MYELOMA ROUNDS DURHAM

Tuesday, March 4, 2025
5:30pm – 8:35pm

Hilton Durham Near Duke University
Durham, NC

This activity is provided by The Leukemia & Lymphoma Society and Medical Learning Institute Inc, in collaboration with the Association of Cancer Care Centers™ (ACCC).

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WELCOMING REMARKS

Cindy Varga, MD
Associate Professor
Atrium Health Levine Cancer Institute
Plasma Cell Dyscrasia Division
Department of Hematology and Oncology
Charlotte, NC

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TARGET AUDIENCE

This activity is intended for hematologists-oncologists, medical oncologists, physician associates, nurse practitioners, nurses and pharmacists involved in the care of patients with myeloma.

EDUCATIONAL OBJECTIVES

At the conclusion of this activity, participants will be better able to:

- Describe the latest developments in myeloma, including current and emerging treatments
- Engage patients and caregivers in clinical trials discussions on newly approved therapies and emerging therapies for myeloma, including combination therapies, CAR T-cell therapy and bi-specific antibodies
- Explain disparities and challenges in diagnosis and treatment of myeloma
- Apply evidence-based treatment strategies for optimal patient care
- Identify patient education and support resources

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AGENDA

5:30 pm	Dinner and Networking
6:30 pm	Welcome and Overview of Program *Cindy Varga, MD*
6:35 pm	Overview of LLS Resources, including the Clinical Trial Support Center *Christen Hawthorne, RN, BSN, BMT-CN*
6:40 pm	Updates in Multiple Myeloma Clinical Research *Eben Lichtman, MD*
6:55 pm	Case Presentation on Bispecifics in the Community and Discussion* Sendhilnathan (Hari) Ramalingam, MD and Cindy Varga, *MD*
7:25 pm	Case Presentation on High-risk Smoldering Multiple Myeloma and Discussion* *Kimberly Burcher, MD and Cristiana Costa Chase, DO*
7:55 pm	Case Presentation on Maintenance Therapy in Transplant Eligible and Discussion* *John Mckay, DO and Sean Ormond, MD*
8:25 pm	Discussion and Wrap-up *All Faculty*
8:35 pm	Conclusion *Cindy Varga, MD*

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***Guest discussants:** Cristina Gasparetto, MD, Yubin Kang, MD, and Peter Voorhees, MD

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ADVISORY GROUP/FACULTY

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Sendhilnathan (Hari) Ramalingam, MD
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Duke Adult Blood and Marrow Transplant Clinic
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Guest Discussants: Cristina Gasparetto, MD, Duke Cancer Institute; Yubin Kang, MD, Duke Cancer Institute; and Peter Voorhees, MD, Atrium Health Levine Cancer Institute .

** Advisory Group and Faculty*

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ADVISORY GROUP & FACULTY DISCLOSURES

*Cindy Varga, MD (Chair), has a financial interest/relationship or affiliation in the form of:
Consultant/Advisor: Janssen
Research Funding: ARCELLX/Kite, Janssen, K36

Kimberly Burcher, MD, has no relevant financial relationships with ineligible companies to disclose for this educational activity.

*Cristiana Costa Chase, DO, has a financial interest/relationship or affiliation in the form of:
Speaker's Bureau: Sanofi

Grace Elsey, PharmD, BCOP, has a financial interest/relationship or affiliation in the form of:
Consultant/Advisor: Jazz Pharmaceuticals (ended 10/2024)

Christen Hawthorne, RN, BSN, BMT-CN, has no relevant financial relationships with ineligible companies to disclose for this educational activity.

*Eben Lichtman, MD, has a financial interest/relationship or affiliation in the form of:
Consultant/Advisor: AbbVie (ended 12/2024)
Research Funding (PI on clinical trials): AbbVie, Bristol Myers Squibb, GlaxoSmithKline, IGI (formerly Ichnos), Poseida, Sanofi

*John Mckay, DO, has a financial interest/relationship or affiliation in the form of:
Consultant/Advisor: BioLineRx, Bristol Myers Squibb, Johnson and Johnson

Sean Ormond, MD, has no relevant financial relationships with ineligible companies to disclose for this educational activity.

Sendhilnathan (Hari) Ramalingam, MD, has a financial interest/relationship or affiliation in the form of:
Research Funding: GlaxoSmithKline

Guest Discussants:
Cristina Gasparetto, MD, has a financial interest/relationship or affiliation in the form of:
Consultant/Advisor: Bristol Myers Squibb, Janssen, Karyopharm, Pfizer, Sanofi
Honorarium: GlaxoSmithKline
Speaker's Bureau: Bristol Myers Squibb, Janssen, Karyopharm, Pfizer, Sanofi

Yubin Kang, MD, has no relevant financial relationships with ineligible companies to disclose for this educational activity.

Peter Voorhees, MD, has a financial interest/relationship or affiliation in the form of:
Consultant/Advisor: AbbVie, Ascentage Pharma, AstraZeneca, Bristol Myers Squibb, GlaxoSmithKline, Johnson and Johnson, Karyopharm, Kite, Pfizer, Regeneron, Sanofi
Research Funding: AbbVie, GlaxoSmithKline, Johnson and Johnson

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**** Part of the faculty and advisory board***
All of the relevant financial relationships of individuals for this activity have been mitigated.

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Disclosure & Conflict of Interest Policy
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Lauren Berger, MPH, has a financial interest/relationship or affiliation in the form of:
Stock Ownership with Bristol Myers Squibb, Gilead Sciences, Inc., Merck & Co., Inc., Organon & Co., Pfizer Inc., and Viatris Inc.

