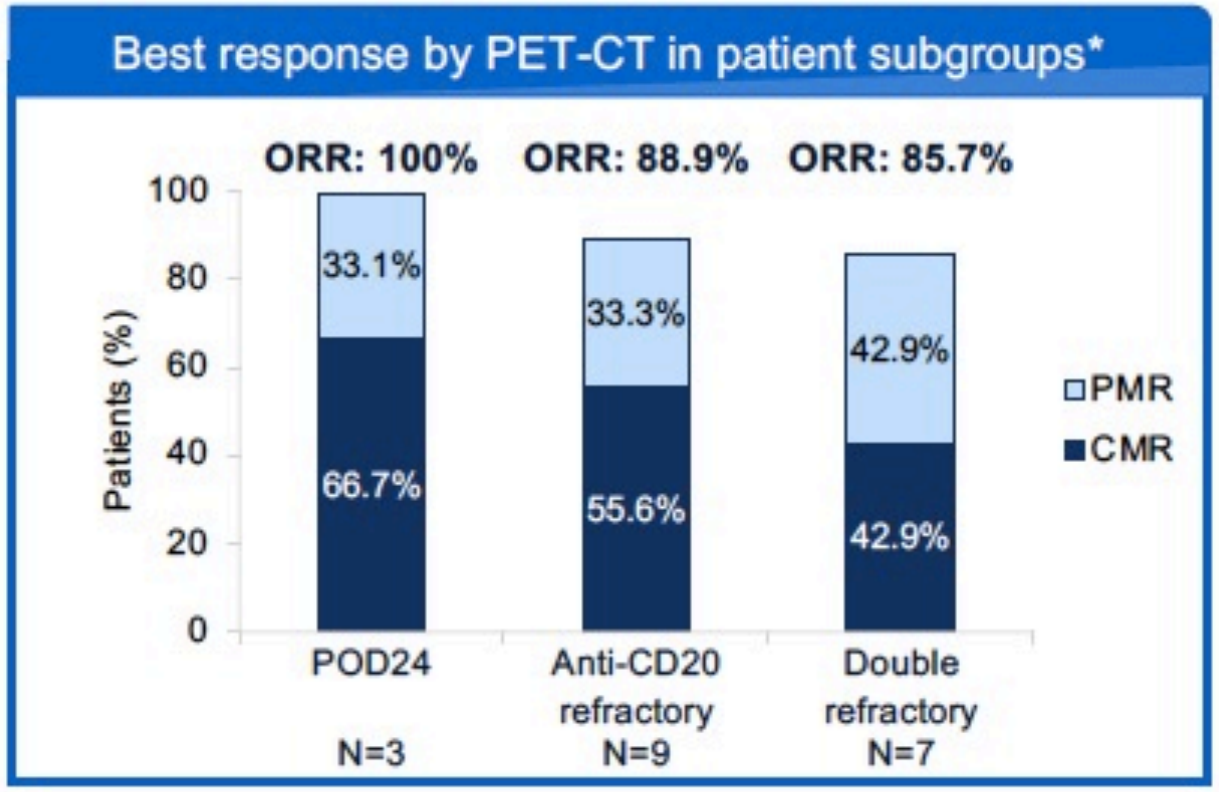
	N=29
Age in years, median (range)	59 (30–79)
Male	13 (44.8%)
Ann Arbor stage at study entry	
I–II	2 (6.8%)
III–IV	27 (93.1%)
FLIPI risk factors at study entry	
0–1	7 (24.1%)
2	8 (27.6%)
3–5	14 (48.3%)
Number of prior lines of therapy, median (range)	1 (1–6)
1 prior line	16 (55.2%)
≥2 prior lines	13 (44.8%)
Refractory to any prior aCD20 therapy	9 (31.0%)
Refractory to any prior aCD20 therapy AND an alkylating agent (double refractory)	7 (24.1%)
POD24	3 (10.3%)

Morschhauser F et al. ASH 2021;Abstract 129.

Mosunetuzumab + Lenalidomide in R/R FL

- Median time to first / best response: 2.5 mo (range: 1.4–5.3) / 2.5 mo (range: 1.4–10.7)





- **High ORR and CMR rate in overall population and in patients with high-risk disease**

Median duration follow-up: 5.4 m

Morschhauser F et al. ASH 2021;Abstract 129.

Agenda

PART 1: Case Presentations and Clinical Decision-Making

- Non-Hodgkin Lymphoma
- Multiple Myeloma

PART 2: Faculty Presentations

- CAR-T in Non-Hodgkin Lymphoma — Dr Flinn
- Bispecifics in Non-Hodgkin Lymphoma — Dr Sehn
- CAR-T in Multiple Myeloma — Dr Munshi
- Bispecifics in Multiple Myeloma— Dr Chari

Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL

Optimal Integration of BCMA-Directed CAR T-Cell Therapy into the Care of Patients with Multiple Myeloma (MM)

Nikhil C. Munshi, MD

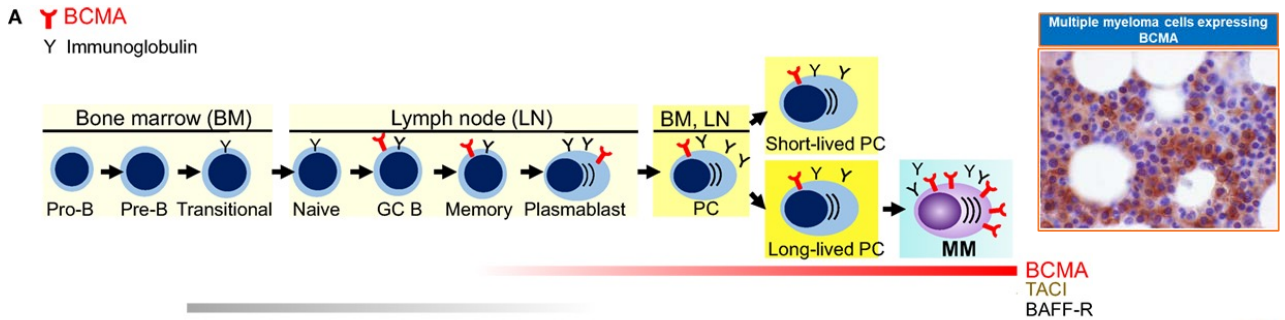
Professor of Medicine
Harvard Medical School

Kraft Family Chair
Director, Basic and Correlative Science
Jerome Lipper Myeloma Center
Dana-Farber Cancer Institute
Boston VA Healthcare System

February 2021 | NP-WWM-IDE-0067

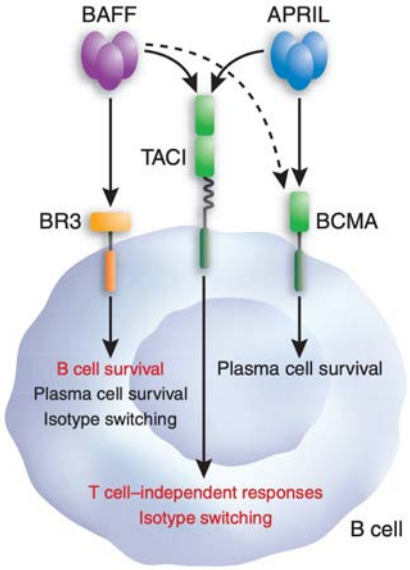
BCMA Is a Selective Plasma Cell Antigen

1

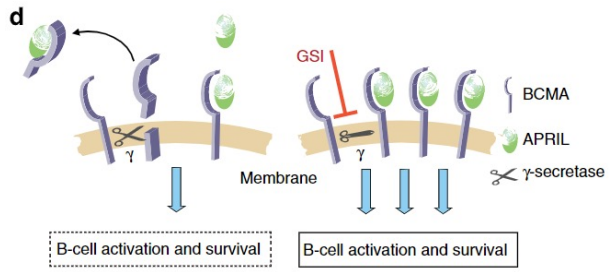


- BCMA expression support survival of long-lived PCs, Ig Class switch and Ab Production

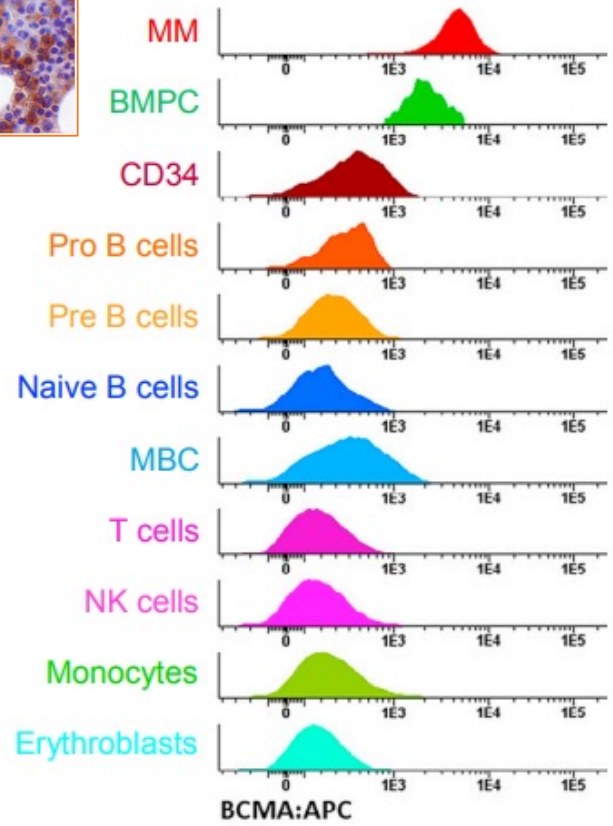
2



3



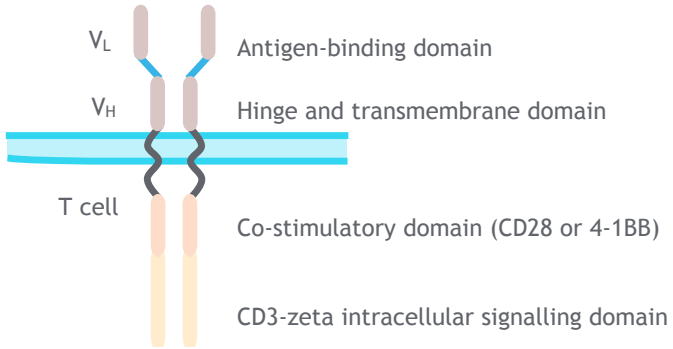
Gamma Secretase Inhibitor JSMD194 (NCT03502577)

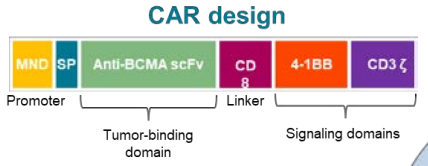


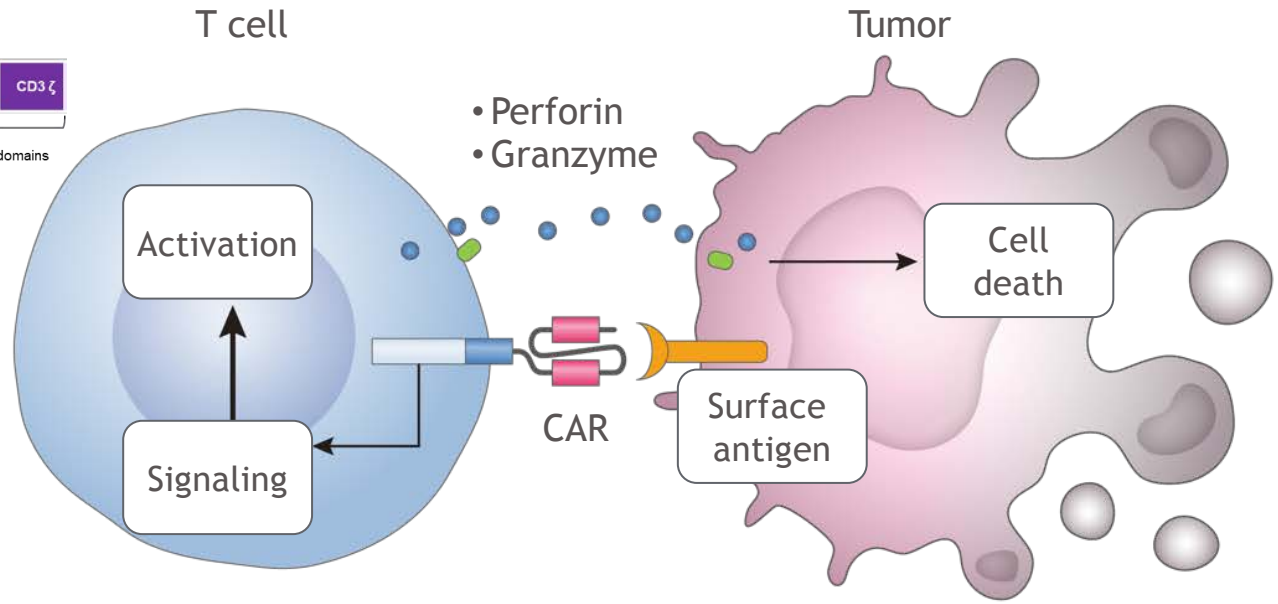
- Promotes proliferation, Survival, associated with immunosuppressive BM microenvironment.
- Expressed nearly universally on MM cells

1.Cho SF et al. Front Immunol 2018;10:1821. 2. Martin F and Dixit VM Nat Genetics 2005.
4. Laurent et al Nat Commun. 2015 Jun 11;6:7333. 5. Seckinger Cancer Cell 2017; 31:396.

Chimeric antigen receptor T cells (CAR T cells) enhance the ability of the immune system to target tumor cells[1]





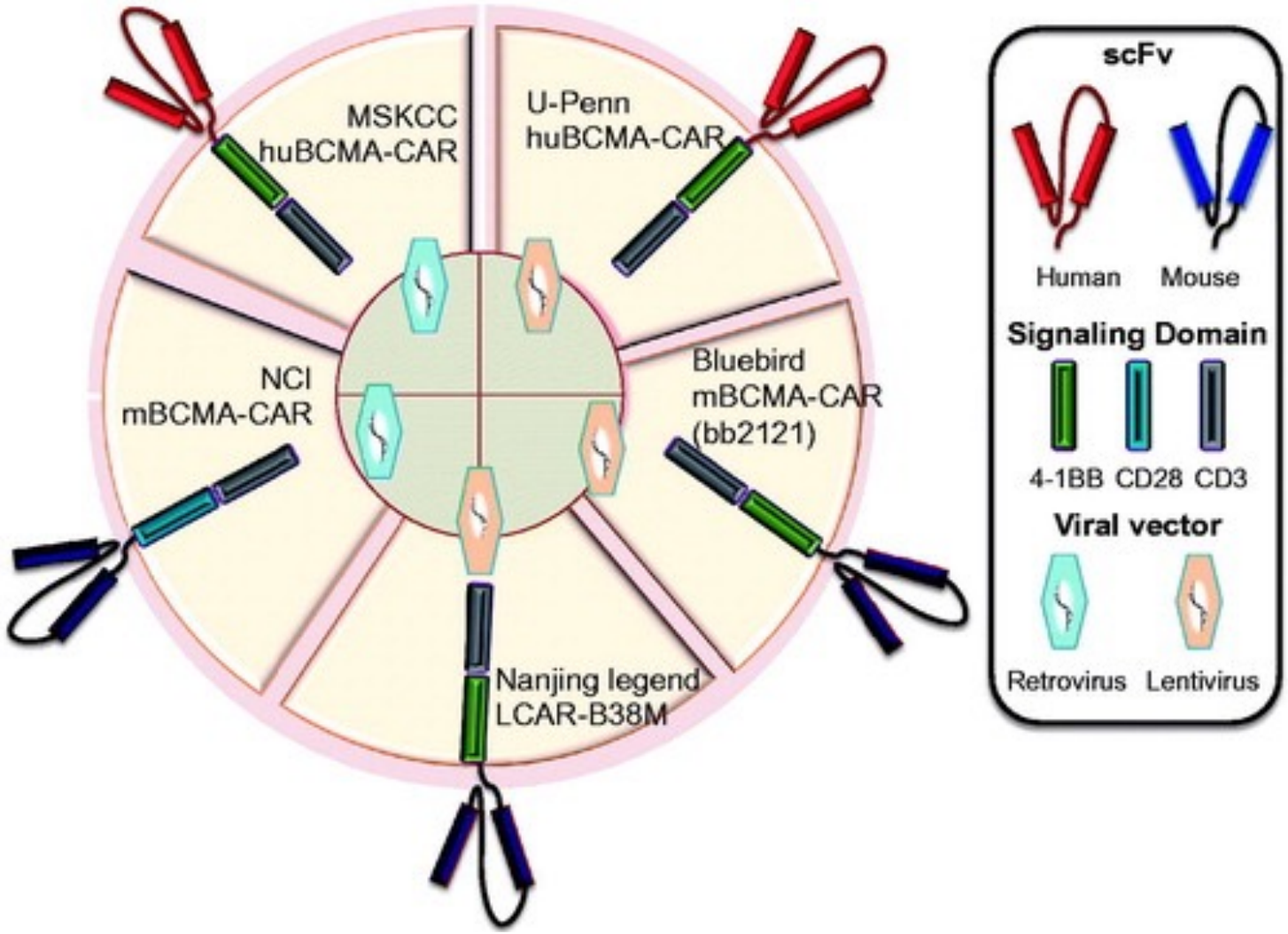


- Exploit **native antibody or T cell recognition** and signaling pathways[1]
- Introduction of unique genes through **viral vectors** to allow recognition of tumor cells[1]
- Dramatic expansion after infusion, and effective tumor cell killing[1,2]

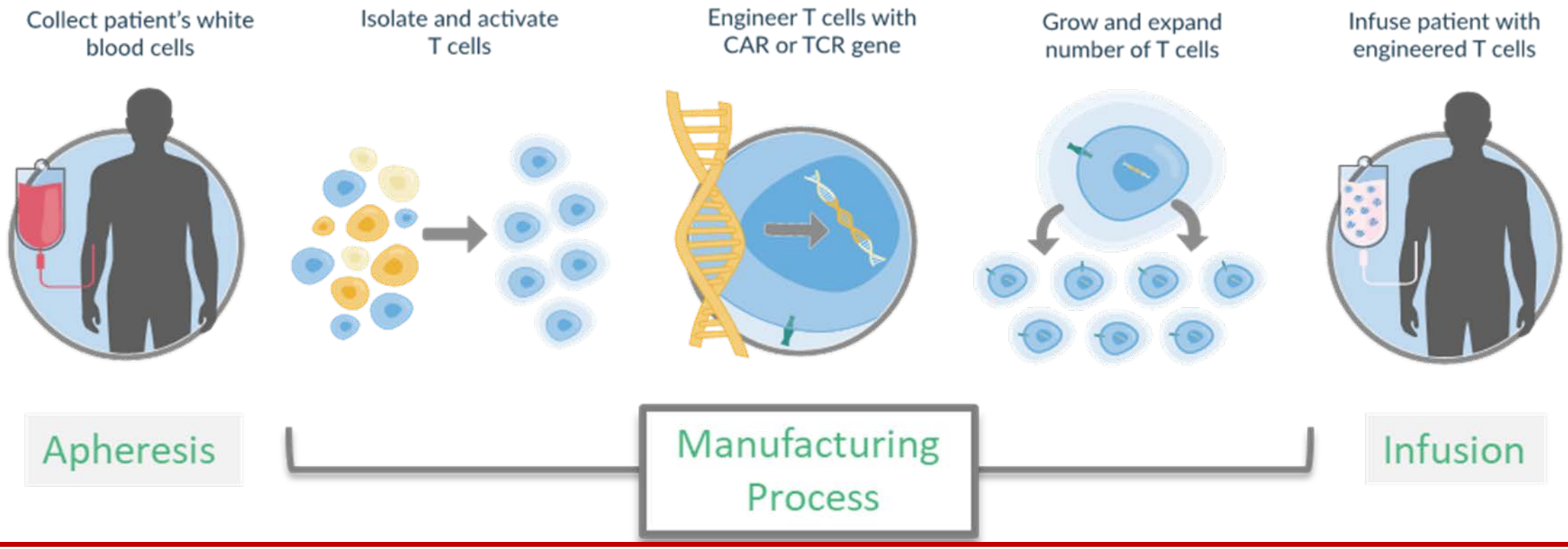
In MM, several BCMA-targeting CAR T cell therapies are in development.

Images extracted from Shinshu University. Available from: www.Shinshu-u.ac.jp/english/topics/research/shinshu_university_a_1.html. Accessed February 2021.
CAR, chimeric antigen receptor.
1. Benmebarek M, et al. Int J Mol Sci. 2019; 20;1283. 2. Munshi NC, et al. Slides presented at ASCO Annual Meeting; May 29-31, 2020; abstract 8503. 3. Madduri D, et al. 62nd ASH Annual Meeting 2020, Presentation #177. 4. NCT03288494. Available from: https://clinicaltrials.gov/ct2/show/NCT03288493. Accessed February 2021. 5. NCT04093596. Available from: https://clinicaltrials.gov/ct2/show/NCT04093596. Accessed February 2021.

BCMA CAR T Studies



ENGINEERED AUTOLOGOUS CELL THERAPY



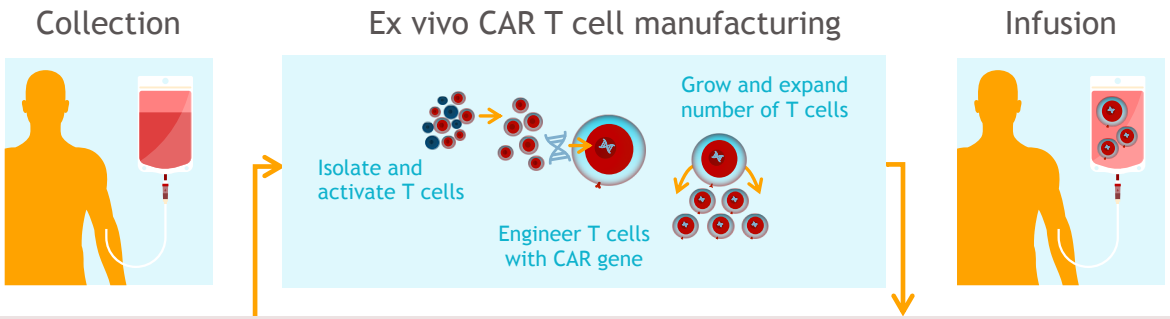
ORIGINAL ARTICLE FREE PREVIEW

The NEW ENGLAND JOURNAL of MEDICINE

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., et al.