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Disclaimer
Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this CE activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this CE activity should not be used by clinicians without evaluation of their patient's conditions and possible contraindications and/or dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

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CE DESIGNATION

Accreditation, Support and Credit
In support of improving patient care, this activity has been planned and implemented by Medical Learning Institute Inc and The Leukemia & Lymphoma Society. Medical Learning Institute Inc 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.

Physician Continuing Medical Education
Medical Learning Institute Inc (MLI) designates this live activity for a maximum of 2.0 *AMA PRA Category 1 Credits™*.
Physicians should claim only the credit commensurate with the extent of their participation in the activity.

MOC Statement
Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2.0 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Participation information will be shared through the ACCME's Program and Activity Reporting System (PARS).

For Physicians requesting MOC credit, the post-test and evaluation are required in their entirety as well as your ABIM ID number, DOB (MM/DD), and a score of 70% or higher is needed to obtain MOC credit.

Physician Associate
Medical Learning Institute Inc has been authorized by the American Academy of PAs (AAPA) to award AAPA Category 1 CME credit for activities planned in accordance with AAPA CME Criteria. This activity is designated for 2.0 AAPA Category 1 CME credits. PAs should only claim credit commensurate with the extent of their participation.

Nursing Continuing Professional Development
Approval for nurses has been obtained by the National Office of The Leukemia & Lymphoma Society under Provider Number CEP 5832 to award 2.0 continuing education contact hours through the California Board of Registered Nursing.

Pharmacy
Medical Learning Institute Inc designates this application-based continuing education activity for 2.0 contact hours (0.2 CEUs) of the Accreditation Council for Pharmacy Education.
Universal Activity Number: JA0007322-9999-25-005-L01-P

Interprofessional Continuing Education Credit
This activity was planned by and for the healthcare team, and learners will receive 2.0 Interprofessional Continuing Education (IPCE) credits for learning and change.

Support Statement
There is no commercial support associated with this activity.

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INSTRUCTIONS FOR CREDIT

There are no fees for participating in or receiving credit for this CE activity. In order to receive credit, learners must participate in the entire CE activity, complete the evaluation form. A certificate of completion will be emailed within 30 days of receipt. If you have questions regarding the receipt of your certificate, please contact us via email at ndane@mlieducation.org.

For information on applicability and acceptance of continuing education credit for this activity, please consult your professional licensing board.

For Physicians requesting MOC credit, the post-test and evaluation are required in their entirety as well as your ABIM ID number, DOB (MM/DD), and a score of 70% or higher is needed to obtain MOC credit.

For Pharmacists, Medical Learning Institute will accept your completed evaluation form for up to 30 days post-activity and will report your participation to the NABP only if you provide your NABP e-Profile number and DOB (MM/DD). Within 6 weeks, you can view your participation record at the NABP website: https://nabp.pharmacy/

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Christen Hawthorne, RN, BSN, BMT-CN
Clinical Trial Nurse Navigator
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Rye Brook, NY

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Our Mission:
Cure blood cancer and improve the quality of life of all patients and their families.

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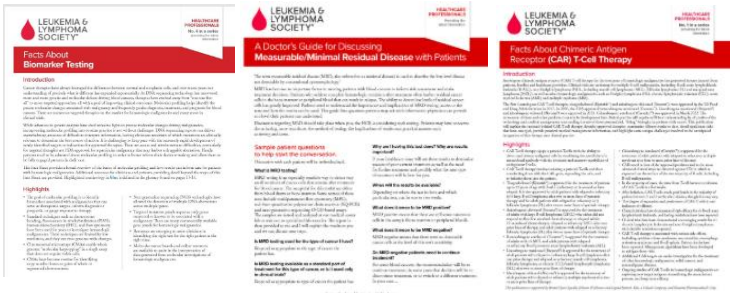
FREE LLS RESOURCES FOR HEALTHCARE PROFESSIONALS

- ❑ CME & CE courses: www.LLS.org/CE
- ❑ Fact Sheets for HCPs: www.LLS.org/HCPbooklets
- ❑ Videos for HCPs: www.LLS.org/HCPvideos
- ❑ Podcast series for HCPs: www.LLS.org/HCPpodcast



Myeloma Fact Sheet Coming Soon!

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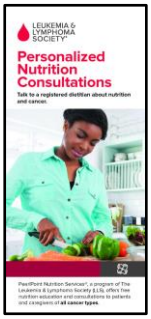
FREE LLS RESOURCES FOR PATIENTS

- **Information Specialists** – Personalized assistance for managing treatment decisions, side effects, and dealing with financial and psychosocial challenges (IRC).
  - www.LLS.org/IRC
- **Nutrition Education Services Center**–Free one-on-one consultations with registered dieticians for patients/caregivers of all cancer types by phone or email.
  - www.LLSnutrition.org
- **Clinical Trial Nurse Navigators** – RNs and NPs provide personalized service for patients seeking treatment in a clinical trial, sift through information and provide information to bring back to their HC team (CTSC).
  - www.LLS.org/CTSC
- **Reach out Monday – Friday, 9 am to 9 pm ET**
  - Phone: (800) 955-4572
  - Live chat and Email: www.LLS.org/IRC
  - HCP Patient Referral Form: www.LLS.org/HCPreferral
- **Webcasts, Videos, Podcasts, Booklets**



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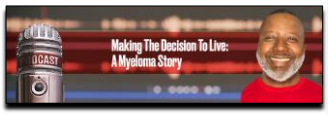
FREE LLS RESOURCES FOR PATIENTS AND CAREGIVERS

- www.LLS.org/Myeloma
- **Webcasts, Videos, Podcasts, booklets**:
  - www.LLS.org/Webcasts
  - www.LLS.org/EducationVideos
  - www.LLS.org/Podcast
  - www.LLS.org/Booklets



- **Support Resources**
  - Financial Assistance: www.LLS.org/Finances
    - Urgent Need
    - Patient Aid
    - Travel Assistance
  - Other Support: www.LLS.org/Support
    - LLS Regions
    - Online Weekly Chats Facilitated by Oncology SW
    - LLS Community Social Media Platform
    - First Connection Peer to Peer Program

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FREE LLS RESOURCES FOR YOUR PATIENTS

- ❑ www.LLS.org/Myelomalink

BOOKLETS AND FACT SHEETS

English – www.LLS.org/Booklets
Spanish – www.LLS.org/Materiales

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CTSC PROCESS FOR SUPPORTING PATIENTS

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HERE TO HELP: LLS COMMITMENT

LLS is committed to providing education and resources to help patients access clinical trials.

CLINICAL TRIAL SUPPORT CENTER

- A team of **highly trained** nurses and nurse practitioners experienced with hematological malignancies and clinical research.
- Provide **education** to patients about clinical trials, treatment options, and other disease specific information.
- Provide patients, families, and their caregivers with a professional, detailed, **individualized** search to discuss with their HCP.
- Provide **guidance** and serve as **advocates** throughout the clinical trial process. Help make connections between the patient and the trial site to facilitate enrollment as appropriate.
- Provide a **personal connection** and develop long term relationships to help better serve our patients.
- We serve as a **bridge** between technology and patients to make accessing clinical trial information easier.

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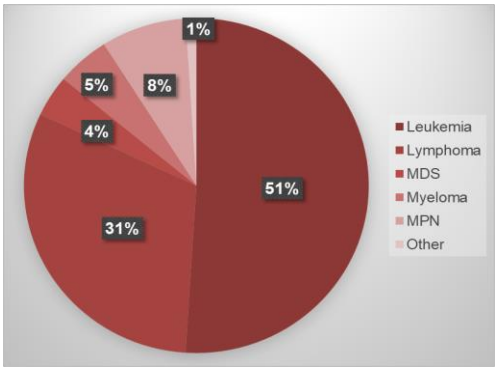
CTSC PATIENT OUTCOMES

- 12 CTSC nurse navigators assisted a total of 1,142 patients
- Nurse navigators had over 10,454 interactions with all patients, caregivers & medical professionals
- **20% of eligible patients enrolled into a clinical trial***
- **Reasons patients did not enroll:**
  - Not clinically indicated for treatment change
  - Team recommended treatment other than trial
  - Insurance constraints
  - No trial available within preferred geography
  - Financial constraints



Disease Category Breakdown of Patients That Entered Into A Clinical Trial

***8-10% of adult cancer patients enroll nationwide annually**

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THE CLINICAL TRIAL SUPPORT CENTER TEAM

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CPNP, MSN, RN, CPHON
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MSN, APRN, AGCNS-BC, OCN, BMTCN
Clinical Trial Nurse Navigator

Michelle Bibo
CTSC Operations Specialist

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HOW TO ACCESS THE CLINICAL TRIAL SUPPORT CENTER

Call the Information Resource Center (IRC) 1-800-955-4572

Patients or caregivers can complete an online referral form at:
https://www.LLS.org/navigation

Healthcare Professionals can complete a referral form at:
https://www.LLS.org/article/clinical-trial-support-center-ctsc-portal-for-healthcare-providers

Email the CTSC directly with questions at: CTSC@LLS.org

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EQUITY IN ACCESS RESEARCH PROGRAM

The Leukemia & Lymphoma Society's (LLS) Equity in Access Research Program was created in 2021 to generate **actionable solutions** to the barriers that prevent all patients from accessing the care they need and deserve. www.LLS.org/EquityinAccess

Program Goals

1) Advance understanding of modifiable, underlying causes of inequitable access to care for blood cancer patients and survivors within the current healthcare system.
2) Generate actionable evidence to assist LLS in advocating for policies and developing programs that tangibly improve the lives of blood cancer patients and survivors.
3) Identify healthcare policies and practices that have the potential to increase equitable access to cancer care and improve the quality of life and outcomes for blood cancer patients and survivors.
4) Cultivate health services researchers in the blood cancer space and contribute to LLS being recognized as a funding and thought leader in this area.

Program Activities

- The program has awarded over $12 million in funding for seminal health services research addressing critical issues such as the cost of oral anticancer medications, the role of health insurance in financial toxicity, and access to clinical trials.
- In 2024 alone, the program awarded $4.8 million to studies testing multi-level interventions to improve clinical trial access and enrollment, with the aim of disseminating those that are effective.

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Application cycle for 2026-2027 academic year will open **June 1, 2025**

- Students must identify as Black/African American, Hispanic/Latino(a), American Indian/Alaska Native, Native Hawaiian/other Pacific Islander
- Applicants must be 2nd – 4th year medical students in good standing at an LCME-accredited medical school.
- Open to U.S. citizens or permanent residents of the U.S. or a U.S. territory
- Award includes
  - $75K for student living expenses
  - $10K for host lab
  - $5K for student relocation costs
  - $6K for student ASH attendance ($3K per year)

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Updates in Multiple Myeloma Clinical Research

Eben Lichtman, MD
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University of North Carolina-Chapel Hill School of Medicine
Associate Member, UNC Lineberger Comprehensive Cancer Center
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Outline

1. NDMM - Induction
   - CEPHEUS
   - GMMG-HD7
   - GMMG-HD10/MajesTEC-5
2. NDMM – Maintenance
   - MajesTEC-4
3. Early relapsed MM
   - DREAMM-7
   - CARTITUDE-4
4. AL amyloidosis:
   - ANDROMEDA
5. Emerging therapies
   - IMMagine-1
   - P-BCMA-ALLO1
   - ISB-2001-101
6. Disparities in MM trials