Overview of the CAR T cell administration process[1,2]



Identify patients eligible for CAR T cell therapy

Evaluation and selection of the patient in the CAR T cell therapy center

Apheresis and transport of cells to CAR T cell manufacturing site

Bridging therapy (post-apheresis, and typically stopped 2 weeks prior to infusion)[2]

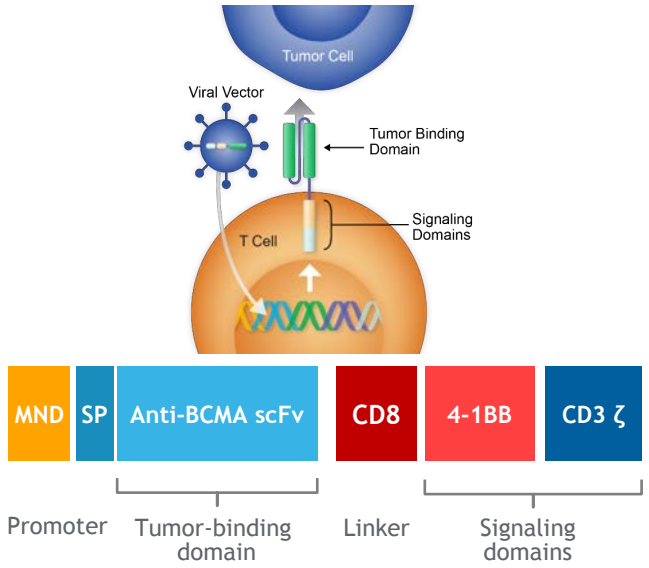
Lymphodepletion therapy (3 consecutive injections 3-5 days before CAR T cell infusion[a])[3,4]

Infusion and monitoring (infusion to Day 28)[3]

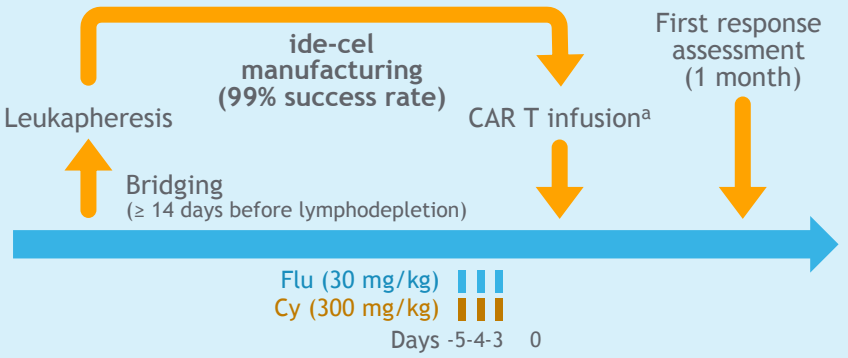
Monitoring medium-term (Day 28-100)[3] and long-term (> Day 100)[3] complications

Image extracted from: Dana-Farber Cancer Institute, How CAR T cell therapy works. Available from: https://www.dana-farber.org/cellular-therapies-program/car-t-cell-therapy/how-car-t-cell-therapy-works/. Accessed February 2020.
Flowchart extracted from: Moran D. The potential of CAR T-cell therapy and the myeloma patient journey. Myeloma Today. Available from: https://indd.adobe.com/view/07583bc3-3af4-4a8d-a142-47cb2c8a6402. Accessed February 2021.
[a]Typically fludarabine/cyclophosphamide.
CAR, chimeric antigen receptor.
1. Moran D. The potential of CAR T-cell therapy and the myeloma patient journey. Myeloma Today. Available from: https://indd.adobe.com/view/07583bc3-3af4-4a8d-a142-47cb2c8a6402. Accessed February 2021.
2. Protocol for: Raje N. N Engl J Med 2019;380:1726-37. 3. Yakoub-Agha I, et al. Haematologica 2020;105:297-316. 4. Turtle CJ, et al. Sci Transl Med. 2016;8:355ra116.

Phase 2 KarMMa Study: Ide-cel in Relapsed Refractory Multiple Myeloma



- RRMM
- ≥ 3 prior regimens
- Previously exposed to:
  - IMiD® agent
  - Proteasome inhibitor
  - Anti-CD38 Ab
- Refractory to last prior therapy per IMWG[b]



Study status as of 14 January 2020

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 (months)

150 × 10^6	18.0
300 × 10^6	15.8
450 × 10^6	12.4
Total	13.3

Endpoints[2,3]

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

Patient characteristics[2]

Time since initial diagnosis, median (range) in yrs		6 (1–18)
No. of prior antimyeloma regimens, median (range)		6 (3–16)
Prior autologous SCT, %	1	94
	> 1	34
Any bridging therapies for MM, %		88
Refractory status, %	Anti-CD38 Ab refractory	94
	Triple refractory	84

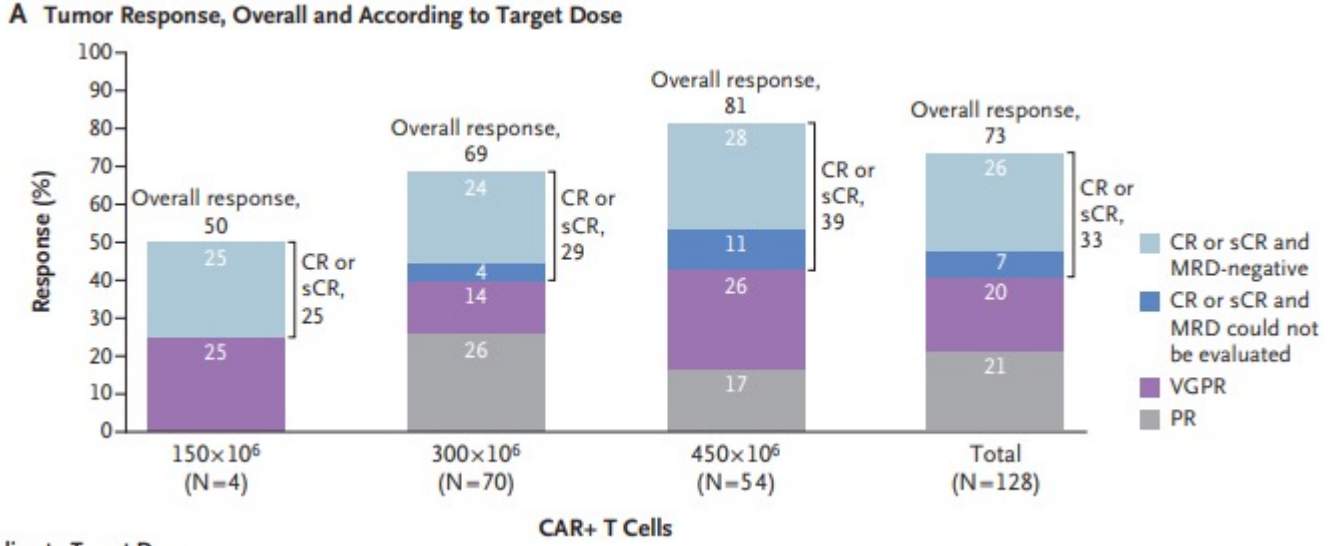
ORIGINAL ARTICLE FREE PREVIEW

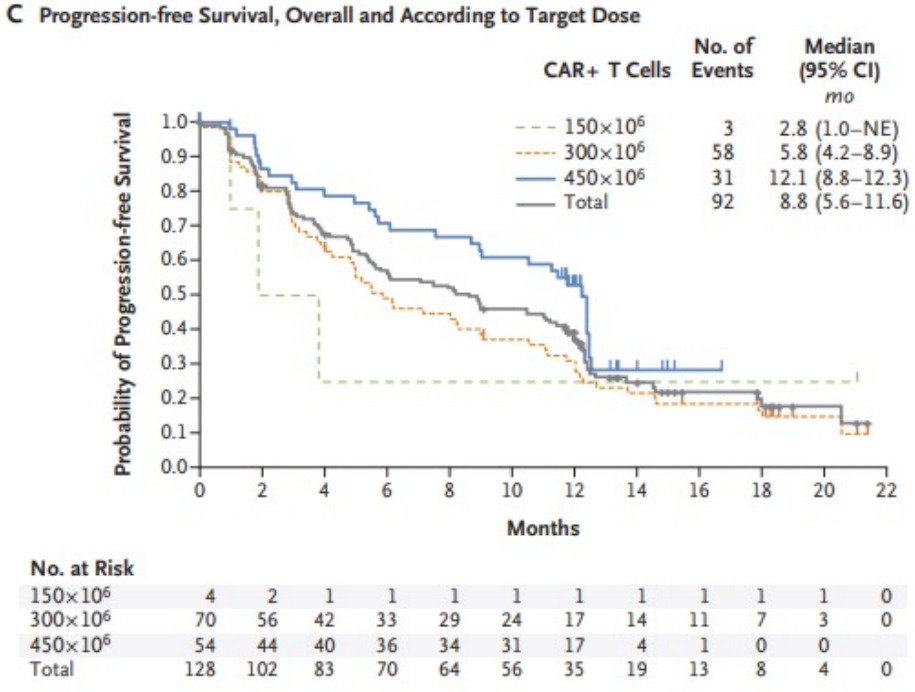
The NEW ENGLAND JOURNAL of MEDICINE

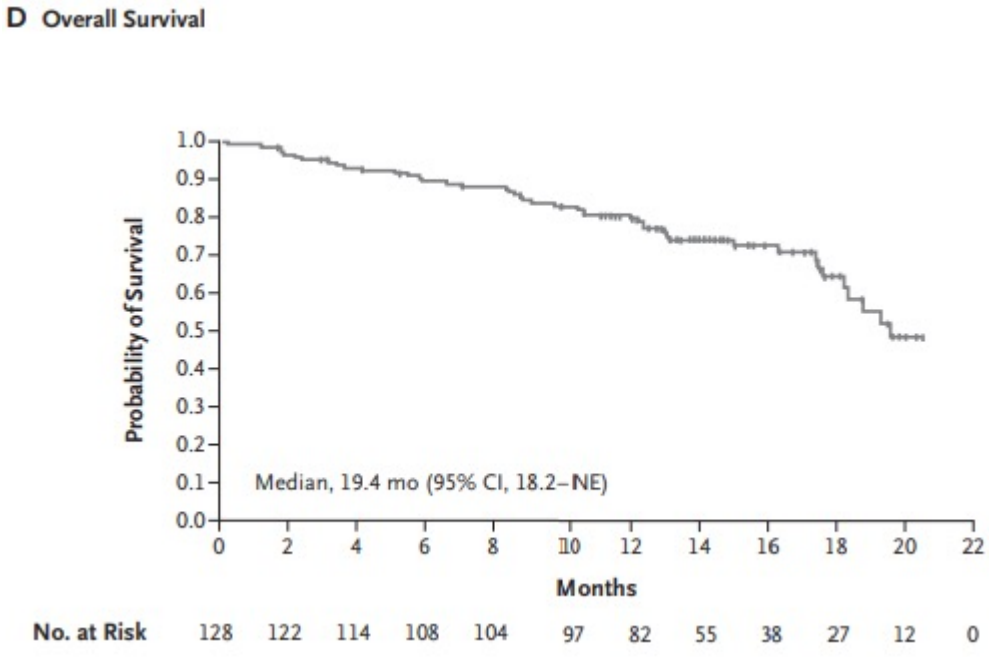
Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma

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., et al.

Ide-cel Delivers High Response Rate and PFS in Relapsed and Refractory Multiple Myeloma







Munshi et al. NEJM 2021 Feb 25;384(8):705-716

Phase 2 KarMMa Study: ASCO 2021 Results

Figure 4. Progression-free survival

PFS by number of prior lines of therapy and in all ide-cel treated patients

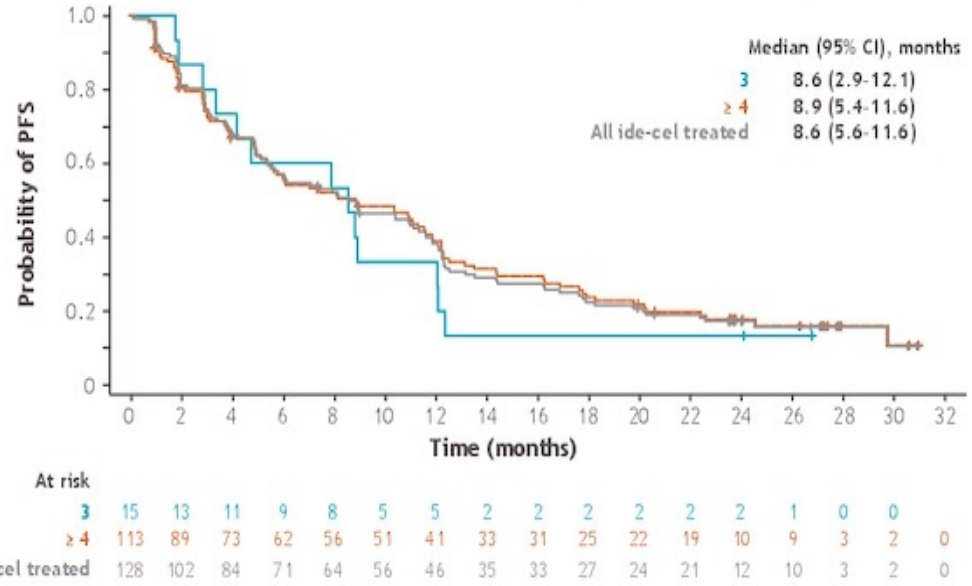
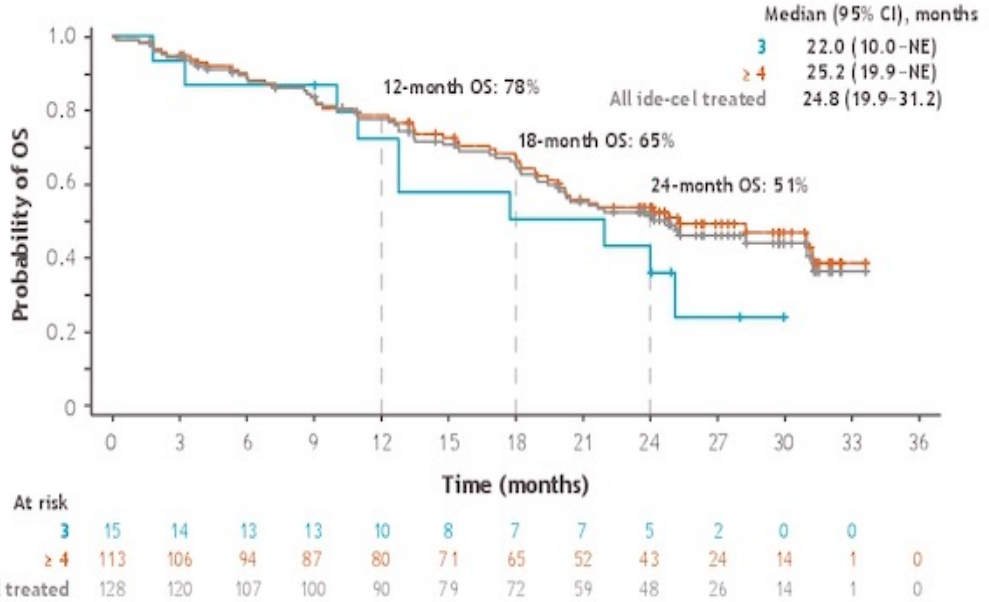


Figure 5. Overall survival

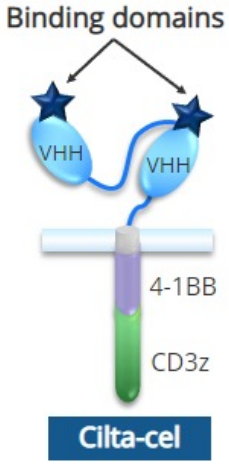
OS by number of prior lines of therapy and in all ide-cel treated patients



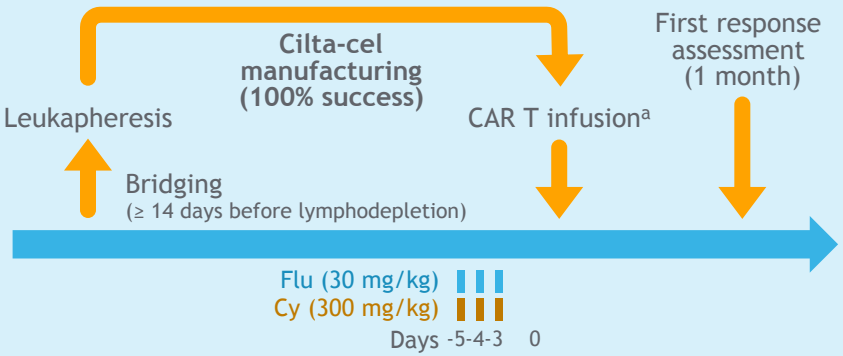
- Median PFS was 8.6 months among all ide-cel treated patients and was similar with 3 and ≥ 4 prior lines of therapy (**Figure 4**)
- Median OS was 24.8 months among all ide-cel treated patients; median OS was 22.0 months and 25.2 months in patients who received 3 and ≥ 4 prior lines of therapy, respectively (**Figure 5**)

Anderson LD et al. ASCO 2021;Abstract 8016.

Phase 1b/2 CARTITUDE-1: Cilta-cel in RRMM



- RRMM
- ≥ 3 prior regimens
- Previously exposed to:
  - IMiD® agent
  - Proteasome inhibitor
  - Anti-CD38 Ab
  - Measurable disease
- Progressive MM per IMWG criteria



18 month F/U

Screened N = 113

Leukapheresed N = 113

↓

Bridging N = 73

Cilta-cel infusion N = 97

↓

Median administered dose: 0.71×10^6 ($0.51–0.95 \times 10^6$) CAR+ viable T cells/kg

Endpoints

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

Patient characteristics[2]

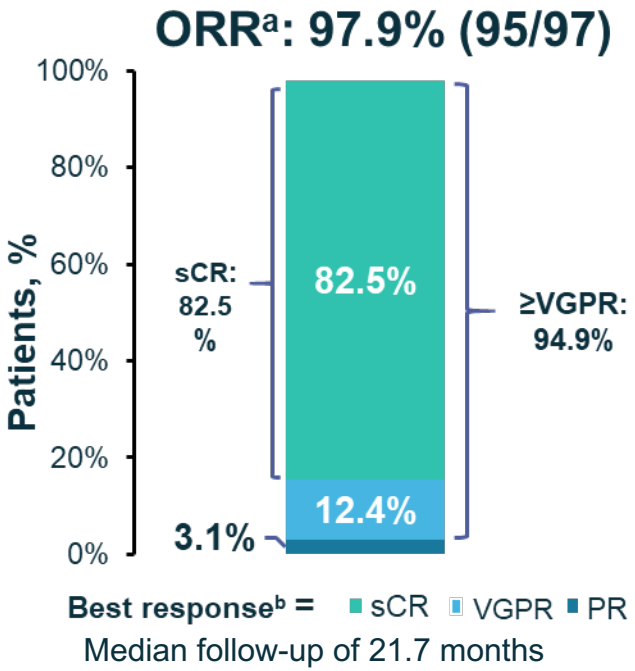
Years since diagnosis, median (range)		5.9 (1.6-18.2)
No. of prior antimyeloma regimens, median (range)		6 (3–18)
Prior autologous SCT, %	1 > 1	89.7 8.2
Any bridging therapies for MM, %		75%
Refractory status, %	Anti-CD38 Ab refractory Triple refractory	99 87.6

THE LANCET
Volume 398, Issue 10297, 24–30 July 2021, Pages 314-324

Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study

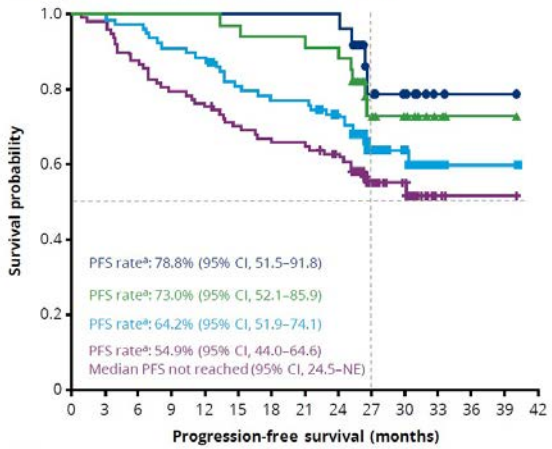
Jesus G Berdeja, Deepu Madduri*, Saad Z Usmani, Andrzej Jakubowiak, Mounzer Agha, Adam D Cohen, A Keith Stewart, Parameswaran Hari, Myo Htut, Alexander Lesokhin, Abhinav Deol, Nikhil C Munshi, Elizabeth O'Donnell, David Avigan, Indrajeet Singh, Enrique Zudaire, Tzu-Min Yeh, Alicia J Allred, Yunsi Olyslager, Arnob Banerjee, Carolyn C Jackson, Jenna D Goldberg, Jordan M Schecter, William Deraedt, Sen Hong Zhuang, Jeffrey Infante, Dong Geng, Xiaoling Wu, Marlene J Carrasco-Alfonso, Muhammad Akram, Farah Hossain, Syed Rizvi, Frank Fan, Yi Lin†, Thomas Martin†, Sundar Jagannath†*

Cilta-cel Achieves Deep Responses in RRMM



Median follow-up of 21.7 months

FIGURE 3: Progression-free survival

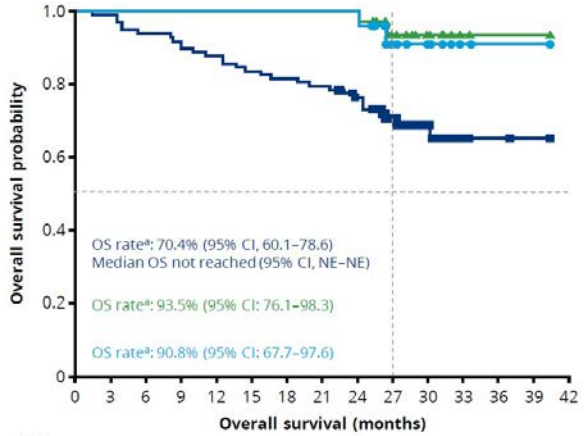


Patients at risk															
MRD negative ≥12 months	24	24	24	24	24	24	24	24	11	8	2	1	1	0
MRD negative ≥6 months	34	34	34	34	34	33	32	32	31	13	10	3	1	1	0
sCR patients	80	80	78	73	71	64	62	61	55	27	17	3	1	1	0
All patients	97	95	85	77	74	67	64	63	57	27	17	3	1	1	0

MRD negative ≥12 months; MRD negative ≥6 months; sCR patients; All patients

[a]27-month PFS rate.