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Newly Diagnosed Multiple Myeloma (NDMM)

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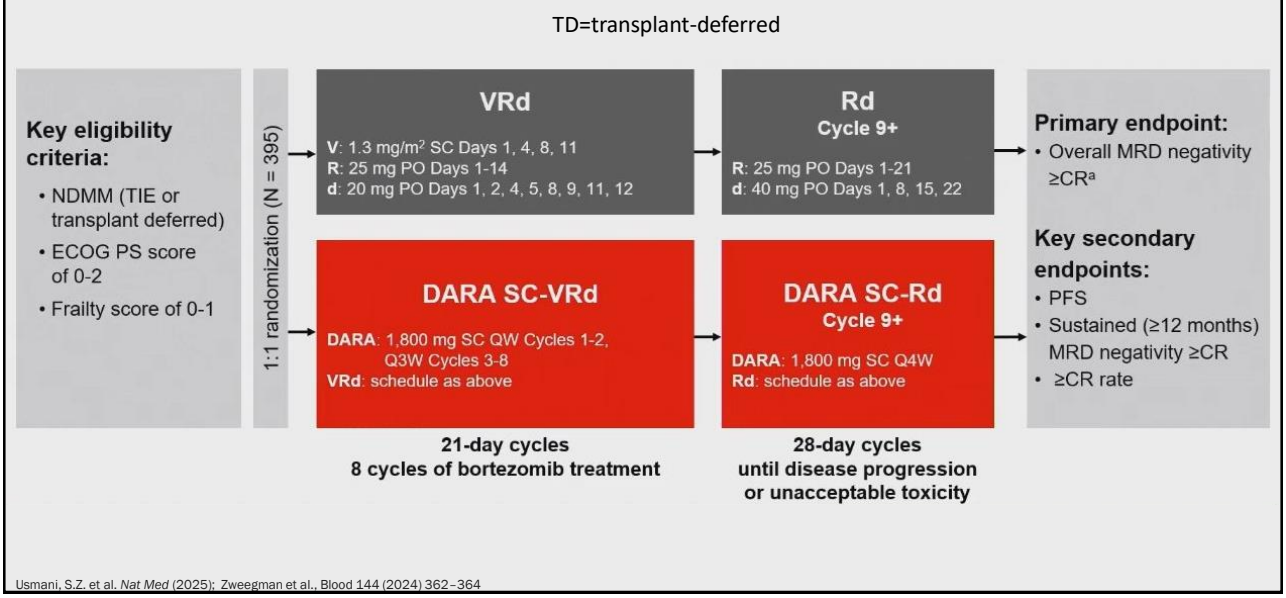
CEPHEUS: VRd +/- Dara, TI-NDMM (~73%) or TD-NDMM (~27%)



Usmani, S.Z. et al. *Nat Med* (2025); Zweegman et al., Blood 144 (2024) 362–364

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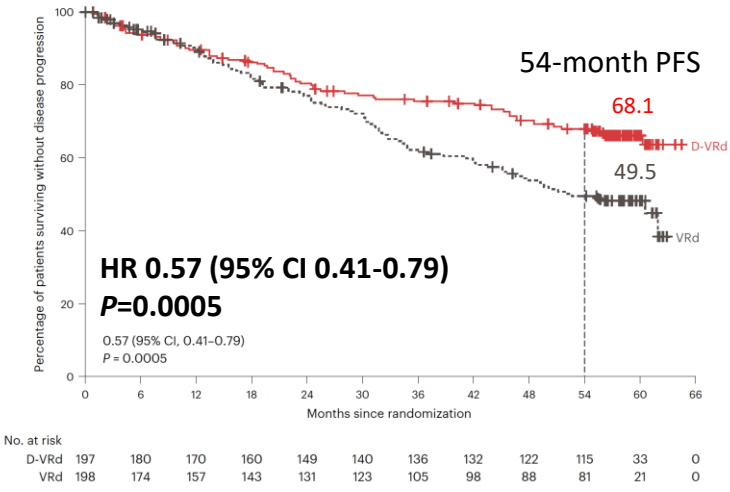
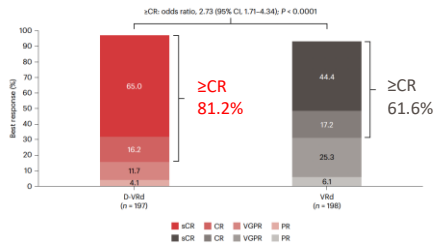
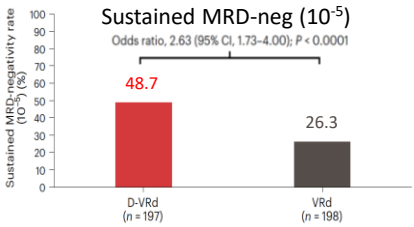
CEPHEUS: D-VRd improves ORR, PFS, MRD-neg Rates







Usmani, S.Z. et al. *Nat Med* (2025); Zweegman et al., Blood 144 (2024) 362–364

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MAIA, IMROZ, CEPHEUS, BENEFIT: Quadruplets Outperform Triplets in TI-NDMM

	MAIA	IMROZ	CEPHEUS	BENEFIT
Induction	**D-Rd vs Rd**	**Isa-VRd vs VRd**	**D-VRd vs VRd**	**Isa-VRd vs Isa-Rd** (V D1,8,15 C1-12; D1,15 C13-18)
Maintenance	---	Isa-Rd vs Rd	D-Rd vs Rd	Isa-R
N	368 vs 369	265 vs 181	197 vs 198	135 vs 135
Median follow-up (y)	5.4	5.0	4.9	2.0
≥CR (%)	51 vs 30	75 vs 64	81 vs 62	58 vs 31
MRD-neg* at 12M (%)	13 vs 4	54 vs 39	43 vs 28	51 vs 21
MRD-neg*, sust. ≥12M (%)	11 vs 2	47 vs 24	49 vs 26	
Median PFS (mo)	62 vs 34	NR vs 54	NR vs 53	NR vs NR
PFS (%)	52 vs 30 @ 60 mo	63 vs 45 @ 60 mo	68 vs 50 @ 54 mo	85 vs 80 @ 24 mo (est)

*10^{-5} sensitivity

Facon et al., EHA 2024; Facon et al., New Eng J 2024; Facon et al., Leukemia 2025; Usmani et al., Nat Med 2025; Leleu et al., Nat Med 2024

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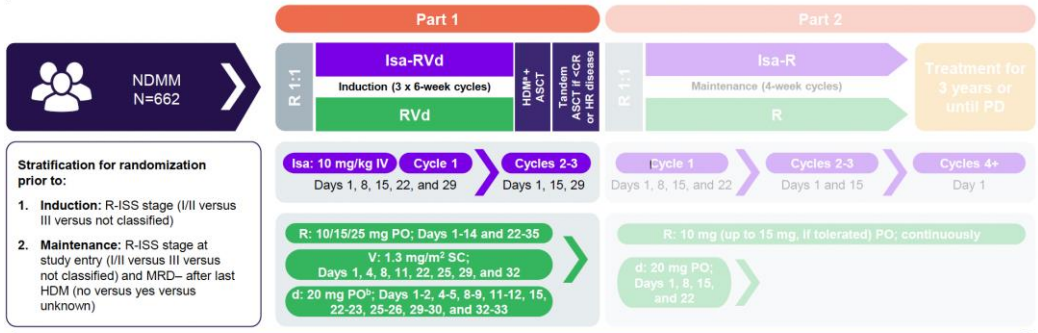
GMMG-HD7: Study Design – Only Phase 3 Study with Second Randomization Before Maintenance



Primary end points[c]: Post-induction MRD– (NGF, 10^{-5}); PFS after second randomization

Key secondary end points: PFS (whole study); OS (whole study and from second randomization); post-induction CR; CR and MRD– after HDM and during and after maintenance therapy

Selected secondary end point: PFS after first randomization

- 18-week induction
- ASCT (tandem if <CR or HR-MM)
- No consolidation
- 2nd randomization (Isa-R vs R)
- Results for 1st randomization only

Goldschmidt et al, Blood. 2024;144 (Supplement 1): 769

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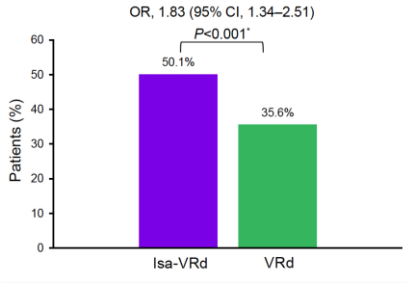
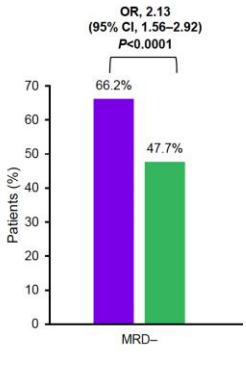
GMMG-HD7: MRD-Negativity

MRD-
post-induction



MRD-
post-ASCT



Goldschmidt et al, Blood. 2024;144 (Supplement 1): 769

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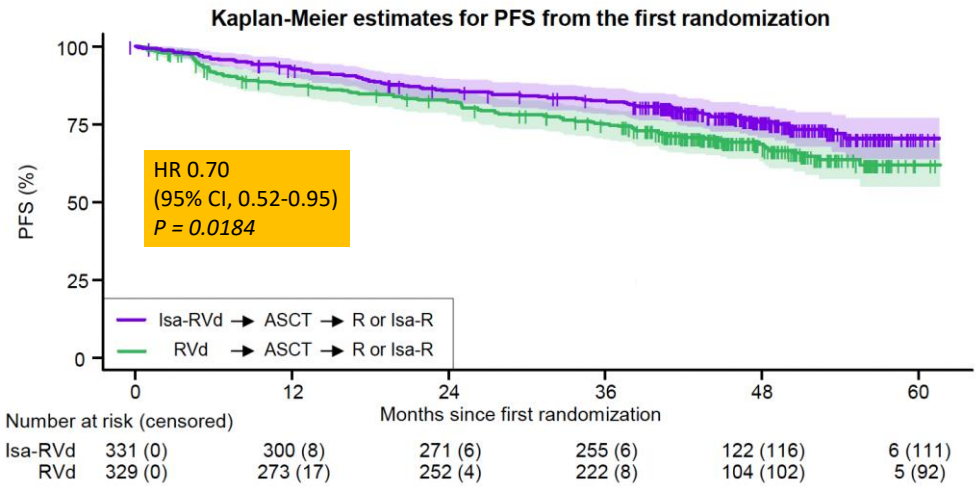
GMMG-HD7: Progression Free Survival