FIGURE 4: Overall survival



Patients at risk															
All patients	97	96	91	88	85	81	79	77	71	42	22	6	2	1	0
Sustained (≥6 mos) MRD neg	34	34	34	34	34	34	34	34	34	18	11	3	1	1	0
Sustained (≥12 mos) MRD neg	24	24	24	24	24	24	24	24	24	13	9	2	1	1	0

All patients; Sustained (≥6 mos) MRD neg patients; Sustained (≥12 mos) MRD neg patients

[a]27-month OS rate.

ASCO 2022 UPDATE	
27-month PFS	**54.9%** (95% CI, 44.0-64.6)
Median PFS	Not reached (95% CI, 24.5-NE)
27-Month OS	**70.4%** (95% CI, 60.1-78.6)
Median OS	Not reached (95% CI, 27.2 months-NE)

ASCO 2022 UPDATE	
27-mo PFS – MRD->12 months	**78.8%** (95% CI, 51.5 – 91.8)
27-Mo OS – MRD->12 months	**90.8%** (95% CI, 67.7-97.6)

Usmani SZ et al. ASCO 2022;Abstract 8028.

CAR-T Cell Toxicities

Comparable baseline features and toxicity, except timing of CRS and delayed neurotoxicity with Cilta-cel

Baseline Features	Cilta-cel[1]	Ide-cel[3]
N	97	128
Target CAR-T Dose	0.75 million/kg	300-450 million
Median Age	61 years	61 years
Median Prior Lines	6	6
Triple Class Refractory	88%	84%
Penta Refractory	42%	26%

Toxicity	Cilta-cel[1]	Ide-cel[3]
CRS (all; grade 3 or 4)	95% (5%)	84% (5%)
Median Onset of CRS	7 days	1 day
ICANS (all; grade 3 or 4)	17% (2%)	18% (3%)
Infections (all; grade 3 or 4)	58% (20%)	69% (22%)
Grade 3 or 4 neutropenia > 1 month*	10%	41%
Grade 3 or 4 thrombocytopenia > 1 month*	25%	48%
Delayed neurotoxicity (all; grade 3 or 4)	12% (9%)	None

Efficacy	Cilta-cel[1]	Ide-cel[3]
ORR; CR rate	98%; 82.5%	73%; 33%
MRD negativity (10^{-5})	58%	26%
PFS	Median NR; 24 m PFS: 60.5%	Median: 8.8 m
OS	Median NR, 24 m OS: 74%	Median: 19 m

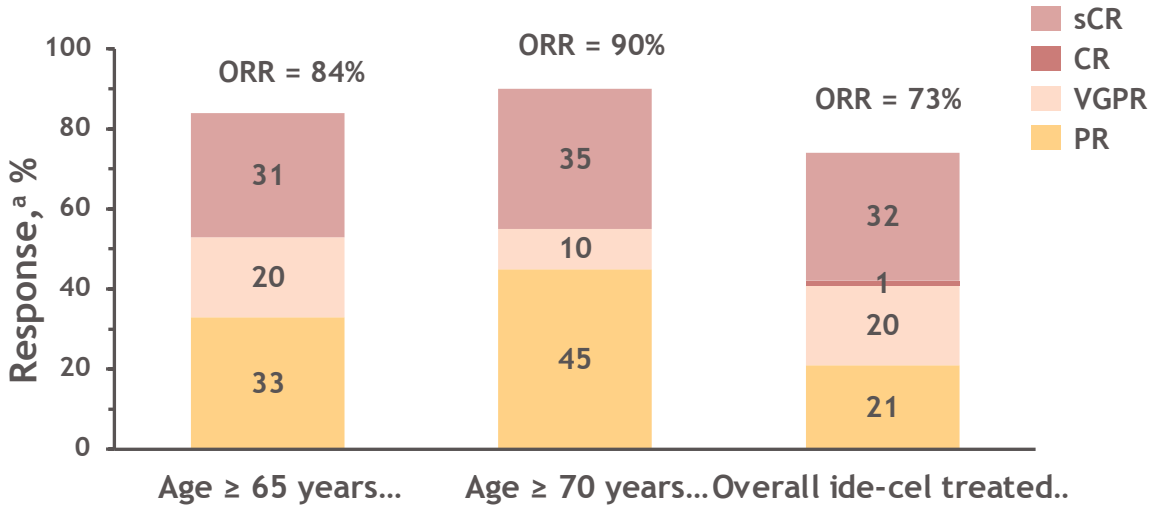
Berdeja et al. Lancet 2021; 398:314. Munshi et al. NEJM 2021; 384(8):705-716.

BCMA CAR T-Cell Therapies: Summary

	CARTITUDE-1[1-2] Cilta-cel Phase 1	CRB-401[3] Ide-cel Phase 1	CRB-402[4] bb21217 Phase 1	LUMMICAR-2[5] CT053 Phase 1b	Allogene[6] (ALLO-715)	CT103A[7] Phase 1/2 Study
Patients	97	62	72	14	42	71
No. of prior regimens, median	6	6	6	6	7	4
Triple refractory, %	87.6	69.4	69	NR	42.9 (penta)	NR
CAR T-cell therapy dose	0.75×10^6 (range, 0.5–1.0 × 10^6)	50, 150, 450, 800 x 10^6	150, 300, 450 x 10^6	1.0/1.5 x 10^8	40, 160, 320, and 480 x 10^6	1.0×10^6
ORR, %	97.9	75.8	69	100	61.5	94.4
CR %	82.5	38.7	36	14.3	78.6	50.7
CRS (all grades), %	94.8	75.8	75	92.9	52.4	93
CRS (grade 3/4), %	4	6.5	1	0	2.4	2.8
Neurotoxicity (all grades), %	20.6	35.5	15	0	2.4	NR
Neurotoxicity (grade 3/4), %	10.3	1.6	4	0	0	NR

(1) Usmani et al. ASCO 2022;Abstract 8028. (2) Martin et al. ASH 2021 abs #549. (3) Yin L et al. ASH 2021;Abs 131. (4) Raje et al. ASH 2021 Abs#548. (5) Chen et al. ASH 2021; abs #2821. (6) Mailankody et al. ASH 2021; abs #651. (7) Li et al. ASH 2021 abs #547.

The Overall Response and safety profile for the elderly groups were comparable with those observed in the overall population

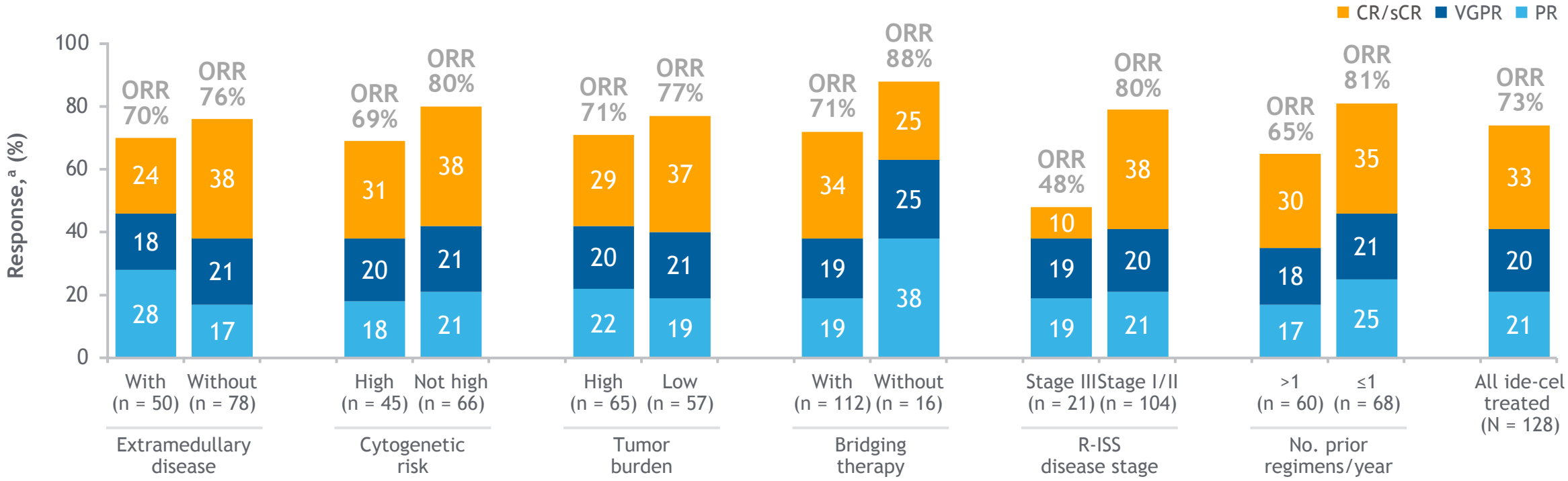


Baseline characteristics[1]		Age ≥65 years (n=45)	Age ≥70 years (n=20)	Overall Ide-cel treated (N=128)
≥ 1 CRS event, n (%)		40 (89)	20 (100)	107 (84)
Max. grade (Lee criteria),[c] n (%)	1	23 (51)	10 (50)	61 (48)
	2	15 (33)	8 (40)	39 (31)
	≥3	2 (4)	2 (10)	7 (5)
Days to onset, median (range)		1 (1-12)	1 (1-12)	1 (1-12)
Days duration, median (range)		5 (1-22)	5 (2-18)	5 (1-63)
≥ 1 neurotoxicity event, n (%)		11 (24)	6 (30)	23 (18)
Max. grade (CTCAE),[d] n (%)	1	6 (13)	5 (25)	12 (9)
	2	1 (2)	0	7 (5)
	3	4 (9)	1 (5)	4 (3)
Days to onset, median (range)		2 (1-6)	2 (1-6)	2 (1-10)
Days duration, median (range)		5 (1-22)	6 (2-16)	3 (1-26)

- Median time to first response was 1.0 month in both elderly groups and in the overall treated population[b]
- Median duration of response was consistent across age groups, ranging from 10.7 to 11.0 months[b]

Data cut-off date: 14 January 2020. [a]Values may not add up to total due to rounding; [b]Time to first response and duration of response were assessed in responders: n = 38 for ≥ 65 years group, n = 18 for ≥ 70 years group, and n = 94 for overall ide-cel treated population. [c]CRS graded according to Lee criteria (Lee DW, et al., *Blood* 2014;124:188-195); [d]Investigator-identified NT events were graded according to the NCI CTCAE v4.03.
CR, complete response; ORR, overall response rate (≥ PR); PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
Berdeja J, et al. Presented at ASH 2020; abstract 1367.

KarMMa subgroup analysis: Ide-cel yielded high response rates in most subgroups, including high-risk patients



- ORR was ≥65% and CR rate was ≥20% across all high-risk subgroups except R-ISS disease stage III
- Presence of extramedullary disease and baseline tumor burden did not substantially affect ORR

Data cutoff date: 14 Jan 2020.
CR, complete response; ORR, overall response rate; PR, partial response; R-ISS, revised International Staging System; sCR, stringent complete response; VGPR, very good partial response.
[a]Sum of CR/sCR, VGPR, and PR rates may differ from the ORR rate due to rounding.
Raje N, et al. Presented at 62nd ASH Meeting 2020. Abstract 3234.

Which patient to Consider?

Identifying patients eligible for CAR T cell therapy

Patient eligibility should be determined prior to leukapheresis

Which patient to Consider? Identifying patients eligible for CAR T cell therapy

Treatment characteristics:

Patients who have received at least four prior MM treatment regimens:[a,1,2]

- Including a PI, an IMiD® agent and an anti-CD38 mAb

Disease characteristics:

Patients who have progressive disease:[1,2]

- Do not need to be refractory to the last treatment regimen; stable disease or minimal response are acceptable
- Do not need traditional measurable disease; imaging is adequate

Patient characteristics:

No age limit for eligibility to receive CAR T cell therapy:[1,3]

- If patients are over 75 then they will be judged on an individual basis

Patients must be willing and able to adhere to the clinic visit schedule and other requirements:[1,4]

- Patients must agree to continued follow-up for gene therapy trials (as mandated by the regulatory guidelines)

[a]Reflecting inclusion criteria in pivotal clinical trials – approved indication may vary.
CAR, chimeric antigen receptor; IMiD® agent, immunomodulatory drug; mAb, monoclonal antibodies; MM, multiple myeloma; PI, proteasome inhibitor.
1. Personal opinion of speaker based on expert panel manuscript pending publication. 2. Shah N, et al. J Immunother Cancer. 2020;8:e000734. 3. Berdeja J, et al. Presented at ASH 2020; abstract 1367. 4. Protocol for: Raje N. N Engl J Med 2019;380:1726-37.

Comorbidities and relevant considerations

Cardiorespiratory

Well managed and compensated cardiorespiratory comorbidities are acceptable.[1,2]

No fixed EF requirement which are liberal than those required for high-dose therapy and transplant.

Renal function

Patients with adequate renal function defined as CrCl ≥ 30 mL/min using Cockcroft-Gault equation, will be included[1-3]

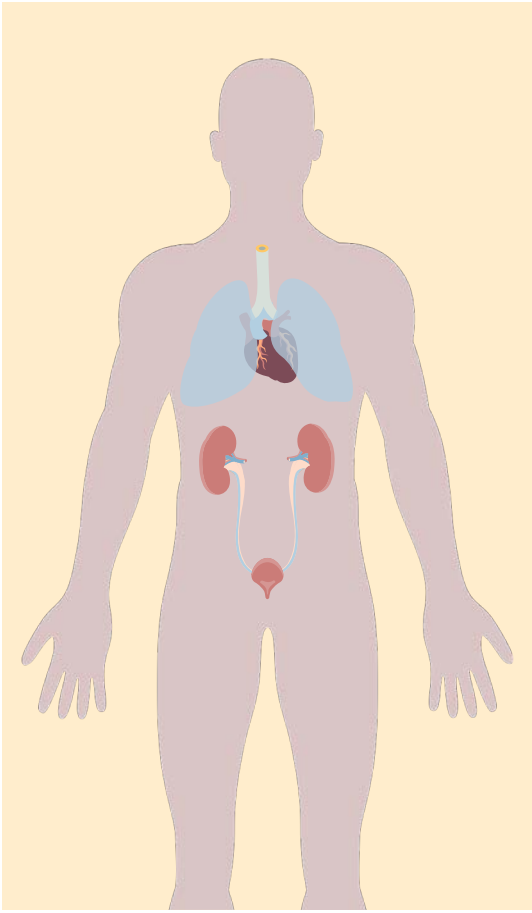
Decreased renal function would require dose reduction for fludarabine and cyclophosphamide during lymphodepletion[1-3]

Viral

CAR T cell therapy should be deferred for patients with active ongoing viral infection, e.g. HCV, HBV or HIV.[1,2]

Immune status

Patients considered for CAR T cell therapy irrespective of recurrent, non-severe infections[1,2]



CAR, chimeric antigen receptor; CrCl, creatine clearance.

1. Personal opinion of speaker based on expert panel manuscript pending publication. 2. Protocol for: Raje N. N Engl J Med 2019;380:1726-37. 3. Shah N, et al. J Immunother Cancer. 2020;8:e000734.

Factors impacting CAR T cell therapy outcomes and the risk of toxicities

Patient on chronic immunosuppressants[a] should be considered with a possibility to hold them during CAR T cell therapy.[1,2]

Ongoing treatment with intermittent topical, inhaled or intranasal corticosteroids is allowed

Patients on anticoagulation should have no active bleeding and should be safe to be taken off anticoagulation[1,2]

Adequate bone marrow function is not a prerequisite for consideration for CAR T cell therapy[1,3]

- There are minimal blood count requirements for a patient to be considered for therapy[1,2]
- A low count (ANC < 1000 cells/mm^3 and/or platelet count < 50,000 mm^3) may impact production of adequate CAR T cells, and may also increase risk of more prolonged cytopenia following lymphodepletion[1,2]

Cilta-cel is not approved by any regulatory agency. Ide-cel is currently approved by the FDA only. AE, adverse event; ANC, absolute neutrophil count; CAR, chimeric antigen receptor.

1. Personal opinion of speaker based on expert panel manuscript pending publication. 2. Protocol for: Raje N. N Engl J Med 2019;380:1726-37. 3. Shah N, et al. J Immunother Cancer. 2020;8:e000734. 4. Munshi NC, et al. Presented at ASCO 2020; abstract 8503. 5. Madduri D, et al. Presented at ASH 2020; abstract 177.

Plans to improve the outcome of CAR T cell therapy

- **Improve the CAR T cell product**
  - PI3K inhibitors - BB21217
- **Reduce turnaround time**
  - Gene editing of allogeneic CAR T cells
  - Allogeneic CAR T cells
  - Quick Production – In vivo growth – PHE885
- **Increase target expression**
  - Resistance mechanisms
  - Gamma-secretase inhibitors for BCMA[7]
  - Find novel targets (e.g. GPRC5D[4])
- **Improve patient selection**
  - Treat at an earlier line of therapy

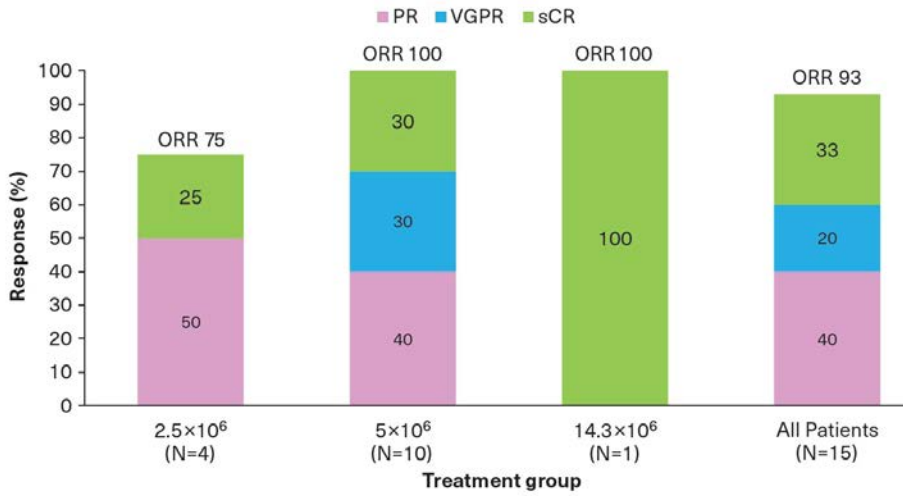
- **Target expression**
  - Resistance mechanisms
  - Gamma-secretase inhibitors for BCMA[7]
  - Find novel targets (e.g. GPRC5D[4])

- **Improve patient selection**
  - Treat at an earlier line of therapy
  - Select CD4:CD8 ratios[2]

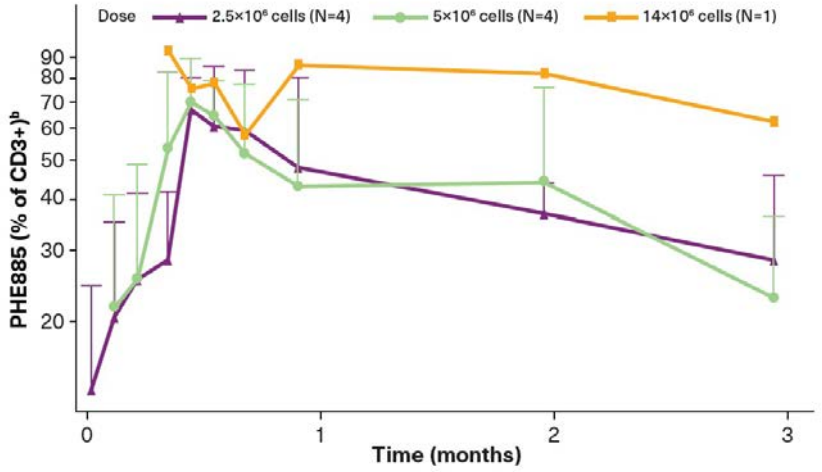
Phase I Study of PHE885, a Fully Human BCMA-Directed CAR-T Cell Therapy for Relapsed/Refractory Multiple Myeloma Manufactured in <2 Days Using the T-Charge™ Platform

- **Anti-BCMA CAR-T cells PHE885 is manufactured using the T-Charge™ platform, which reduces ex vivo culture time to about 24 hours and takes <2 days to manufacture the final product, thereby relying entirely on in vivo expansion after CAR-T cell infusion**

Figure 2. Summary of Tumor Response by ORR[a]

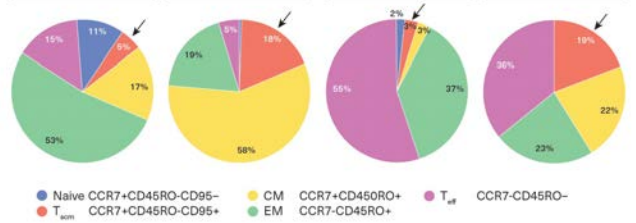


Cellular Kinetics of PHE885 by Flow Cytometry



T-Charge™ Process Preserves T-Cell Stemness in Final Product

Figure 6. PHE885 Product Stemness

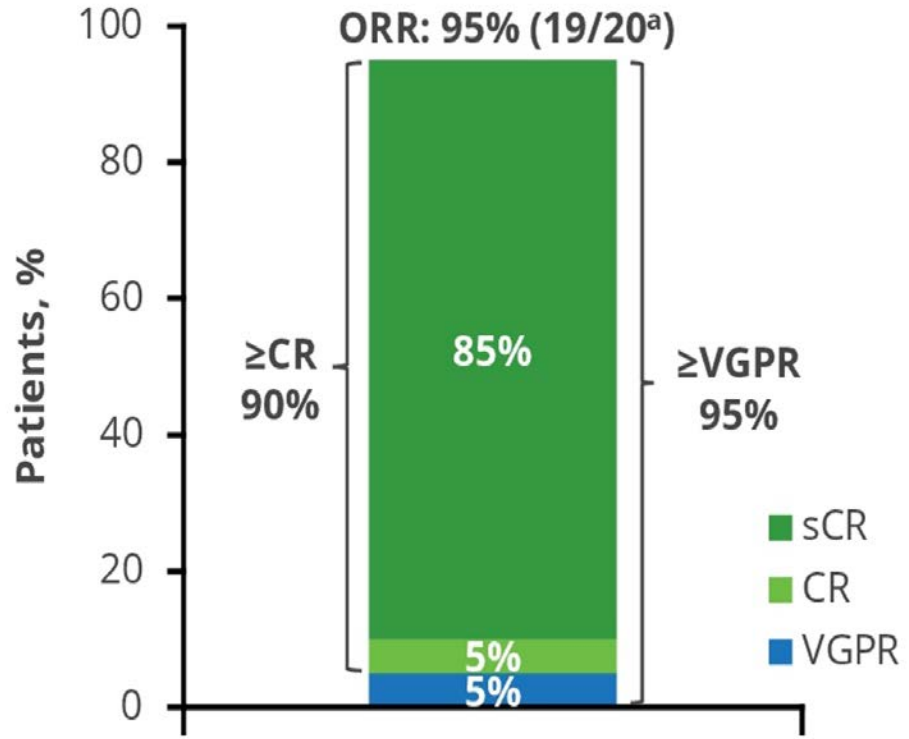


- **A Shift Toward Naive/Tscm Phenotype Is Observed in Patients Following PHE885 Treatment**
- **A shift to Tscm/Tnaive population in both CD4 and CD8 T cells in the >VGPR group but not PD group**

Sperling et al ASH 2021;Abstract 3864.

Efficacy and Safety of Cilta-cel in Lenalidomide-Refractory Patients with Progressive Multiple Myeloma after 1-3 Prior Lines of Therapy: CARTITUDE-2 Cohort A

Overall response rate



[a]One patient demonstrated a minimal response.
sCR, stringent CR

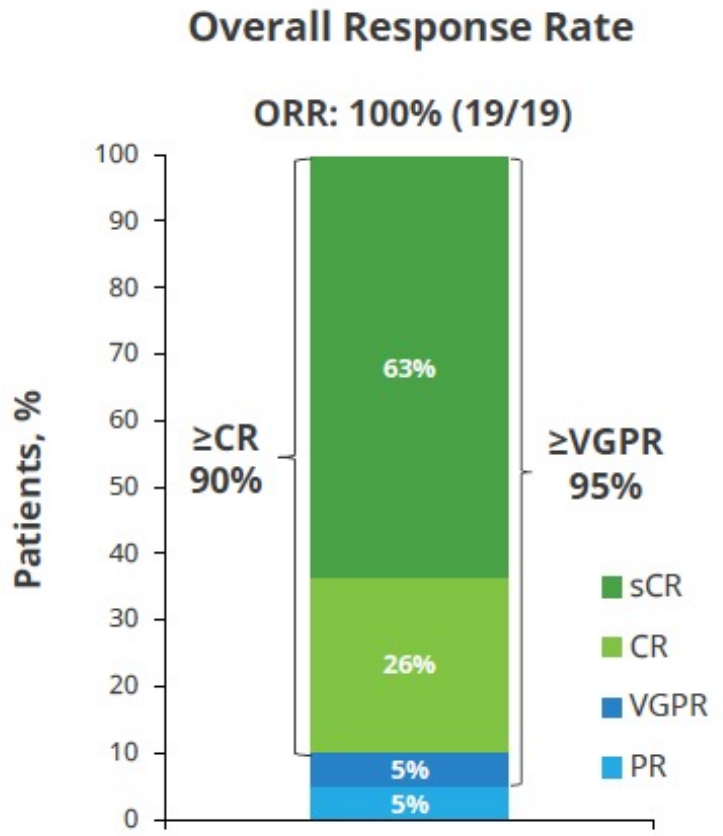
Adverse events

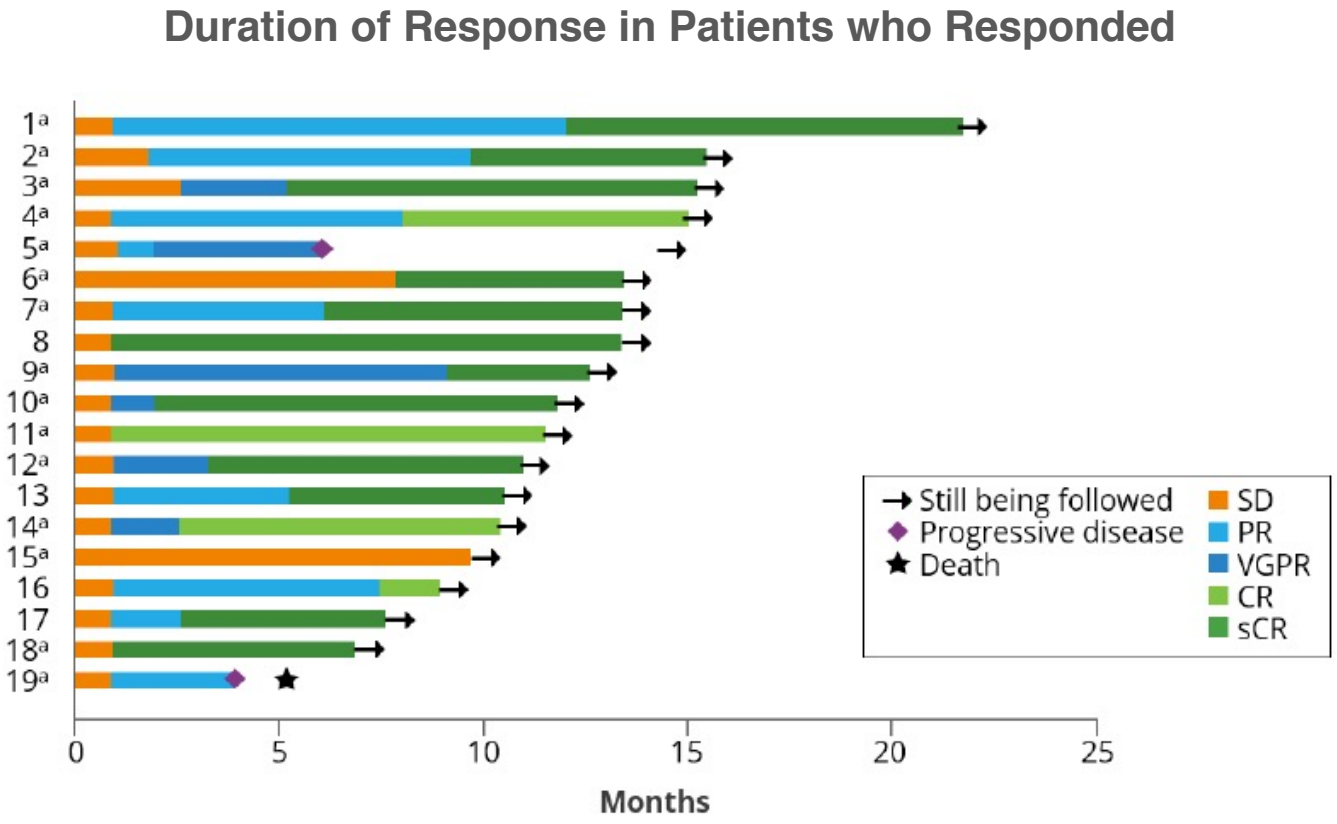
AEs ≥20%, n (%)	N=20	
	Any Grade	Grade 3/4
Hematologic		
Neutropenia	19 (95)	19 (95)
Thrombocytopenia	16 (80)	7 (35)
Anemia	15 (75)	9 (45)
Lymphopenia	14 (70)	14 (70)
Leukopenia	11 (55)	11 (55)
CAR-T-related AEs		
CRS	19 (95)	2 (10)
Neurotoxicity	6 (30)	1 (5)
ICANS	3 (15)	0
Other	3 (15)[a]	1 (5)

[a]One patient had peripheral sensorimotor neuropathy, one had anosmia and dysgeusia, and one had facial paralysis.

Hillengaas J et al. EHA 2022;Abstract P959. Einsele H et al. ASCO 2022;Abstract 8020.

CARTITUDE-2, Cohort B: Cilta-cel in Patients With Multiple Myeloma and Early Relapse After Initial Therapy





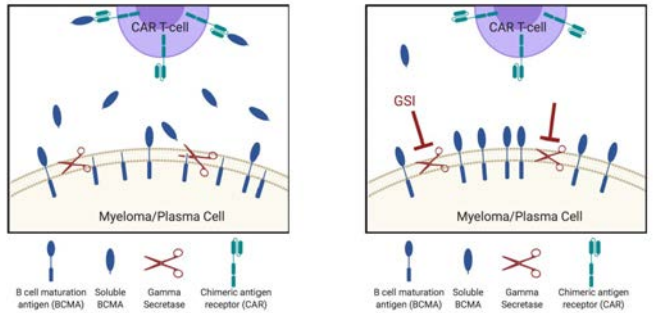
- Of the 15 patients with MRD-evaluable samples at 10^{-5} threshold, 14 (93.3%, [95% CI, 68.1–99.8]) were MRD negative

- Median time to first response: 1.0 month (range, 0.9–9.7)
- Median time to best response: 5.1 months (range, 0.9–11.8)
- Median DOR was not reached
- 12-month PFS rate was 89.5% (95% CI, 64.1–97.3)

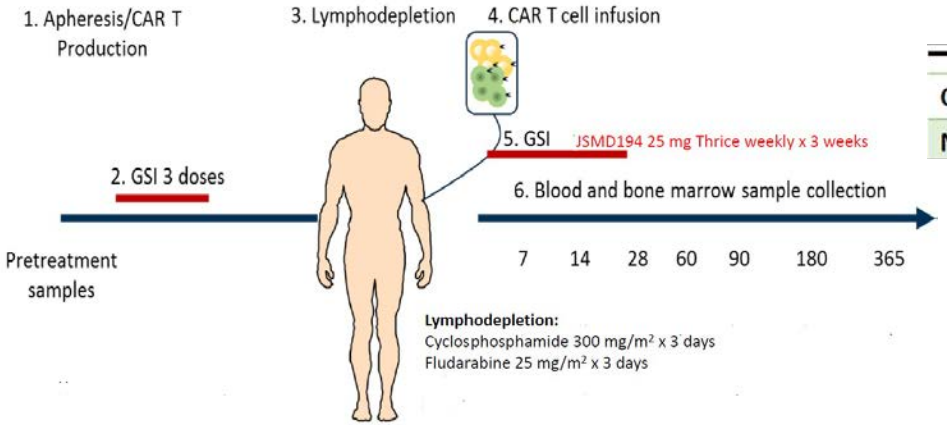
Agha ME et al. EHA 2022;Abstract S185

Fully Human BCMA CAR T Cells in Combination with a Gamma Secretase Inhibitor to Increase BCMA Expression in R/R Multiple Myeloma

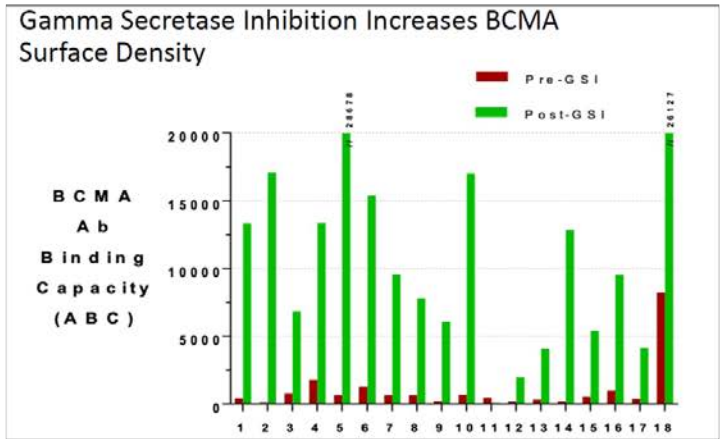
Gamma Secretase Cleaves BCMA from Plasma Cells



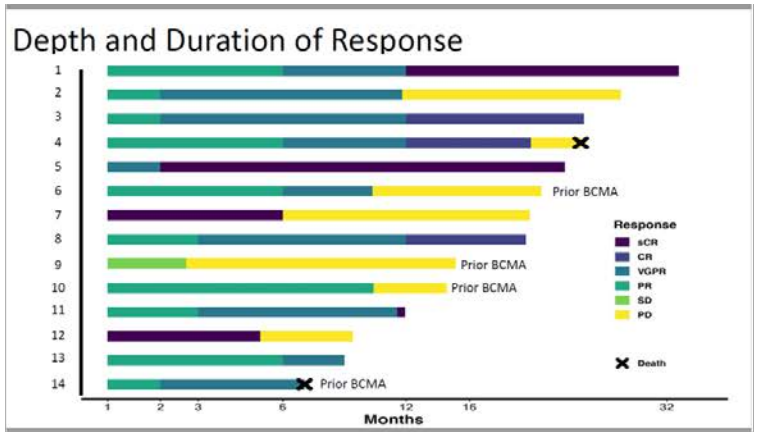
Study Design



Gamma Secretase Inhibition Increases BCMA Surface Density



Depth and Duration of Response



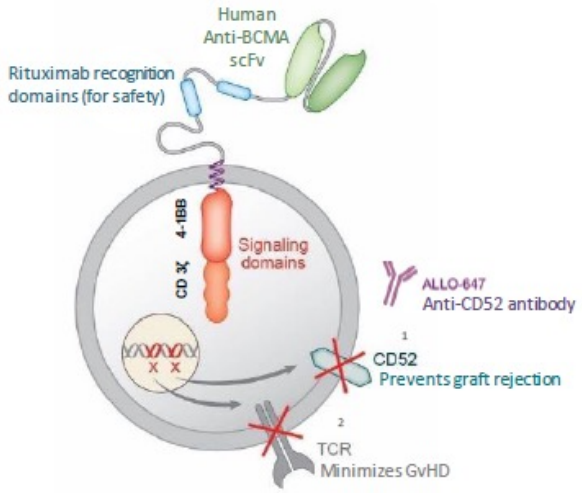
CRS (any grade)	17 (94%)
Neurologic Δ from baseline*	12 (66%)

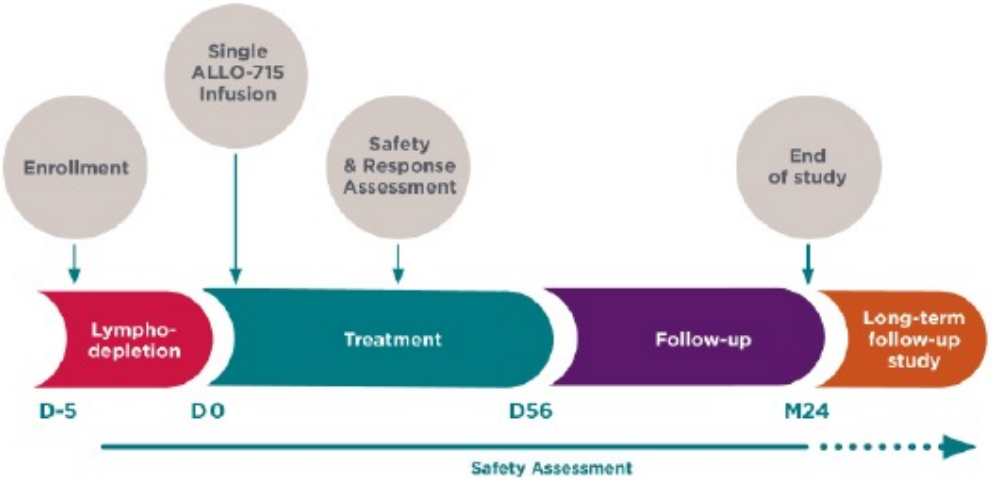
Cytokine Release Syndrome (ASTCT Grading)

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
9 (50%)	6 (33%)	4 (22%)	1 (6%)	0 (0%)

Cowan et al ASH 2021.

Phase 1 Data Validates the Feasibility of Allogeneic Anti-BCMA ALLO-715 Therapy for Relapsed/Refractory Multiple Myeloma





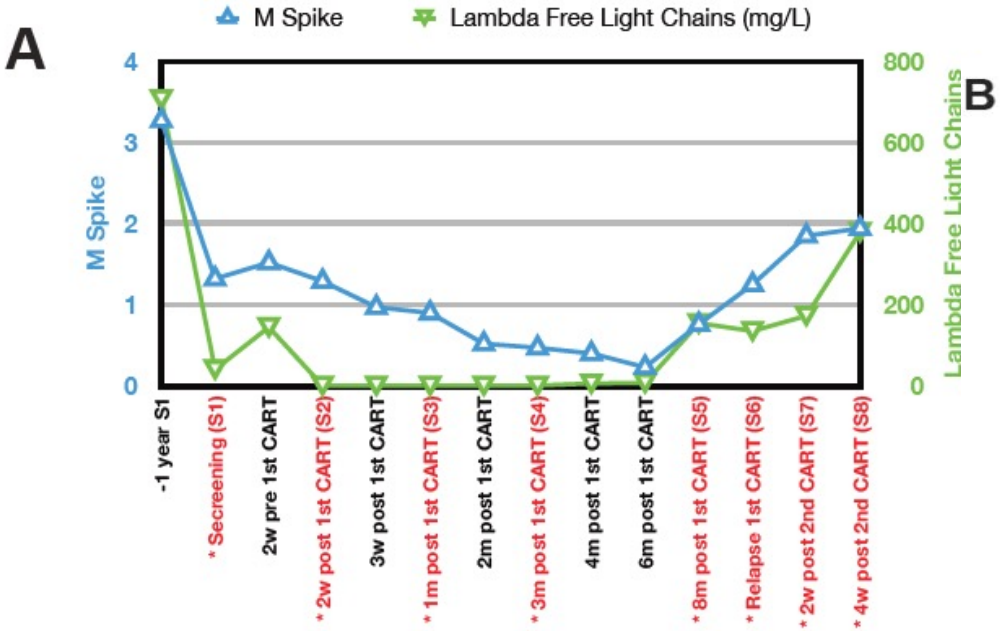
ALLO-715 Dose Escalation: 40, 160, 320, 480 x 10^6 CAR+ T cells	
Lymphodepletion Regimens (FCA, CA†)**	**Doses**
Fludarabine	30 mg/m²/day x 3 days
Cyclophosphamide	300 mg/m²/day x 3 days
ALLO-647	13 to 30 mg x 3 days

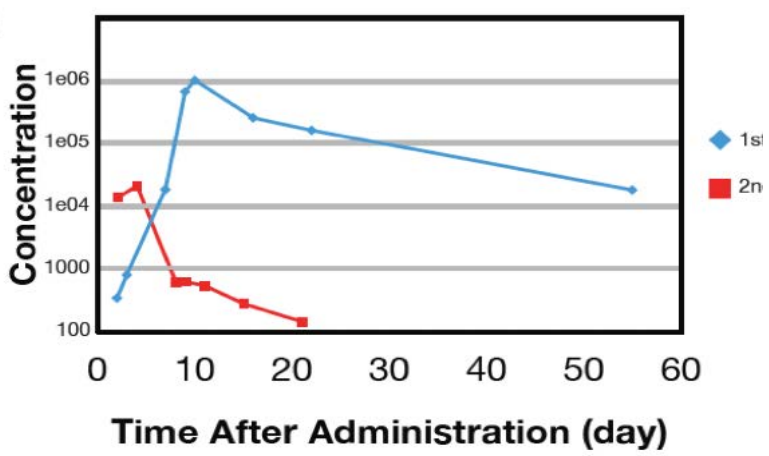
Cell Dose & LD Regimen	DL3 (320M CAR+ T Cells)*				DL4 (480M CAR+ T Cells)	
	FCA39 N=11	FCA60 N=10	FCA90 N=3	FCA ALL N=24	FCA39 N=3	FCA60 N=3
ORR†, n (%) (95% CI)	7 (64) (31, 89)	8 (80) (44, 98)	2 (67) (9, 99)	17 (71) (49, 87)	1 (33) (0.8, 91)	2 (67) (9, 99)
VGPR+ Rate, n (%)	5 (46)	5 (50)	1 (33)	11 (46)	0	2 (67)
CR/sCR Rate, n (%)	3 (27)	3 (30)	0	6 (25)	0	0
mDOR, months (95% CI)	8.3 (3.4, 11.3)	NE (5.6, NE)	3.1 (2.4, 3.1)	8.3 (3.4, 11.3)	1.4 (NE, NE)	NE (1.5, NE)