Goldschmidt et al, Blood. 2024;144 (Supplement 1): 769

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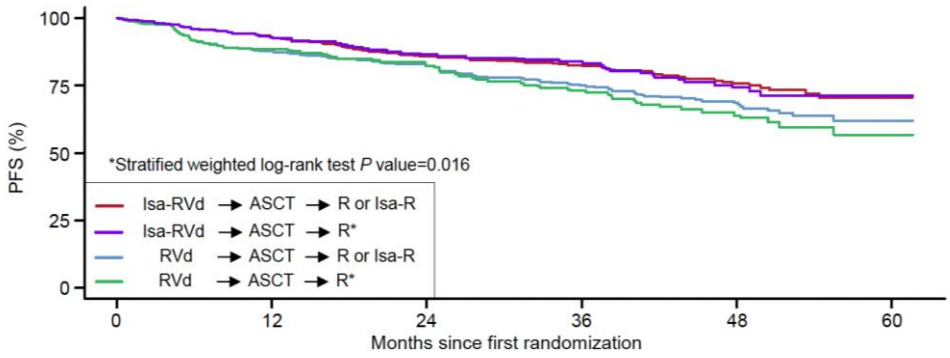
GMMG-HD7: PFS Benefit of Isa-RVd vs RVd When Accounting for Second Randomization



Weighted risk set estimator accounting for the second randomization confirms a significant benefit for Isa-RVd vs RVd induction followed by SoC lenalidomide maintenance therapy only

Goldschmidt et al, Blood. 2024;144 (Supplement 1): 769

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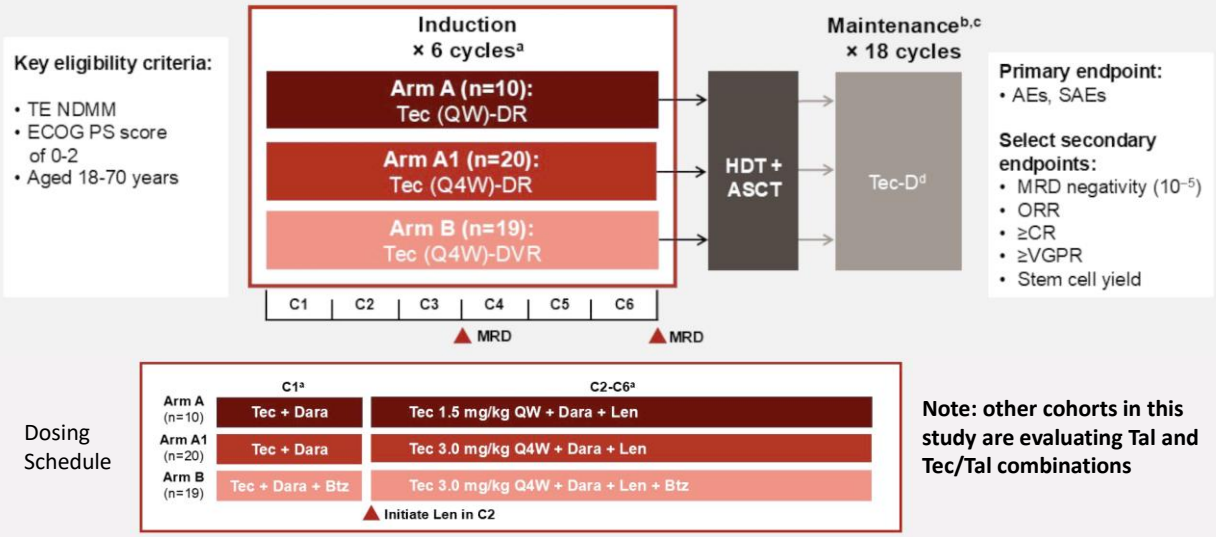
GMMG-HD10/MajesTEC-5: Study Design – Teclistamab-Based Induction



Raab et al, Blood. 2024;144 (Supplement 1): 493

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GMMG-HD10/MajesTEC-5: Safety

- Neutropenia 63% (57% grade 3/4)
- CRS 65% (all grade 1/2)
- Infections 80% (35% grade 3/4)
  (no treatment discontinuation, no grade 5 infections)
- 90% received ≥1 dose IVIg

Raab et al, Blood. 2024;144 (Supplement 1): 493

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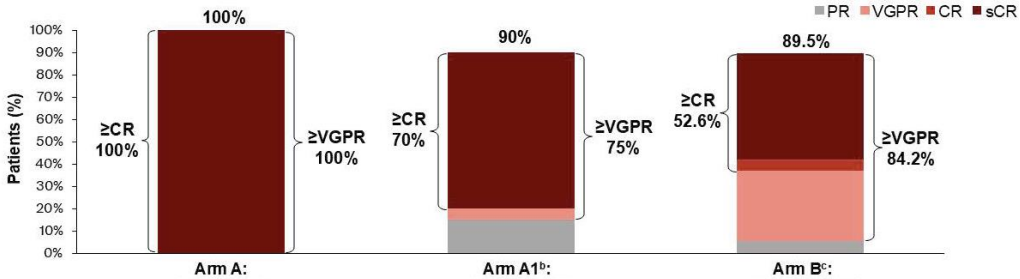
GMMG-HD10/MajesTEC-5: Efficacy



	Arm A: Tec (QW)-DR n=10	Arm A1[b]: Tec (Q4W)-DR n=20	Arm B[c]: Tec (Q4W)-DVR n=19
Induction complete, n	10	5[d]	8[e]
Induction ongoing, n	0	14	10

- 100% evaluable patients MRD-negative (10^{-5}) by C3
- Stem cell mobilization was feasible