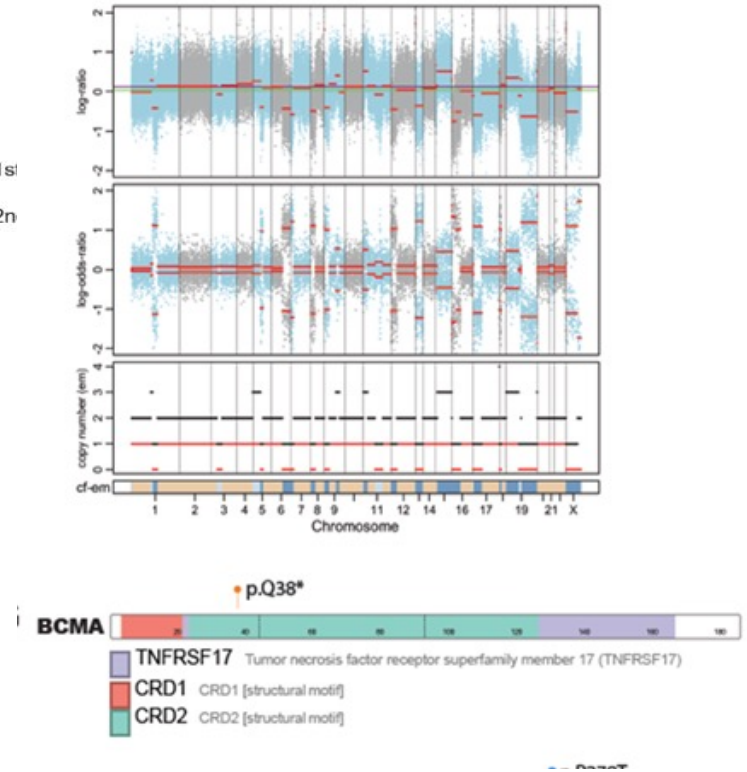
TEAE of Interest* (N=43)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	All Grades
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cytokine Release Syndrome	13 (30)	10 (23)	1 (2)	0	0	24 (56)
Neurotoxicity†	4 (9)	2 (5)	0	0	0	6 (14)
Graft-versus-Host Disease	0	0	0	0	0	0
Infection‡	3 (7)	10 (23)	7 (16)	0	3 (7)	23 (54)
Infusion Reaction to ALLO-647	7 (16)	5 (12)	0	0	0	12 (28)

11 (46%) were VGPR+, of those 6 (25%) were CR/sCR

Biallelic BCMA Loss Confers Resistance to BCMA CAR T Cells



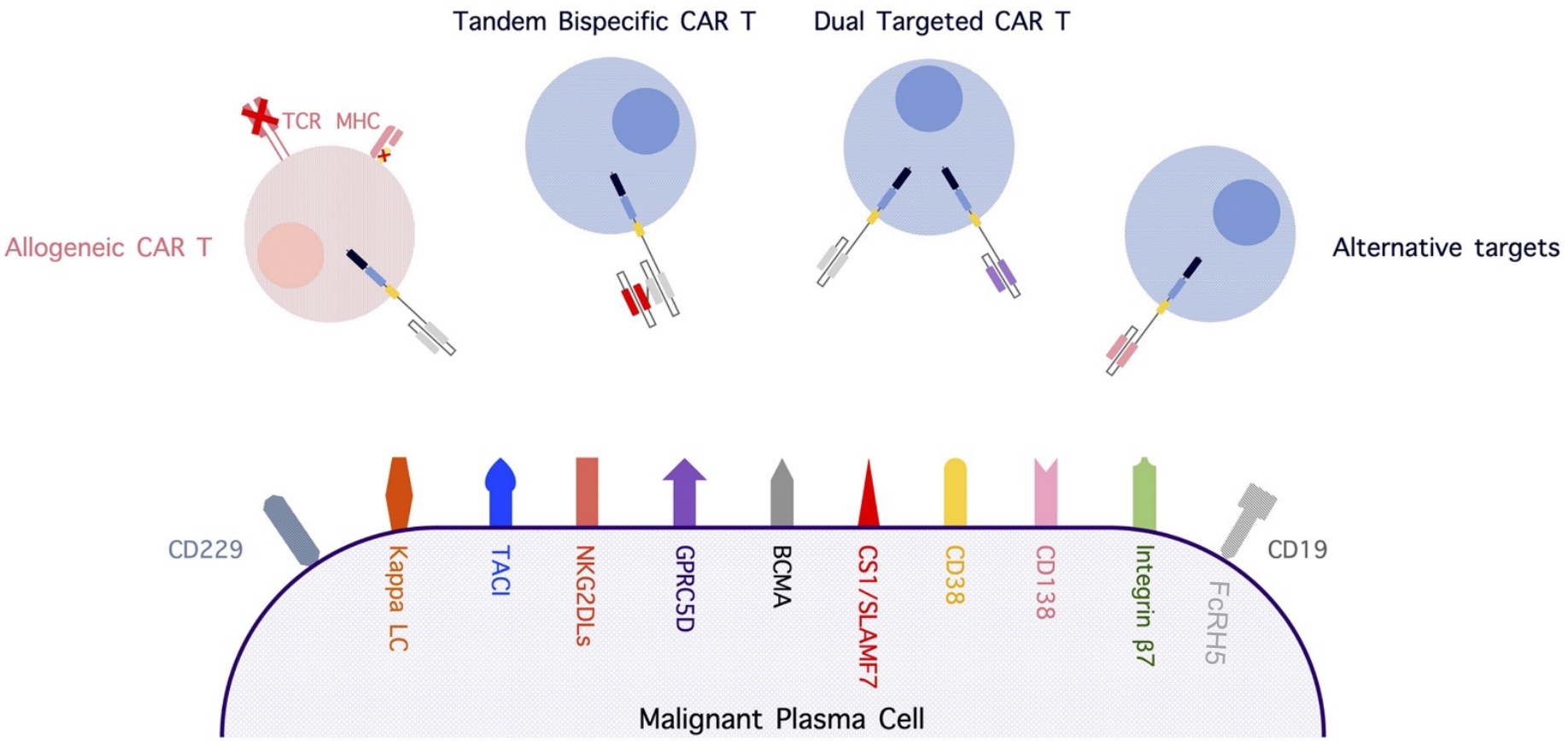




Dual targeting to avoid resistance: GPRC5D, CD19, FcHR5, CD38, CD138, SLAMF-7

Samur et al Nat Comm 2021

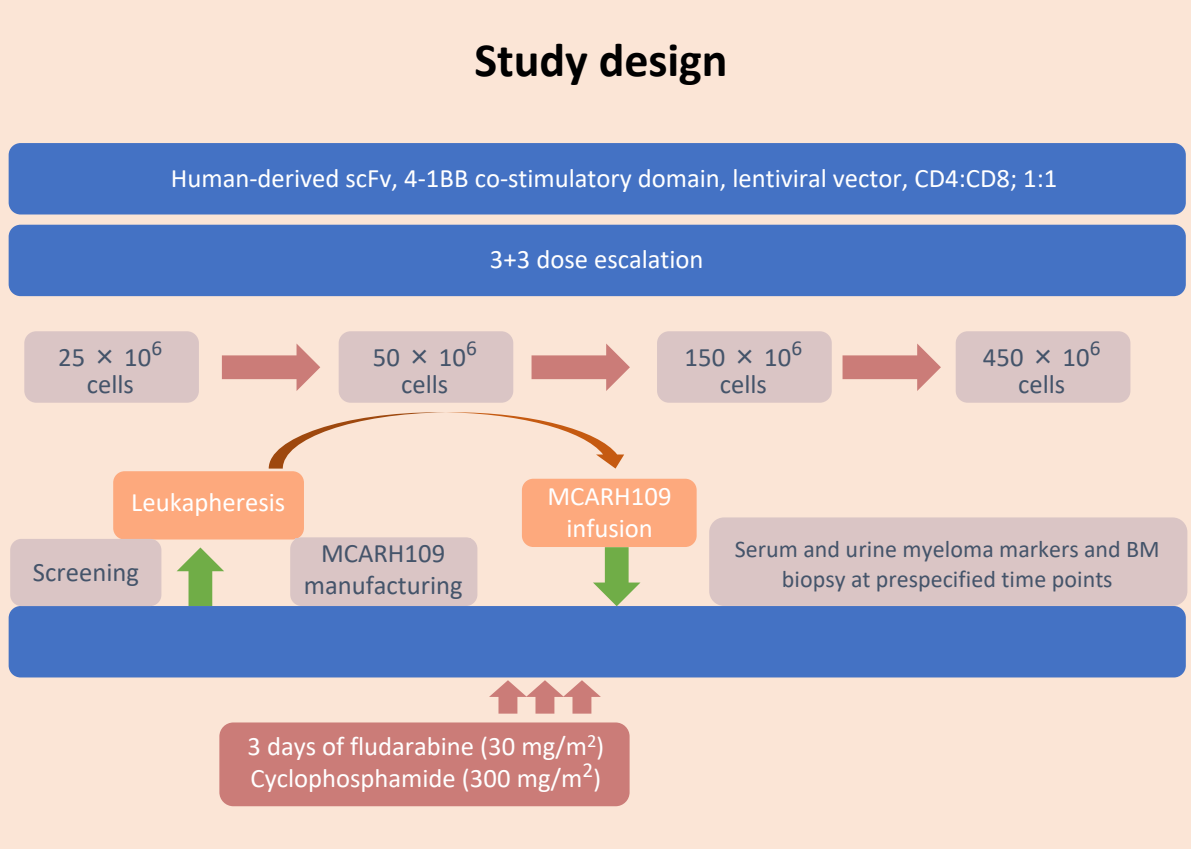
Future of CAR T Cells and/or BiTES in Multiple Myeloma



Kitsada Wudhikarn, Sham Mailankody, Eric L. Smith, Future of CAR T cells in multiple myeloma, Hematology Am Soc Hematol Educ Program, 2020, Figure 1.

American Society of Hematology
Helping hematologists conquer blood diseases worldwide

GPRC5D targeted CAR T cell therapy in RRMM Clinical response (n = 16)



Response, n (%)	25 X10^6 CAR+ T cells (n = 3)	50 X10^6 CAR+ T cells (n = 3)	150 X10^6 CAR+ T cells (n = 5)	450 X10^6 CAR+ T cells (n = 5)	Total (N = 16)
≥ PR	1 (33)	3 (100)	2 (40)	5 (100)	11 (69)
≥ VGPR	1 (33)	2 (67)	0 (0)	4 (80)	7 (44)
≥ CR	0 (0)	1 (33)	0 (0)	3 (60)	4 (25)
MRD negativity	2 (67)	2 (67)	2 (40)	2 (50)	8 (50)

Response, n (%)	Prior BCMA therapy (n = 10)	Prior CAR T therapy (n = 8)
≥ PR	8 (80)	6 (75)
≥ CR	3 (30)	3 (38)
BM MRD negativity[a], n (%)	5 (50)	2 (25)

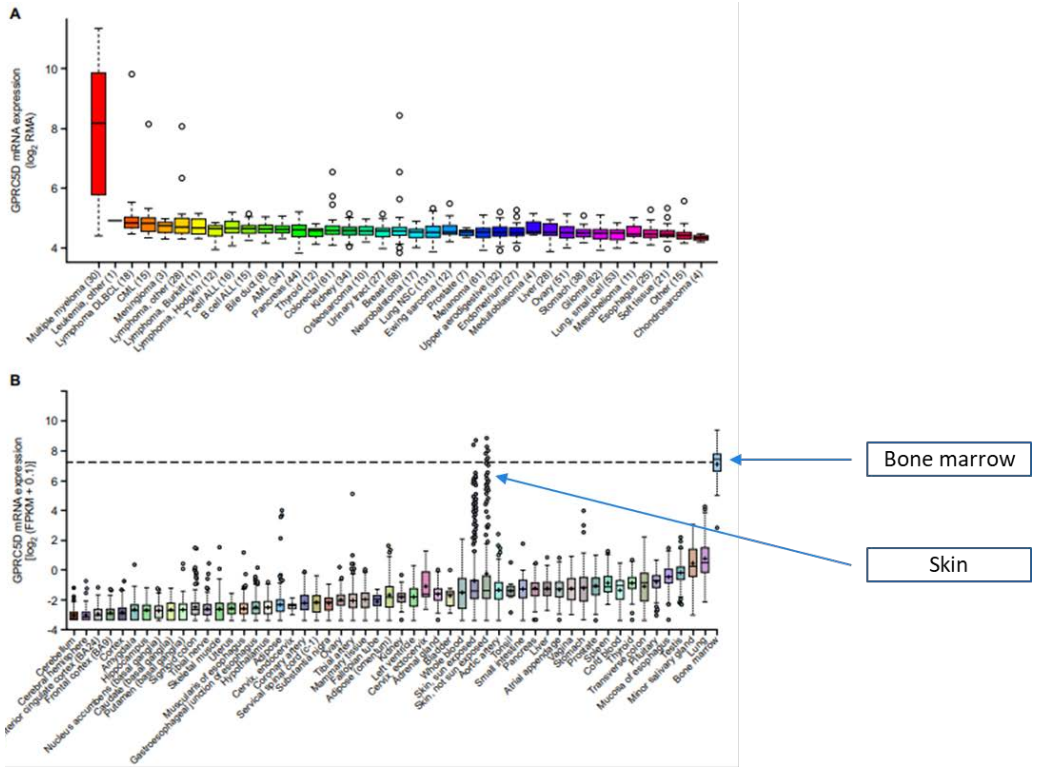
Investigational only, not approved.

[a] MRD assessment by multicolour flow cytometry (sensitivity: 1 in 105).

scFv, single-chain variable antibody fragments.

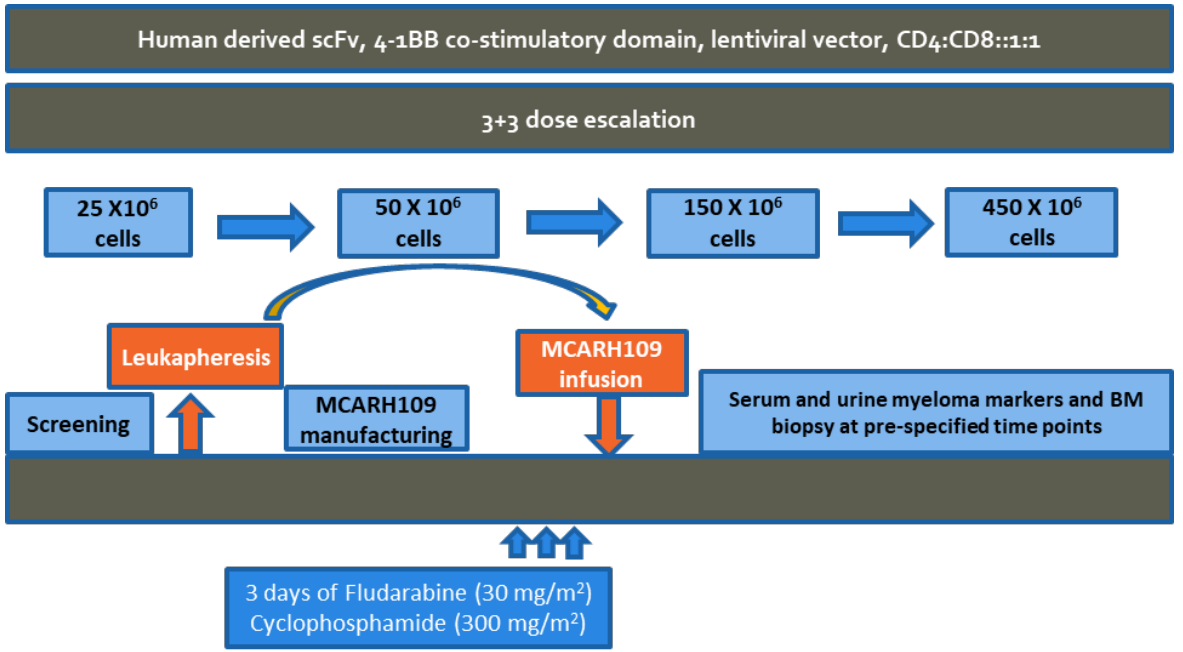
Mailankody S, et al. Presented at ASH 2021; abstract 827.

Phase I First-in-Class Trial of MCARH109, a G Protein Coupled Receptor Class C Group 5 Member D (GPRC5D) Targeted CAR T Cell Therapy in Relapsed or Refractory Multiple Myeloma



Smith EL. et al. Science Translational Medicine 2019

Study Design



Key eligibility criteria:

- 3 or more lines of therapy; Prior PI, IMiD, CD38 antibody-based therapy
- Prior BCMA and CART allowed; Non-secretory myeloma allowed

Conclusion

- Incredible effectiveness of CAR-T cell therapy is achieving impressive responses
- Innovative patient selection and intervention under investigation
- Task for us is to sustain/maintain the great responses achieved with CAR-T cell infusion
- Understanding mechanisms of resistance and developing alternatives will lead to curative outcome in MM

Agenda

PART 1: Case Presentations and Clinical Decision-Making

- Non-Hodgkin Lymphoma
- Multiple Myeloma

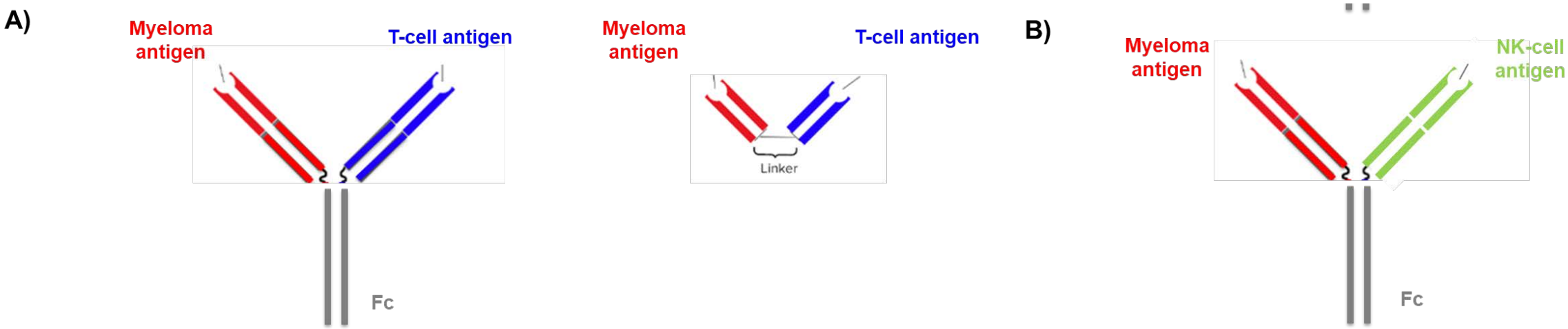
PART 2: Faculty Presentations

- CAR-T in Non-Hodgkin Lymphoma — Dr Flinn
- Bispecifics in Non-Hodgkin Lymphoma — Dr Sehn
- CAR-T in Multiple Myeloma — Dr Munshi
- Bispecifics in Multiple Myeloma— Dr Chari

BCMA and Non-BCMA Bispecific Antibodies Under Investigation in MM

Ajai Chari, MD
Professor of Medicine (Hematology and Medical Oncology)
Icahn School of Medicine at Mount Sinai
Director, Clinical Research
Multiple Myeloma Program
Associate Medical Director
The Tisch Cancer Institute Clinical Trials Office
New York, New York

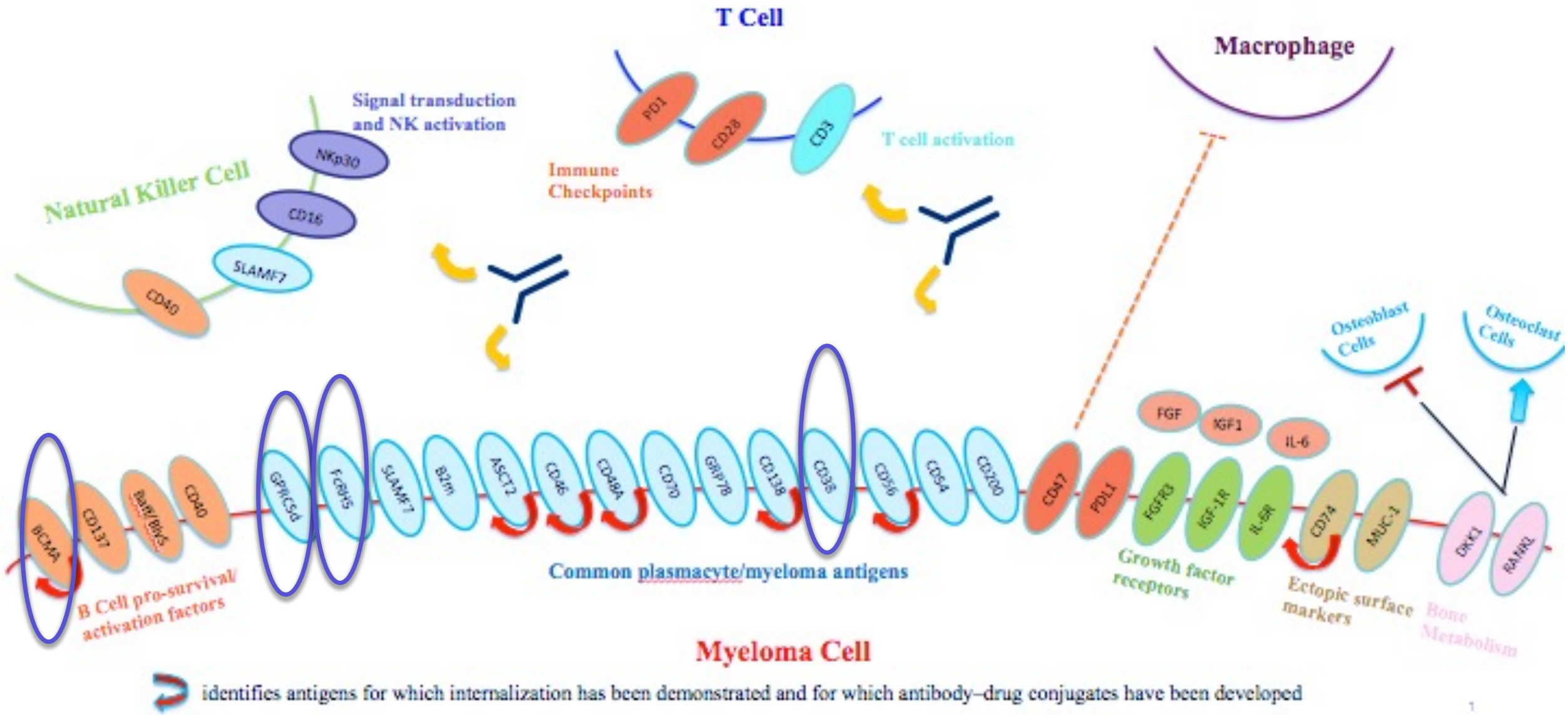
Bispecific Antibodies



- These are only representative schematics and constructs vary in **antigen-binding domains** and **dimerization** (homodimers vs heterodimers) resulting in differences in **antigen-binding sites** (valency), **geometry, size**, and **flexibility**
  - **Fc portion** provides stability in circulation allowing for intermittent (instead of continuous) dosing, and can also promote ADCC and complement activation
  - all these variables can result in different pharmacokinetic and pharmacodynamic properties
- T-cells brought into close proximity to cells expressing MM antigen to form an immunologic synapse and promote cell-mediated cytotoxicity via release of perforin and granzymes
- Bispecific NK-cell engagers under development

Lancman, et al. ASH 2020.

Bispecific Targets in Multiple Myeloma



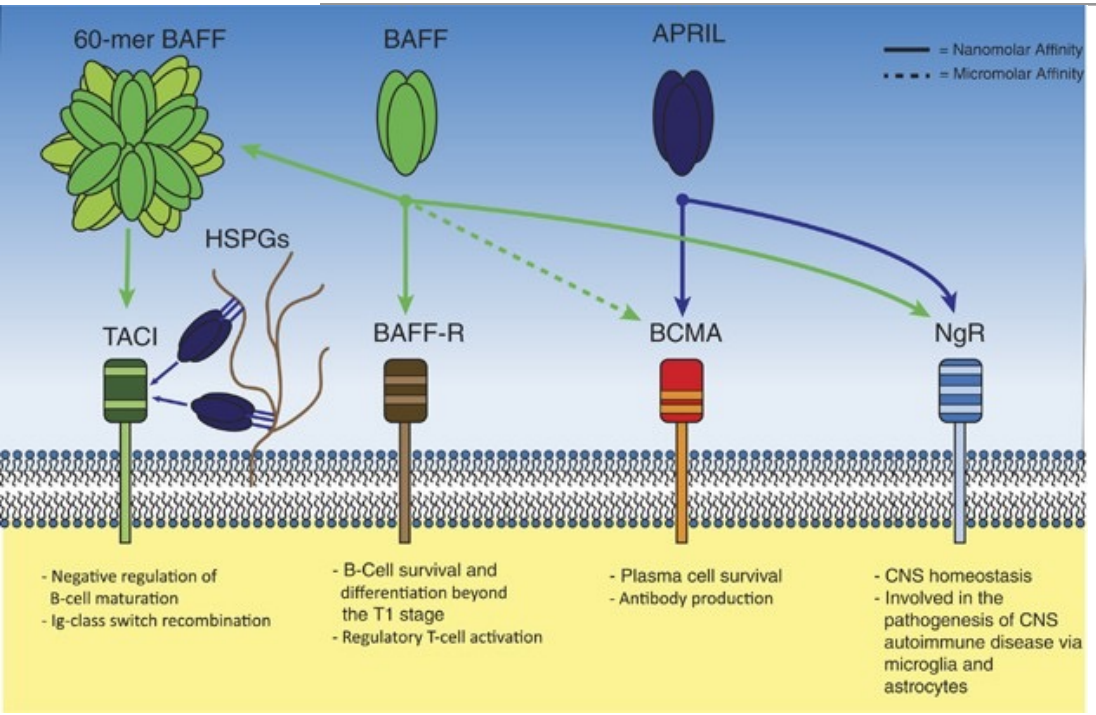
identifies antigens for which internalization has been demonstrated and for which antibody–drug conjugates have been developed

Bispecific Antibodies Clinical Trials in Multiple Myeloma

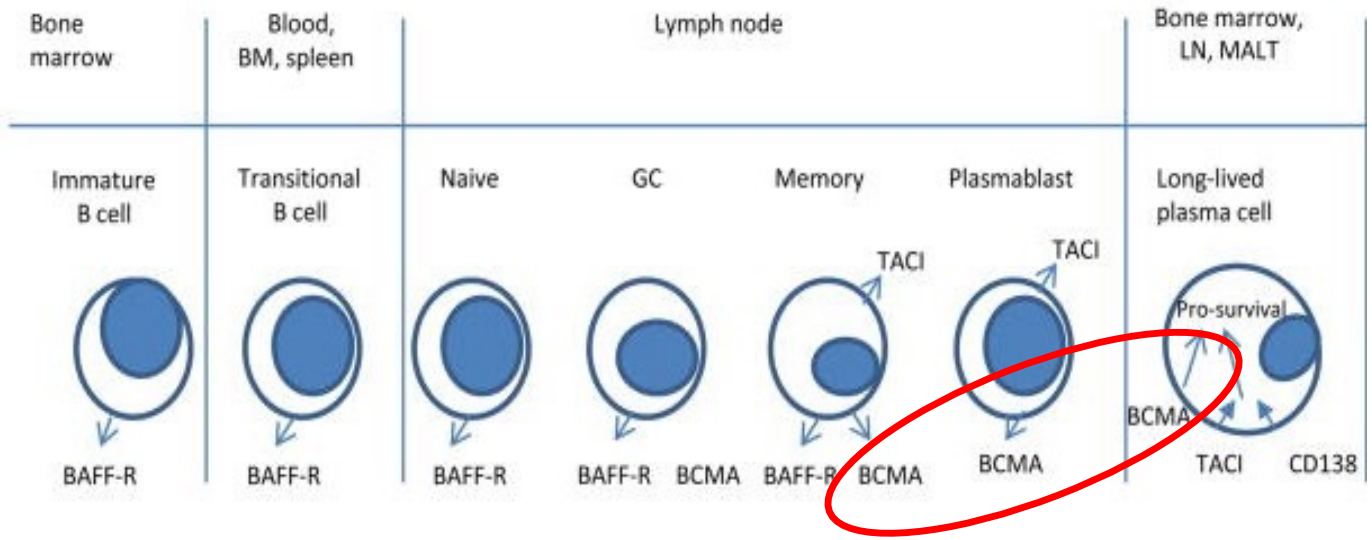
Agent		Targets	Phase	Clinical Trial Number	Status
	AMG420	BCMAxCD3	I	NCT03836053	Completed
Pavurutamab	AMG701	BCMAxCD3	I/II	NCT03287908	Ongoing
Alnuctamab	CC93269	BCMAxCD3	I	NCT03486067	Ongoing
Elrantamab	PF06863135	BCMAxCD3	I	NCT03269136	Ongoing
Linvoseltamab	RGN5458	BCMAxCD3	I/II	NCT03761108	Ongoing
Teclistamab	JNJ64007957	BCMAxCD3	Ib I	NCT04108195 NCT03145181	Ongoing Ongoing
	TNB-383B	BCMAxCD3	I	NCT03933735	Ongoing
Talquetamab	JNJ64407564	GPRC5dxCD3	Ib I	NCT04108195 NCT03399799	Ongoing Ongoing
Cevostamab	BFCR4350A	FCRH5xCD3	I	NCT03275103	Ongoing
	GBR1342	CD38xCD3	I/II	NCT03309111	Ongoing
	AMG424	CD38xCD3	I	NCT03445663	Closed

Updated from Lancman, et al. ASH 2020.

BCMA (B-cell maturation antigen)



- Receptor for BAFF and APRIL
- Expressed on mature B cell subsets, PC's, and plasmacytoid DC's
- Maintains plasma cell homeostasis
  - BCMA-/- mice have normal B cell #s, impaired PC survival



Hengeveld et *al Bl Cancer J* 2015 ; Maus, June, *Clin Can Res* 2013

Bispecific Antibodies: BCMAxCD3

Bispecific Antibody	AMG-701	CC-93269	Elranatamab	HPN217	REGN5458	JNJ-64007957 (Teclistamab)	TNB-383B
Treatment	Weekly IV	Weekly IV	Weekly SC	Weekly IV	Weekly IV	Weekly IV or SC	IV q3w
Patients	n= 85	n= 19	n= 94	N=37	n=49	n= 165	n= 58
Median prior lines	6	6	5	NR	5	5	6
Triple-class refractory	62%	IMiD 84%, PI 90%, Dara 89%	95.7%	NR	100%	77.8%	64%
ORR at therapeutic dose	26% all patients 5/6 (83%) most recent cohort	10/12 (83%) ≥ 6mg IV	60.6% 76 mcg SC (RP2D)	7/13 (53%) 2150 ug or higher	5/8 (63%) 96mg IV	63% CR: 39.4% MRD-: 26.7% 1500ug/kg SC (RP2D)	12/15 (80%) 40-60 mg IV
Duration of Response	17/21 (81%) ongoing at median 5.6 months	NR	NR	NR	14/19 (74%) ongoing at median 6 months	18.4 months (14.9-NE) PFS: 11.3 (8.8-17.1)	22/27 (81%) ongoing at median 4.5 months
AEs, (All/(Gr 3+) **CRS** **Infections** **Neutropenia** **Anemia** **Thrombocytopenia** **Deaths** **Other**	 64% (9%) (17%) 25% 42% 21% 4 (5%) Neurotoxicity 8% (0%)	 90% (5%) NR (26%) NR (53%) NR (42%) NR (21%) 1 (5%)	 59% (0%) 52% (22%) 38% (37%) 44% (34%) 29% (20%) 1 PN 16% (1%)	 24% (0%) NR NR 46% (38%) NR NR	 39% (0%) 47% (18%) 16% (14%) 37% (22%) 18% (6%) 3 (6%) Neurotoxicity 12% (0%)	 72% (0.6%) 76% (45%) 71% (64%) 52% (37%) 40% (21%) 4 (3%) ISR 32% (0%) Neurotoxicity 15%	 45% (0%) 21% (14%) 19% (16%) 21% (17%) 17% (14%) 2 (3%)

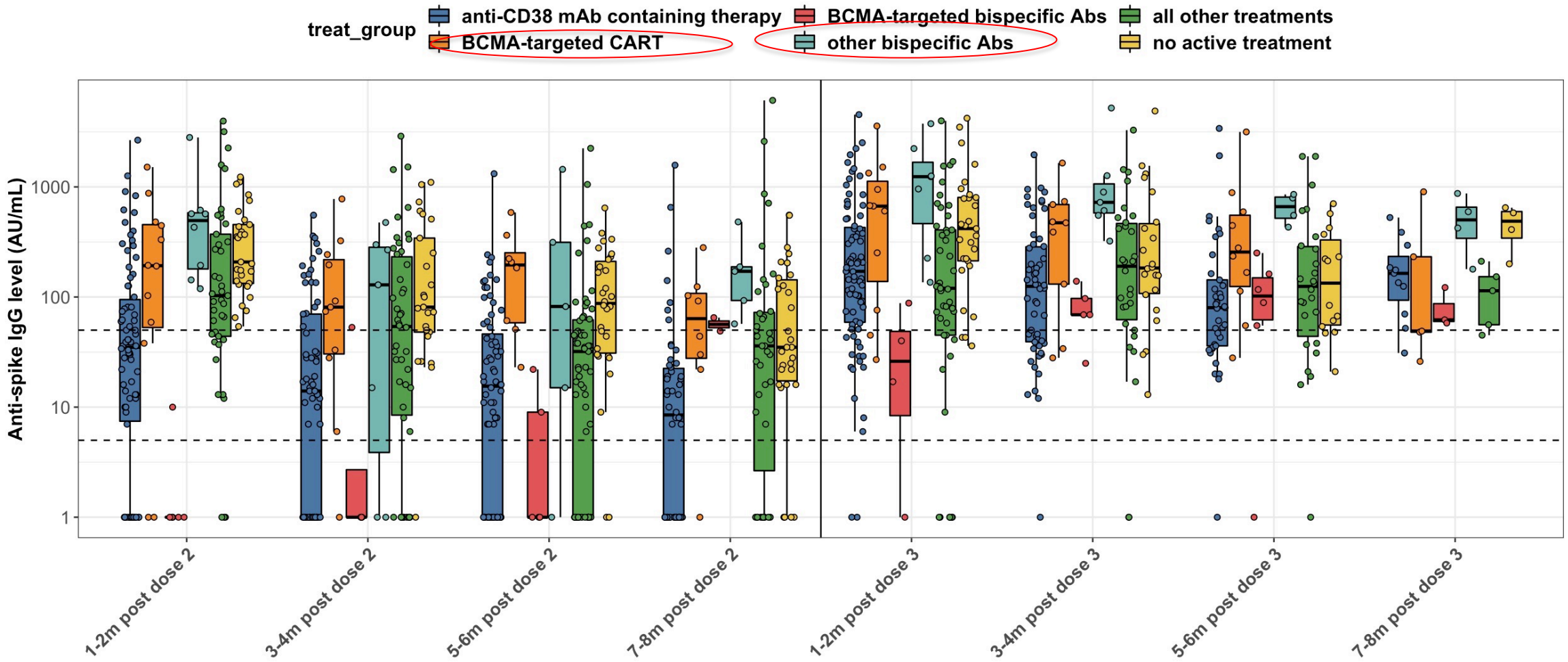
Topp et al, *J Clin Oncol.* 2020; Harrison et al, ASH 2020; Costa et al, ASH 2019; Lesokhin et al, ASCO 2022; Madan et al. ASH 2021;; Zonder et al ASH 2021; Moreau et al. *N Engl J Med.* Jun 5 2022. Kumar S, et al. ASH 2021

Bispecific Combinations

Bispecific Antibody	JNJ-64007957 (Teclistamab)	Teclistamab + daratumumab
Treatment	Weekly IV or SC	Dara SC 1800 mg Tec SC 1.5–3 mg/kg QW or Q2W
Patients	n= 165	n= 46
Median prior lines	5	6
Triple-class refractory	77.8%	74% Penta-refractory: 63%
ORR at therapeutic dose	63% CR: 39.4% MRD-: 26.7% 1500ug/kg SC (RP2D)	29/37 (78%)
Duration of Response	18.4 months (14.9-NE) PFS: 11.3 (8.8-17.1)	NR
AEs, All (Gr 3+) **CRS** **Infections** **Neutropenia** **Anemia** **Thrombocytopenia** **Deaths** **Other**	 72% (0.6%) 76% (45%) 71% (64%) 52% (37%) 40% (21%) 4 (3%) ISR 32% (0%) Neurotoxicity 15%	 61% (0%) 63% (28%) 54% (50%) 48% (28%) 33% (28%) 2 (3%) Neurotoxicity 2%

Moreau et al. *N Engl J Med.* Jun 5 2022; Rodriguez-Otero P et al. ASCO 2022: Abstract 8032.

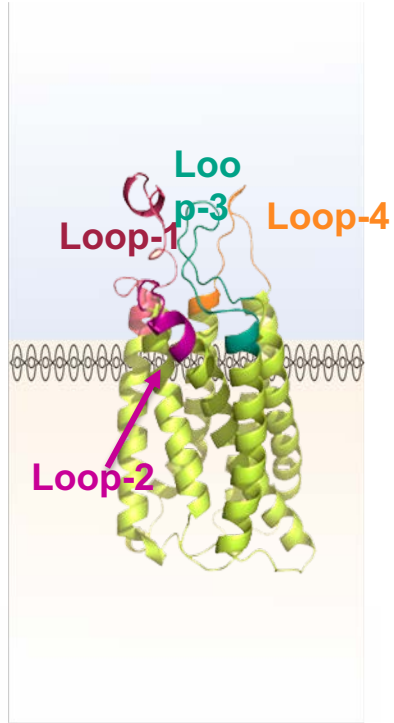
Longitudinal dynamics of anti-spike IgG response diminished most prominently in BCMA-bispecific antibody-treated patients



Van Oekelen, O et al. Immune Effector Cell Therapies in MM Workshop, Boston, MA, May 2022

GPRC 5d Expression and Prognosis

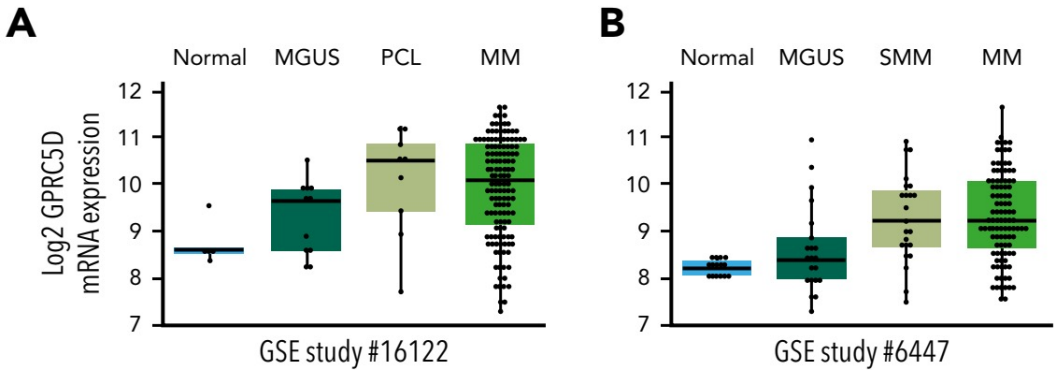
- G-protein–coupled receptor class 5member D(GPRC5D) is a type-C 7-pass transmembrane receptor protein
  - Orphan receptor - ligand and signaling mechanism unknown
  - No known shed peptides or extracellular domain shedding (reduced risk for sink effect)



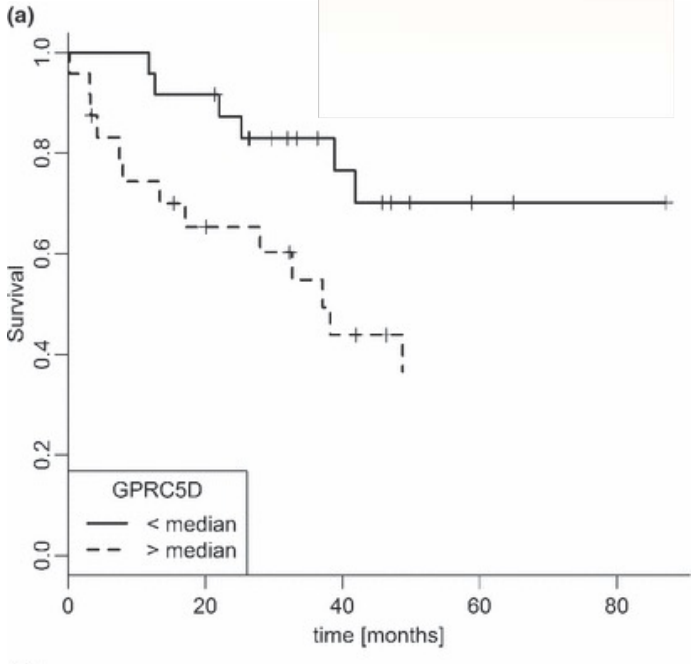
- Predominantly expressed in cells with a plasma-cell phenotype, including the majority of malignant plasma cells from patients with MM