Raab et al, Blood. 2024;144 (Supplement 1): 493

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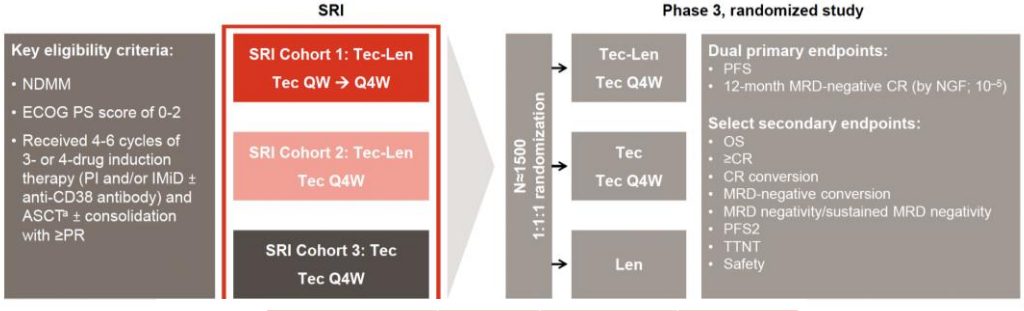
MajesTEC-4: Study Design Teclistamab-Based Maintenance



	Cycle 1	Cycle 2	Cycles 3-6	Cycles 7-26
Cohort 1: Tec-Len Tec QW → Q4W	Tec step up[a] + Tec 1.5 mg/kg on D8, D15, and D22	Tec 1.5 mg/kg QW + Len	Tec 3.0 mg/kg Q2W + Len	Tec 3.0 mg/kg Q4W + Len
Cohort 2: Tec-Len Tec Q4W	Tec step up[a] + Tec 1.5 mg/kg on D8 and D15	Tec 3.0 mg/kg Q4W + Len		
Cohort 3: Tec Tec Q4W	Tec step up[a] + Tec 1.5 mg/kg on D8 and D15	Tec 3.0 mg/kg Q4W		

- Len was initiated at 10 mg/day[b] from Cycles 2 to 4, followed by 15 mg/day in Cycles 5 to 26, if tolerated
- 2-year fixed-duration maintenance regimen[c]

Zamagni et al, Blood. 2024;144 (Supplement 1):494

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MajesTEC-4: Neutropenia, Infections

	Cohort 1: Tec-Len (QW → Q4W) (N=32)		Cohort 2: Tec-Len (Q4W) (N=32)		Cohort 3: Tec (Q4W) (N=30)	
Median follow-up, mo	21.1		9.2		9.2	
TEAEs,[a] n (%)	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**
Neutropenia	30 (93.8)	30 (93.8)	21 (65.6)	20 (62.5)	17 (56.7)	14 (46.7)
Any infection	30 (93.8)	12 (37.5)	25 (78.1)	9 (28.1)	23 (76.7)	6 (20.0)
Most common infections[b]						
URTI	20 (62.5)	1 (3.1)	13 (40.6)	0	8 (26.7)	0
COVID-19	12 (37.5)	1 (3.1)	5 (15.6)	0	9 (30.0)	1 (3.3)
Pneumonia	9 (28.1)	4 (12.5)	3 (9.4)	0	2 (6.7)	1 (3.3)
Nasopharyngitis	6 (18.8)	0	0	0	3 (10.0)	0

- Hypogammaglobulinemia[c] reported in:
  - Cohort 1: 31 (96.9%) patients
  - Cohort 2: 25 (78.1%) patients
  - Cohort 3: 28 (93.3%) patients
  - All received ≥1 dose of IVIg or SCIg
- One grade 5 COVID-19 TEAE occurred in Cohort 2
- Infection prophylaxis, including Ig replacement, was strongly recommended[d]

Zamagni et al, Blood. 2024;144 (Supplement 1):494

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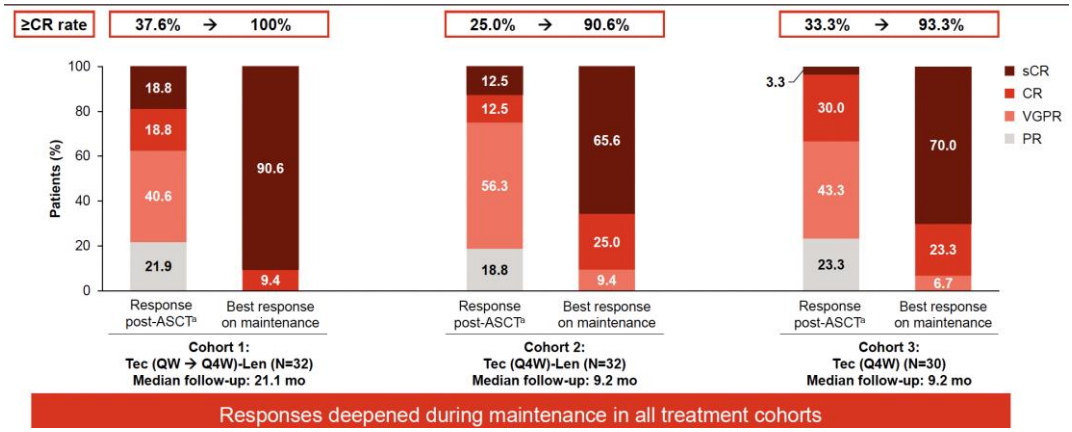
MajesTEC-4: Response Post-ASCT, Best Response on Maintenance