- High GPRC5D expression associated with poor prognosis

GPRC mRNA expression



Pillarisetti K et al. Blood 2020;135(15):1232-1243



Atamaniuk J et al. Eur J Clinical Invest 2012;42(9):953-60

G-protein–coupled Receptor Class 5 member D(GPRC5D) Expression

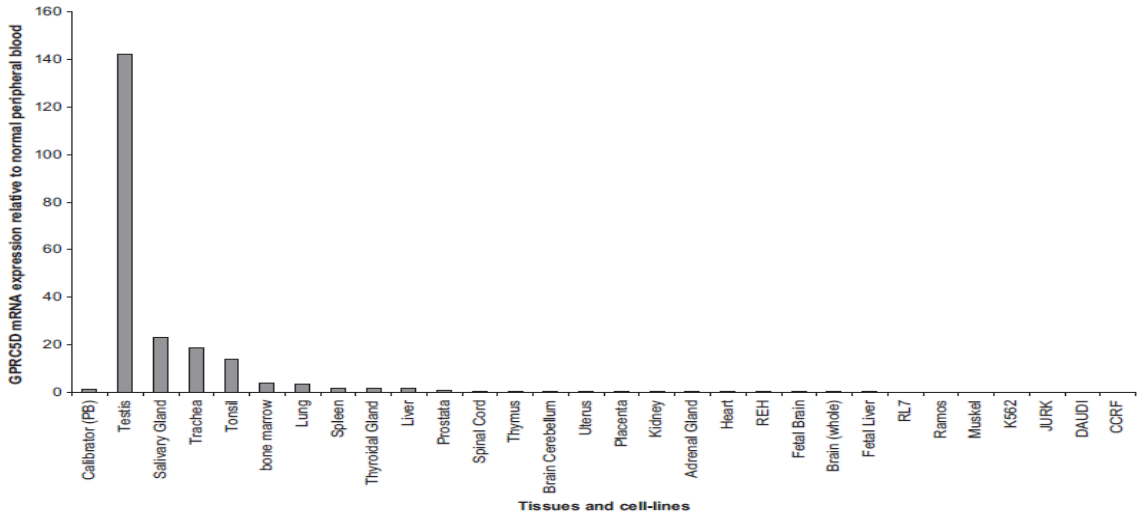
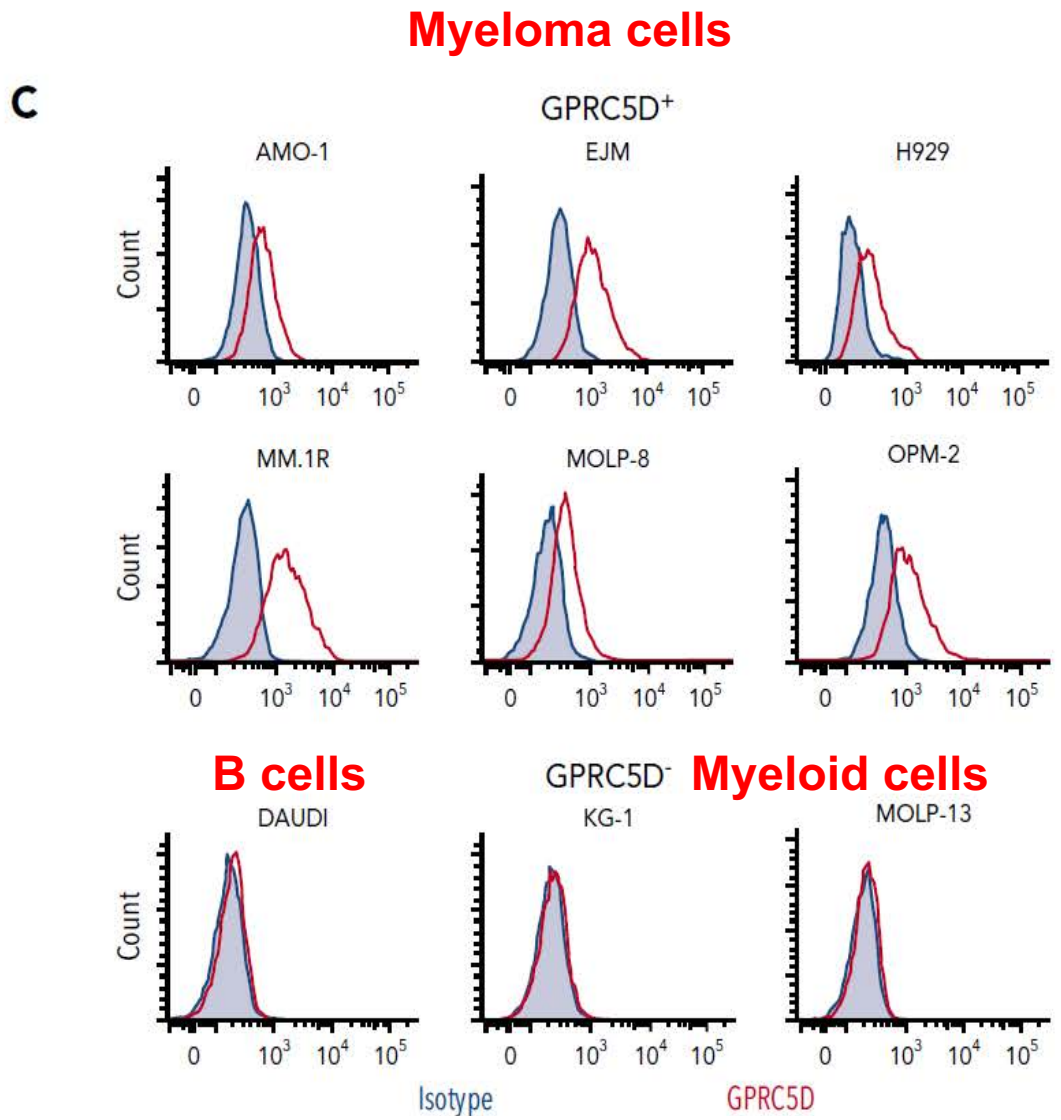


Figure 3 Expression of GPRC5D in different tissues and cell lines relative to normal peripheral blood. *x*-axis shows all analysed tissues, cell lines and controls. The *y*-axis represents GPRC5D mRNA expression relative to peripheral blood. Tissue samples showed highest results in testis (142-fold). Lower levels were found in salivary gland (23-fold), trachea (19-fold) and in tonsil (14-fold). In bone marrow and lung tissue, very low levels were detected (3·6-fold and 3·5-fold). Spleen, thyroid gland and prostate showed expressions, ranging from 0·9-fold to 1·5 fold. No expressions were found in uterus, spinal cord, kidney, adrenal gland, brain cerebellum, brain (whole), heart, foetal liver, foetal brain, thymus and placenta. In all cell lines, no expressions were detected.

Atamaniuk, et al. *Eu J Clinical Investigation* 2012

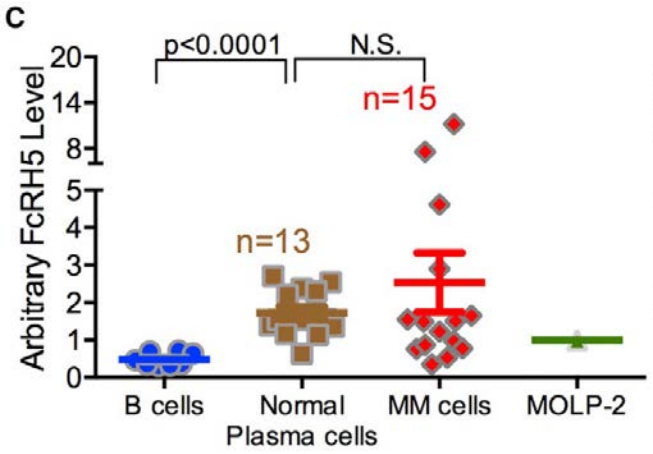


Pillarisetti, et al. *Blood* 2020

Fc receptor-homolog 5 (FcRH5) Protein and mRNA expression

- Surface protein in immunoglobulin superfamily, closely related to Fc receptors
- Ligand(s) for FcRH5 are unknown, but implicated in proliferation and isotype expression in the development of antigen-primed B cells
- FcRH5 protein and mRNA over-expressed in malignant plasma cells

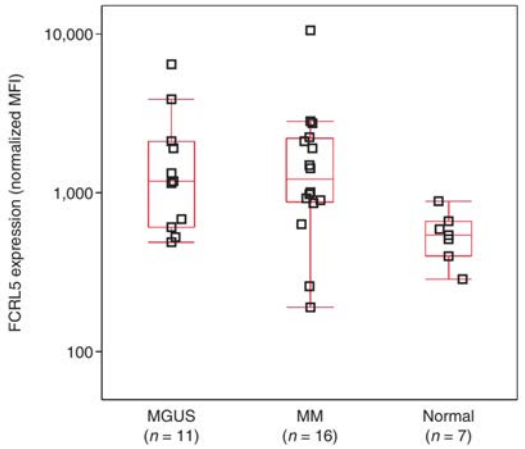
FcRH5 protein expression by flow cytometry



MGUS, monoclonal gammopathy of undetermined significance

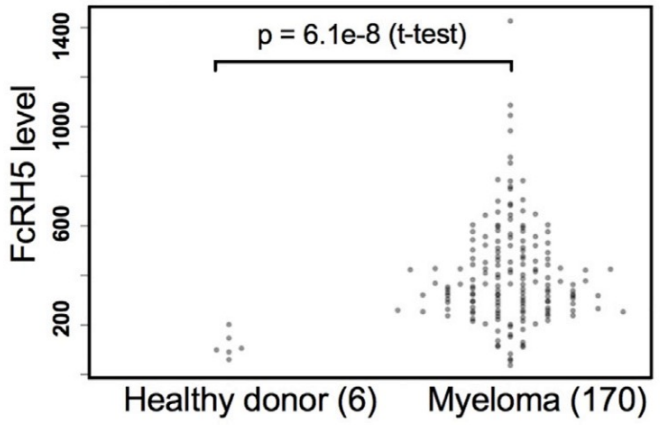
Li J et al. Cancer Cell 2017;31(3):383-395

FcRH5 protein expression by flow cytometry



Elkins K et al. Mol Cancer Ther 2012;11(10):2222-32

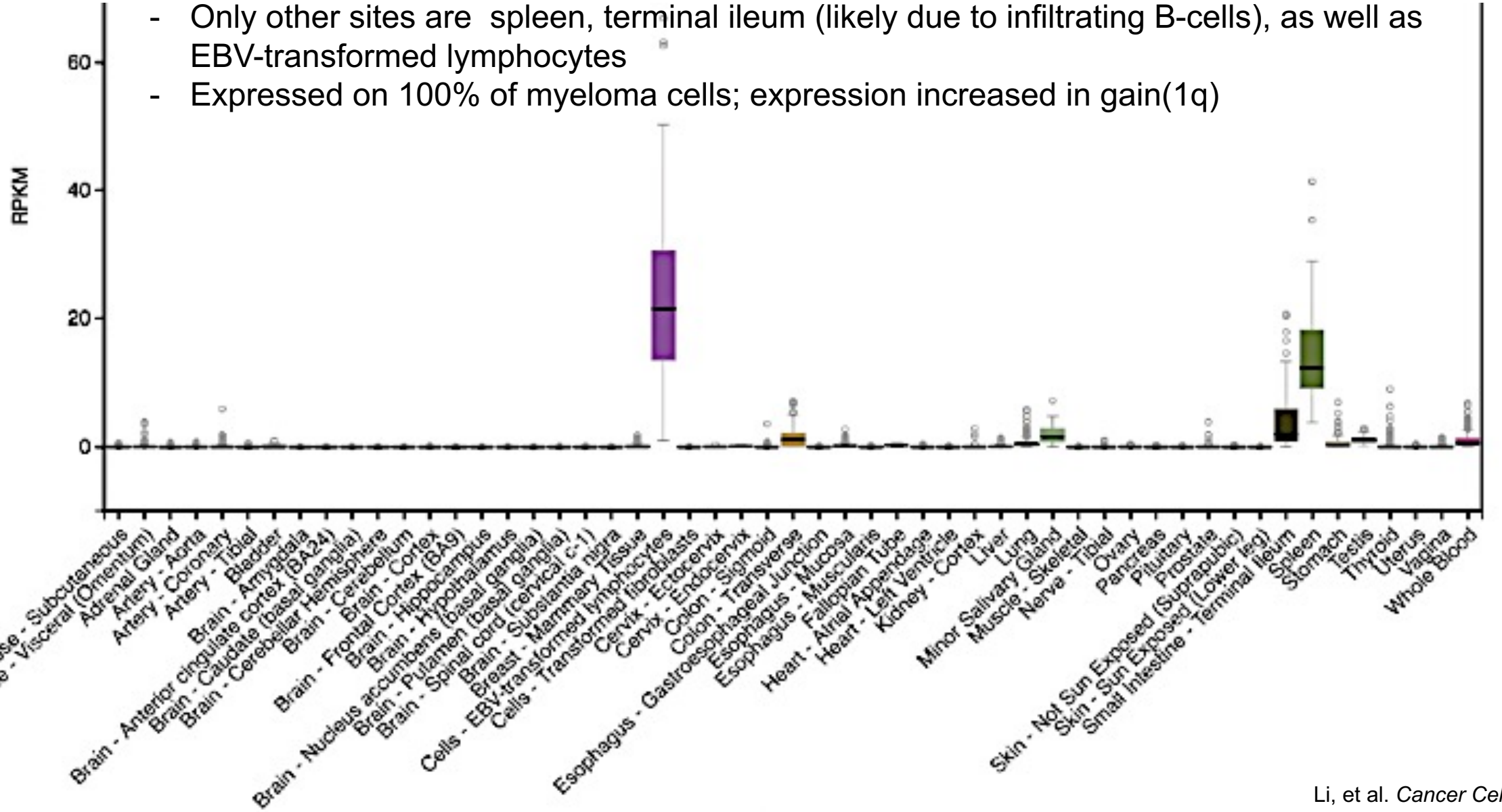
FcRH5 mRNA expression in CD138+ plasma cells



Li J et al. Cancer Cell 2017;31(3):383-395

Fc Receptor Homolog 5 (Fcrh5) Expression

- Expressed in B-cell lineage, from pre-B cells to plasma cells
- Only other sites are spleen, terminal ileum (likely due to infiltrating B-cells), as well as EBV-transformed lymphocytes
- Expressed on 100% of myeloma cells; expression increased in gain(1q)



Li, et al. *Cancer Cell* 2017

Non-BCMA-Targeted Bispecific Antibodies

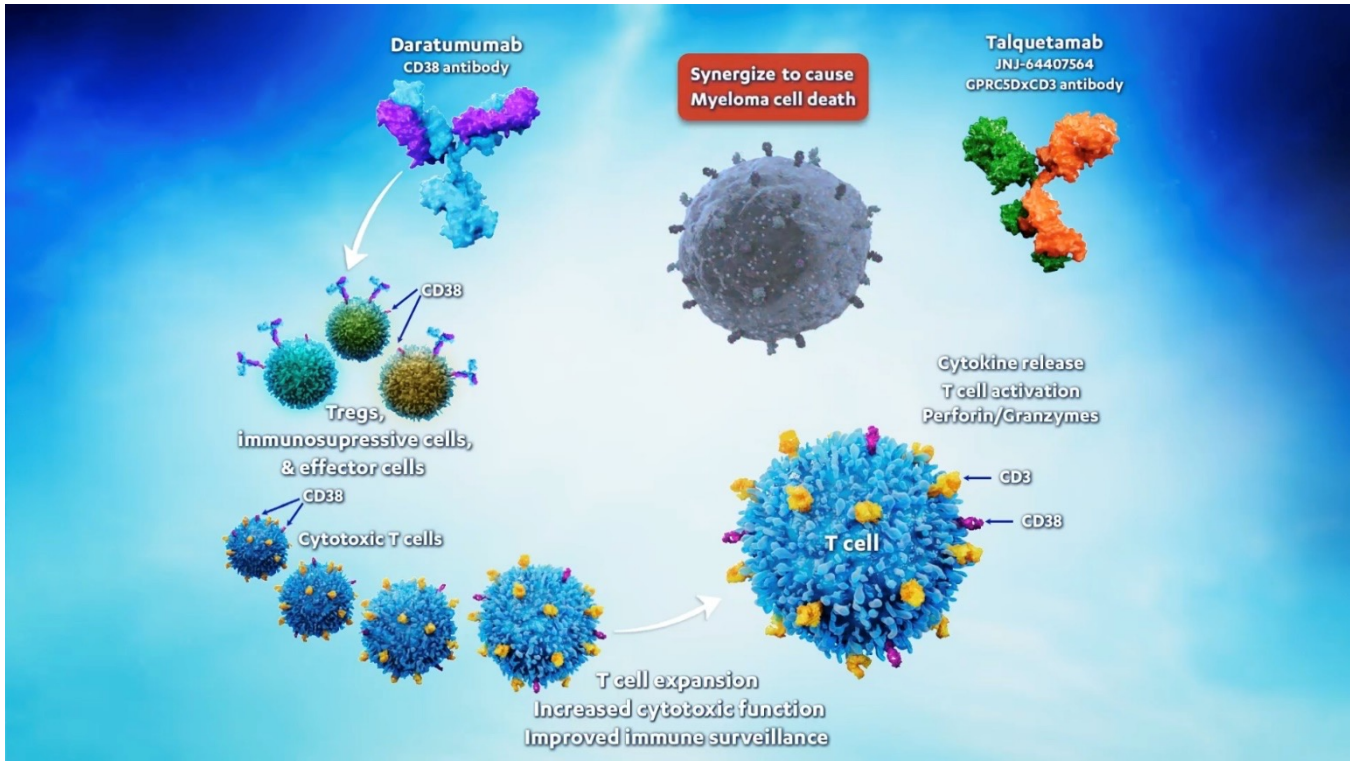
Bispecific Antibody	Anti-GPRC5d Talquetamab[a] Phase 1 MonumenTAL-1 Study		Anti-FcRH5 Cevostamab[c] Phase 1
Treatment	405 µg/kg SC QW (RP2D)	800 µg/kg SC QW	IV q3w
Patients	n=30	n=44	n=161
Median prior lines	6	5	6
Prior BCMA therapy	27%	16%	33%
Triple-class refractory	100%	98%	85%
Penta-drug refractory	80%	68%	68%
ORR at therapeutic dose	**21/30 (70%)**	**28/44 (64%)**	**132-198 mg: (56.7%)**
AEs, (All/(Gr 3+)			
CRS	77% (3%)	80% (0%)	80% (2%)
Infections	47% (7%)	34% (9%)	43% (19%)
Neutropenia	67% (53%)	36% (23%)	18% (16%)
Anemia	60% (27%)	36% (8%)	32% (22%)
Thrombocytopenia	37% (23%)	20% (8%)	% not reported
Deaths	33% (5%)	0%	6 (3.7%)
Dysgeusia	60% (N/A	36% (N/A)	Diarrhea 26% (1%)
Other	83%)	75%	
	Skin-related and nail disorders 75% G3 rash 7.5%		

- Minnema MC et al. ASCO 2022: Abstract 8015;

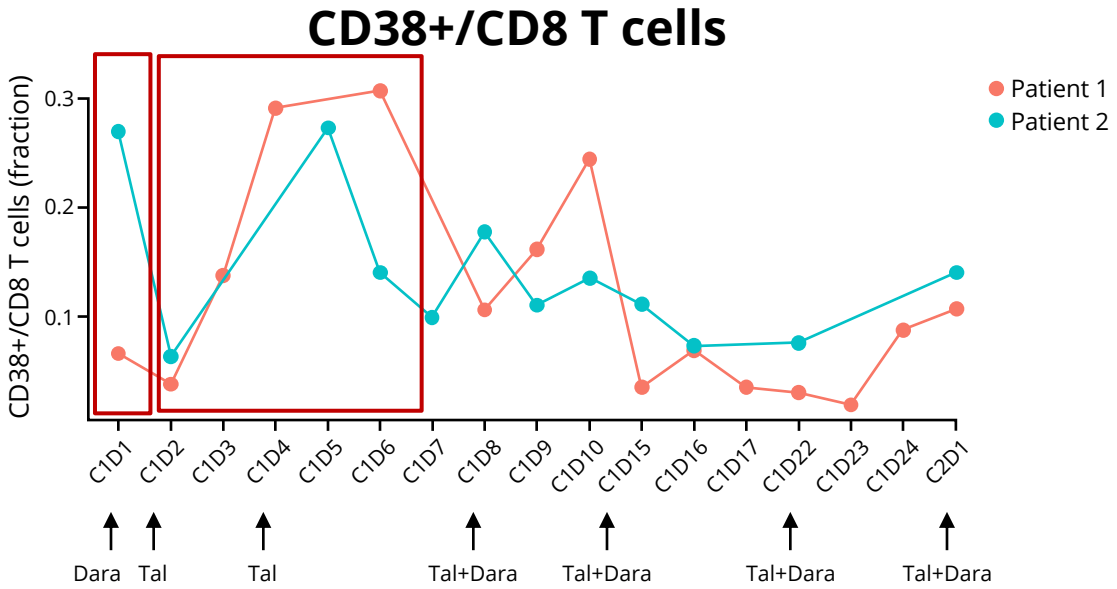
Trudel S et al, ASH 2021: Abstract 157.

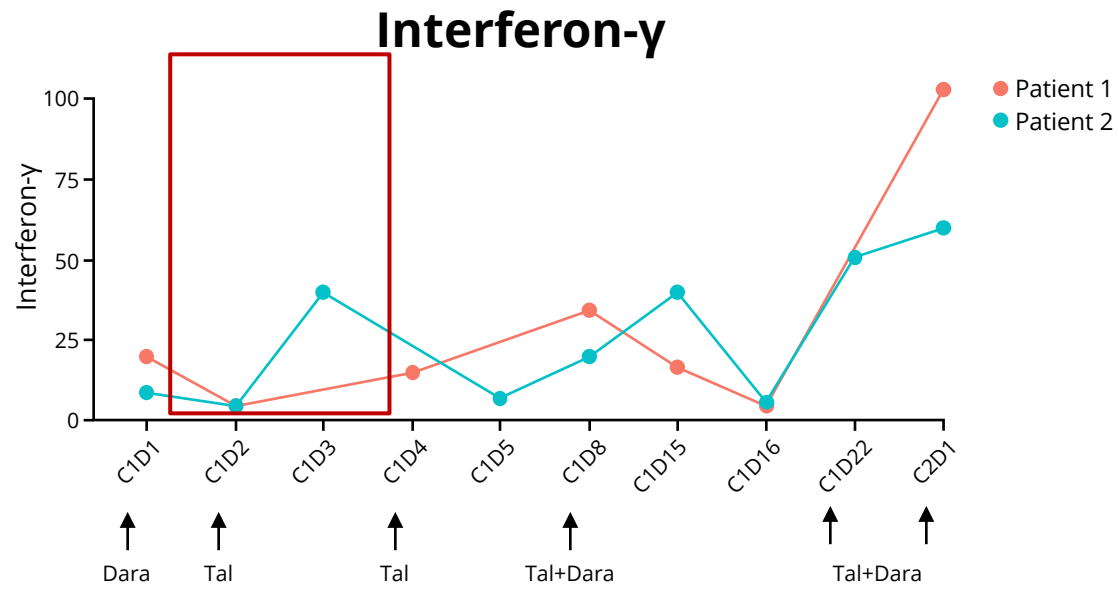
Talquetamab and Daratumumab: Rational Combination Partners

- Daratumumab (dara) is a human IgG1κ mAb targeting CD38 with a direct on-tumor and immunomodulatory mechanism of action[1]
  - Dara monotherapy leads to T cell expansion and enhanced T cell cytotoxic potential[2]
  - Talquetamab (tal; JNJ-64407564) is a novel, first-in-class antibody that binds to GPRC5D and CD3 receptors, mediating T cell recruitment, activation, and subsequent lysis of GPRC5D+ MM cells[3]
- The combination of tal and dara has the potential to yield synergistic clinical efficacy
  - Preclinical studies showed the addition of dara enhanced tal-mediated lysis of MM cells[4]



TRIMM-2: Tal + Dara Leads to Induction of CD38+/CD8+ T cells and Peripheral T-Cell Activation





- Peripheral T cell activation was observed with tal + dara, as evidenced by upregulation of CD38+/CD8+ T cells
  - The proportion of CD38+/CD8+ T cells declined after initial dara dosing on C1D1, consistent with previous data
  - **Notably, tal administration led to induction of CD38+ T cells after C1D2 despite concurrent dara treatment**
- Induction of pro-inflammatory cytokines was observed following tal dosing in presence of dara
- The pharmacokinetic profile of tal in the presence of dara was consistent with the profile observed in the phase 1 tal monotherapy (MonumenTAL-1)

.Chari et al ASH 2021, abstract 161

Non-BCMA-Targeted Bispecific Antibodies

Bispecific Antibody	Anti-GPRC5d Talquetamab[a] Phase 1 MonumenTAL-1 Study		Anti-GPRC5d Talquetamab + Daratumumab Phase 1b TRIMM 2 Study [b]
Treatment	405 µg/kg SC QW (RP2D)	800 µg/kg SC QW	400 qwk & 800 ug/kg q2wk
Patients	n=30	n=44	n=29
Median prior lines	6	5	6
Prior BCMA therapy	27%	16%	**55%**
Triple-class refractory	100%	98%	79%
Penta-drug refractory	80%	68%	66%
ORR at therapeutic dose	**21/30 (70%)**	**28/44 (64%)**	**17/21 (81%)**
AEs, (All/(Gr 3+)			
CRS	77% (3%)	80% (0%)	55% (0%)
Infections	47% (7%)	34% (9%)	35% (10%)
Neutropenia	67% (53%)	36% (23%)	41% (31%)
Anemia	60% (27%)	36% (8%)	31% (21%)
Thrombocytopenia	37% (23%)	20% (8%)	35% (21%)
Deaths	33% (5%) 0%		0
Dysgeusia	60% (N/A	36% (N/A)	48% (N/A)
Other	83%) Skin-related and nail disorders 75% G3 rash 7.5%	75%	Skin & nail 65% G3 rash 10%

- Minnema MC et al. ASCO 2022: Abstract 8015; Chari A et al, ASH 2021: Abstract 161;

Conclusions

- Historically, 20-30% ORR and PFS of 3-4 months in unmet need of RRRM for novel agent to attain accelerated approval in US
- T cell redirection therapies are generating unprecedented response rates and bispecifics with wide therapeutic index
- TNF super family includes the plasma cell specific B-cell maturation antigen (BCMA) receptor for the ligands BAFF and APRIL that regulate B cell activation
- Anti BCMA off the shelf bispecifics ORR ~ 60-80% in phase 1 studies with wide therapeutic index - but very competitive market and differentiating factors will be
  - **Time to market, efficacy, safety** (CRS, neuropathy, infections), **convenience** (outpt/ability to give in community, priming, route, and frequency), and **cost** (especially if IVIG required)
  - Lack of COVID vaccine response and COVID deaths warrants vaccination prior to start and reinforcement of Mab SQ prophlyaxis, po/Mab IV outpt therapy, convalescent plasma inpt therapy

Conclusions

- Cevostamab novel agent encouraging, minimal non heme toxicity, ? COVID/infection
- Talquetamab novel agent, lack of infection, oropharyngeal/cutaneous supportive care cocktail
- Given pt selection (non explosive disease at consent and adequate labs at LD), bridging chemo , CART PFS will need to be > 1 year to be competitive with bispecific in ITT analysis
- Combination strategies + dara (highest BCMA exposure population to date) +/- pom very encouraging
- Data in earlier lines of therapy, high risk, PK of extramedullary and heavy tumor burden, RCTs eagerly awaited

Appendix – Additional Faculty Cases

Case Presentation – Dr Flinn: A 72-year-old man with mantle cell lymphoma

- 10/20 Diagnosed with stage 4 mantle cell lymphoma including bulky adenopathy, bone marrow involvement and cutaneous nodules
- Pathology revealed mantle cell lymphoma, Ki-67 = 60%, no TP53 abnormalities, complex cytogenetics
- RDHAOx X 4 with plan for auto BMT but progressed
- Zanubrutinib X 2 months with PD
- 11/21 Brexu-Cel
- Course complicated Grade 1 CRS and Grade 2 ICANs
- Day 30 PET reveals CR. Remains in CR 9 months later

Case Presentation – Dr Sehn: A 69-year-old woman with Stage IVA follicular lymphoma

- **69 yo female with history of stage 4A follicular lymphoma diagnosed in 2012, not requiring therapy**
- **In September 2020 (age 77 years), she developed a rapidly enlarging thigh mass (>10 cm), with biopsy confirming DLBCL (GCB subtype, not double-hit) in keeping with transformation**
- **Treated with R-CHOP x 6 cycles (dose reduced) achieving a CR**
- **She was well until January 2022 when she had local recurrence as well as diffuse lymphadenopathy, biopsy confirmed DLBCL**
- **She received R-GDP x 1 cycle with minimal benefit**

Case Presentation – Dr Sehn: A 69-year-old woman with Stage IVA follicular lymphoma (continued)

- **In June 2022, she received CAR T-cell therapy (with tisa-cel), which was well tolerated**
- **Course complicated by persistent cytopenias, and red cell transfusion requirement**
- **PET scan at 1 month demonstrates a CR**

Case Presentation – Dr Sehn: A 33-year-old woman with primary mediastinal B-cell lymphoma

- **33 yo female**
- **Presented with bulky mediastinal mass in May 2020 (14 cm with local extension into lung), elevated LDH**
- **Biopsy: PMBCL**
- **Treated with DA-EPOCHR x 6 for bulky stage 4 disease**
- **Post-treatment PET showed excellent response with only minor focal uptake in mediastinum, Deauville 4**
- **She was initially observed, but PET/CT at 3 months showed evidence of progression**

- **In Feb 2021, she received R-GDP x 2 with plan for ASCT**
- **Due to further progression, transplant cancelled**

Case Presentation – Dr Sehn: A 33-year-old woman with primary mediastinal B-cell lymphoma (continued)

- **In May 2021, she received CAR T-cell therapy (with axi-cel), which was well tolerated**
- **No significant complications**
- **PET scan demonstrated a CR, which has persisted for >1 year**

Case Presentation – Dr Flinn: A 37-year-old man with follicular lymphoma

- 5 years ago presented with axillary adenopathy, Stage 4 disease with bone marrow involvement
- PMH significant for type 1 diabetes
- BR X 6 PET – CR
- Maintenance rituximab X 2 years
- PD 6 months after completing rituximab
- CVP X 6 with PR but progresses 3 months later
- 5/21 starts on CD20 bispecific antibody
- Initial PET scan concerning for PD but remained on treatment and achieved Deauville of 3 and Deauville of 1
- Course complicated by COVID and joint infection. Despite being off therapy for 3 months remains in CR
- AEs including rash and peeling skin on palms of hands

Case Presentation – Dr Flinn: A 75-year-old woman with Richter's Transformation

- 75 yo woman originally diagnosed with SLL, 17p deletion, MYB deletion, mutated IGHV
- Enrolled on trial with Idelalisib but 8 months later is diagnosed with Richter’s transformation
- RCHOP X 6 achieves CR
- 30 months later relapses with DLBCL
- Receives 1 year of CD20 bi-specific antibody and achieves CR
  - Only significant AEs are infusion reaction with first infusion, rash and fatigue
- Maintains remission for 14 months but develops recurrence in rectus muscle of right eye

Case Presentation – Dr Sehn: A 78-year-old man with Grade I-II follicular lymphoma

- **78 yo male**
- **Presented with diffuse lymphadenopathy above and below the diaphragm, and bilateral pleural effusions in Feb 2013**
- **Cervical LN biopsy: follicular lymphoma grade 1-2, bone marrow biopsy positive**
- **Treated with R-CVP, progressed after 3 cycles**
- **Switched to clinical trial and received Bendamustine and Obinutuzumab x 6 cycles and achieved a CR (followed by Obinutuzumab maintenance x 2 y)**
- **In April 2018, at age 83 years, had evidence of progressive lymphadenopathy (>8 cm in abdomen), with fatigue and abdominal pressure, no evidence of transformation**

Case Presentation – Dr Sehn: A 78-year-old man with Grade I-II follicular lymphoma (continued)

- **Treated with mosunetuzumab monotherapy on phase I/II trial**
- **Received 8 cycles per protocol, achieving a CR, and has been on observation ever since**
- **No relevant toxicity, but developed neutropenia that persisted post-therapy and gradually resolved**

Case Presentation – Dr Munshi: CAR T Cell Therapy Eligibility

5/8/2017 **70 year old male with Initial Diagnosis IgG Kappa Multiple myeloma, R-ISS-2, Creatinine – 3.1**

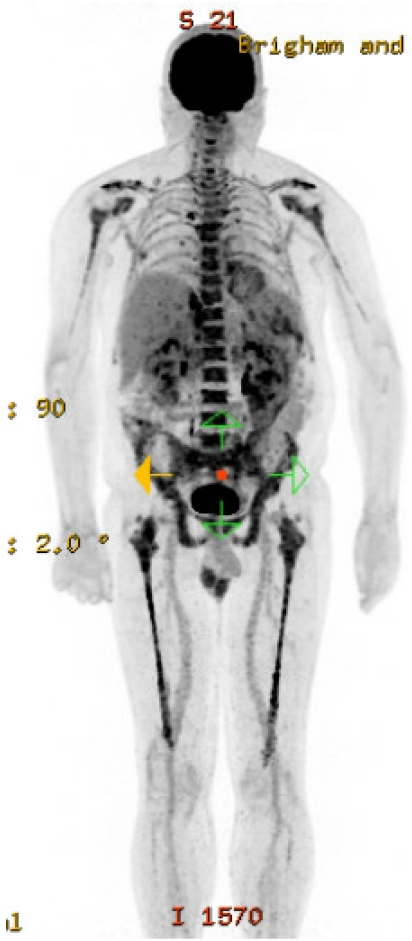
5/12/2017 - 9/8/2018	Initially VCD followed by RVD -> RD maintenance - VGPR with Creatinine 1.6
10/2018 - 1/2019	Carfilzomib+Pomalidomide+Dexamethasone
1/23/2019 - 4/5/2020	Daratumumab+Pomalidomide+Dexamethasone
4/5/2020 - 8/2020	Elotuzumab+Pomalidomide+Dexamethasone
8/2020 - 8/30/2020	**Radiation -** XRT to Pancreas
8/20/21 - 12/23/2021	Carfilzomib+Pomalidomide+Dexamethasone

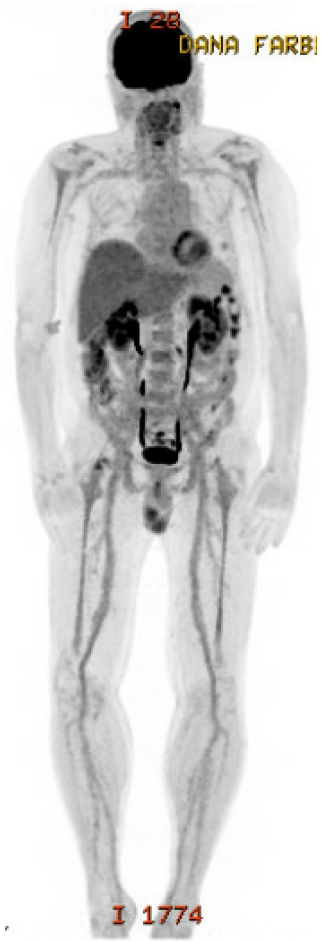
Relapsed with New extramedullary disease, Creatinine 3.1, Ejection fraction 49%, SFLR 631 (Kappa FLC – 6220 mg/dL)

Case Presentation – Dr Munshi: Post CAR T management

- 69 year old male
- 07/2017 - RVDx6 followed by HDT and ASCT – PR and RD maintenance
- 02/2018 - relapsed- Daratumumab with PD
- 05/2018 - Venetoclax with carfilzomib and Dex.
- 07/2019 - progressive disease – eligible for CAR-T protocol
- Following lymphodepletion CAR-T infusion was postponed due to high grade fever with High CRP.
- Fever eventually considered due to aggressive myeloma
- He did develop CRS and required one infusion of Toci

Ref. Range	7/02/19	7/19/19	8/2019	9/2019	10/2019	11/2019
Lambda FLC(mg/L)	10,079.8	752.8	24.9	11.8	34.6 (H)	117.7 (H)





07/03/2019 08/08/2019

7/10/2019
CAR-T
Infusion

- **Started on Elotuzumab, Thalidomide and Dex**
- **Excellent response sustained over 15 months**

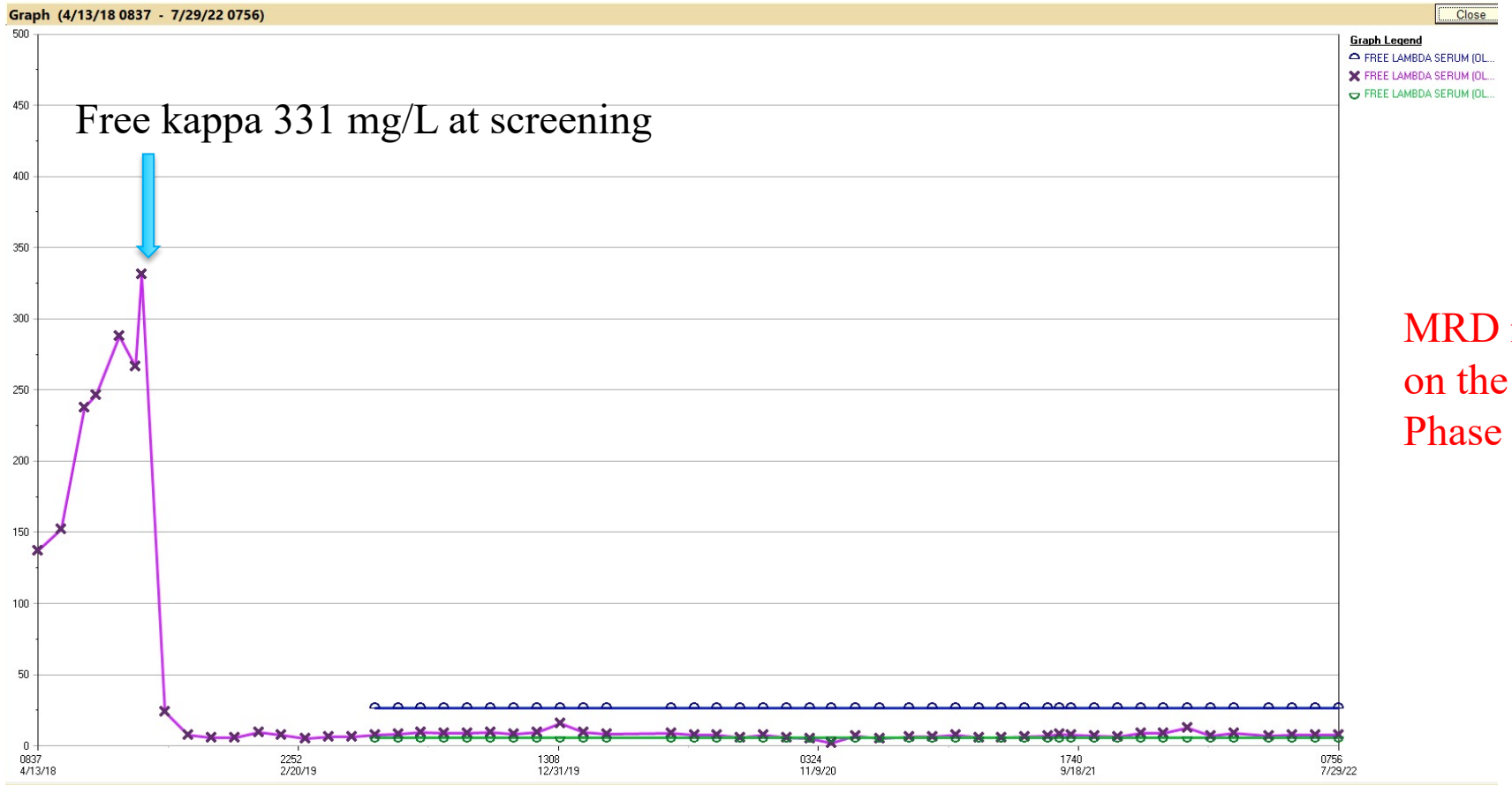
Case Presentation – Dr Chari: Triple Class Refractory MM Patient on Talquetamab

IgG lambda MM ISS 1 (B2M 2.86) and DS 1A. cyto/FISH not reported

63 yo F Hg 10.8, IgG 2236 mg/dl, m spike 1.59 mg/dl, lambda 3279 mg/L BM Bx 1/6/12 50% lambda PC.

1. First line therapy: RVD 7/10/12 X 3, S/P mel 200 m/g/m2 ASCT 08/10/2012 with VGPR+, followed by Len maintenance with PD10/26/2015
2. Second line therapy: atezolizumab PDL1 Ab + len 10 mg C1D1 11/24/2015 x 5 cycles then PD
3. Third line therapy: Elo/Pom/Dex trial C1D1 4/27/16 x13 cycles then PD.
4. Fourth line therapy: Dara SC study C1D1 5/23/17 x9 cycles then PD .
5. Fifth line therapy: C1 Dara (IV)/Bortezomib 2/9/18- * 6 cycles then Dara/Ixa/Dex 4/13/18 with PD
6. Sixth line therapy: Talquetamab IV C1D1 8/16/18 @ 1.5 mcg/kg c/b grade 1 CRS treated with toci. Grade 1-2 cytopenias during C1-2, transient grade 1 dysgeusia * 2-3 days (no weight loss), grade 1 nail changes recently resolved.

Case Presentation – Dr Chari: Triple Class Refractory MM Patient on Talquetamab (Continued)

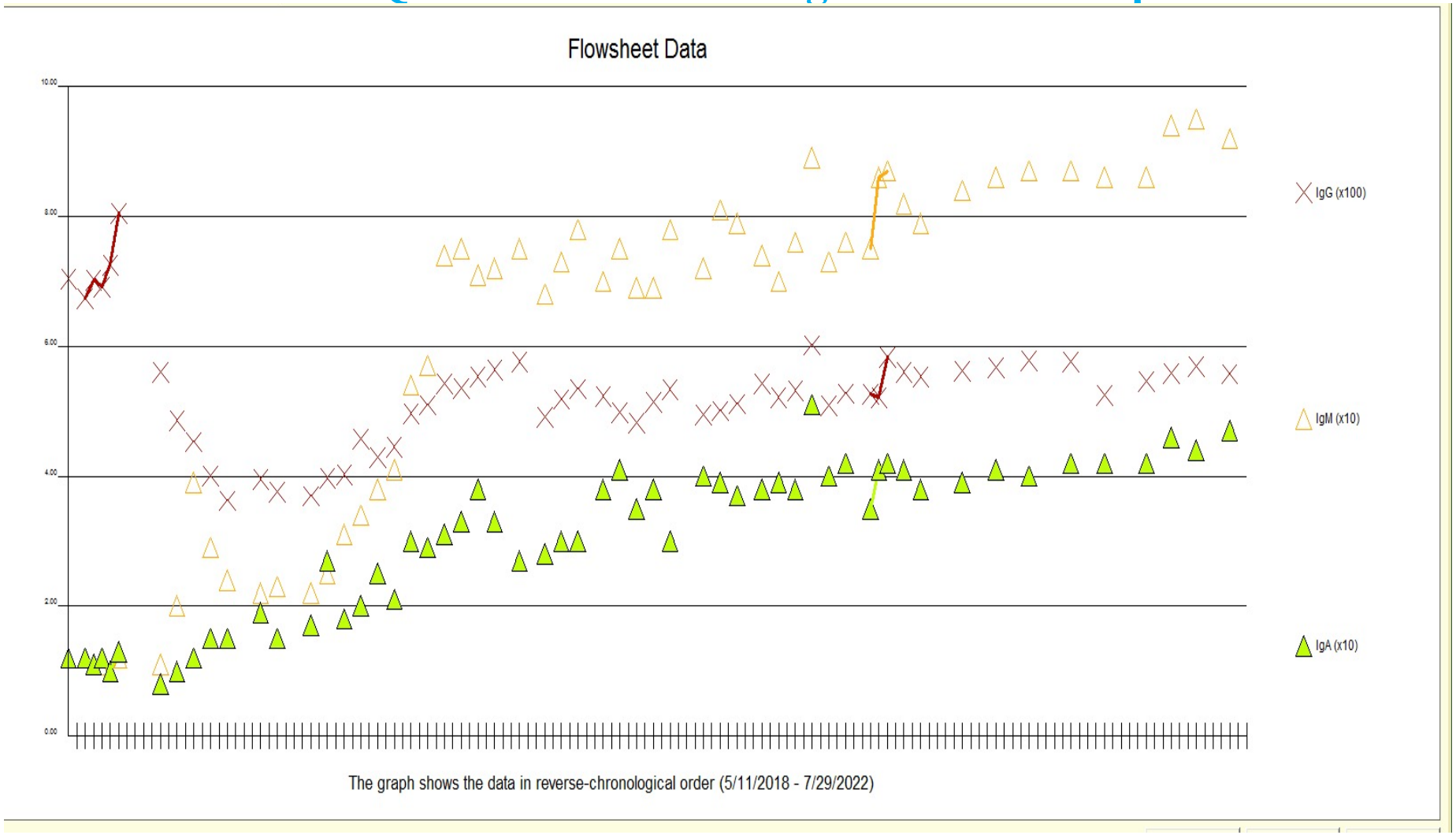


MRD neg sCR for 4 years+ on the lowest dose of a Phase 1 *dose escalation* study

	6/25/2019	2/17/2021
% MRD +	0.0000	0.0000
NON-AGGREGATE EVENTS	9388963	5960471
ABNORMAL PC EVENTS	0	0

Case Presentation – Dr Chari: Triple Class Refractory MM Patient on Talquetamab (Continued)

Triple Class Refractory MM Patient on Talquetamab: Quantitative Immunoglobulins on Talquetamab Over Time



+COVID antibodies in response to vaccinations

Meet The Professor

Optimizing the Management of Small Cell Lung Cancer

Thursday, August 11, 2022
5:00 PM – 6:00 PM ET

Faculty

Jacob Sands, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

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

RTP
RESEARCH
TO PRACTICE