Zamagni et al, Blood. 2024;144 (Supplement 1):494

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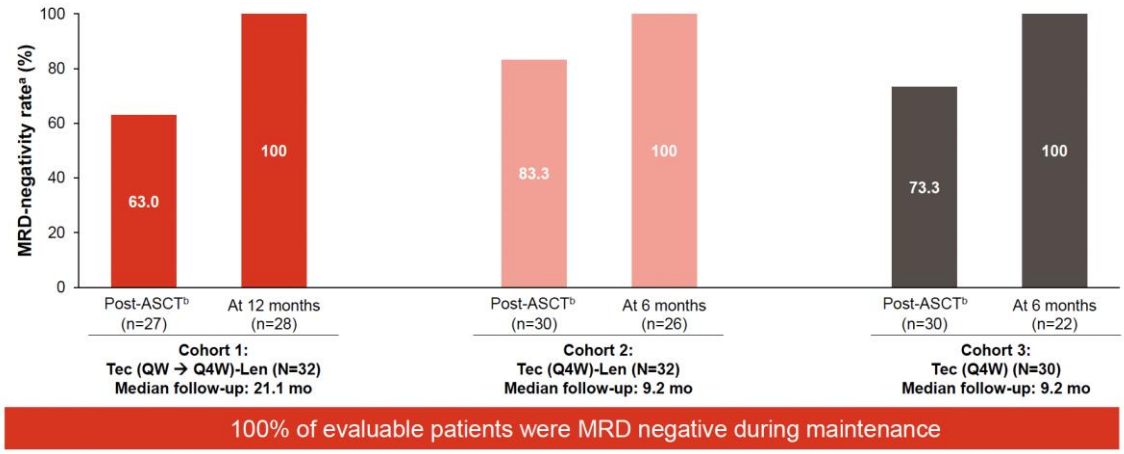
MajesTEC-4: MRD-Negativity (10^{-5}) Rates



Zamagni et al, Blood. 2024;144 (Supplement 1):494

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Early Relapsed MM

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DREAMM-7: Ph3 BelaVd vs DaraVd (2L+)

RRMM
≥1 prior line
BCMA-naïve
Dara-sensitive
(N = 494)

- Belamantamab mafodotin + Bortezomib + Dexamethasone (BVd) (n = 243) — Belantamab mafodotin
- Daratumumab + Bortezomib + Dexamethasone (DVd) (n = 243) — Daratumumab

51% received 1 prior line, 38% 2-3 prior lines
- **84% prior IMiD**
  - 54% prior thladomide
  - 52% prior lenalidomide
  - 34% lenalidomide-refractory
- **88% prior PI**
- **1.4% prior daratumumab**

Primary endpoint: PFS
Key secondary endpoints: OS, DoR, MRD negativity

Hungria et al., N Engl J Med 2024 Aug 1;391(5):393-407
Hungria et al, Blood. 2024;144 (Supplement 1): 772

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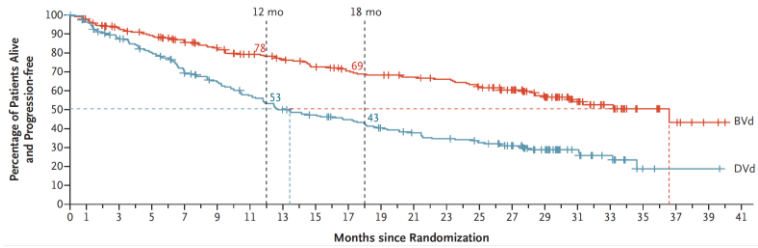
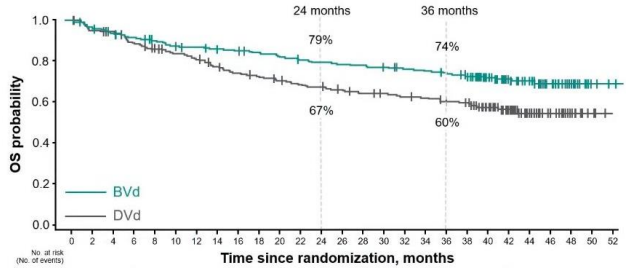
DREAMM-7: Overall Survival

PFS



Median PFS
36.6 vs 13.4 mo
HR 0.41 (95% CI, 0.31–0.53)
***P* < 0.001**

OS



36-month OS
74 vs 60%
HR 0.58 (95% CI 0.43-0.79)
***P* = 0.00023**

Hungria et al., N Engl J Med 2024 Aug 1;391(5):393-407
Hungria et al, Blood. 2024;144 (Supplement 1): 772

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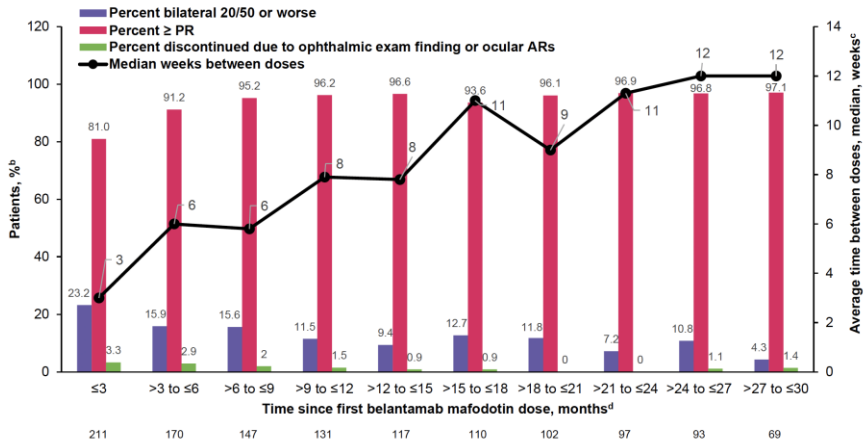
DREAMM-7: Responses, Ocular Events, Dosing Interval



- Median time between doses increased with treatment duration
- Response rates (best confirmed response ≥ PR in each interval) remained high throughout treatment
- 23% of patients experienced 20/50 or worse events in the first 3 months; prevalence generally decreased thereafter
- The rate of treatment discontinuation due to ocular events was low

Results from the primary analysis (data cutoff: October 2, 2023)

Hungria et al., N Engl J Med 2024 Aug 1;391(5):393-407
Hungria et al, Blood. 2024;144 (Supplement 1): 772

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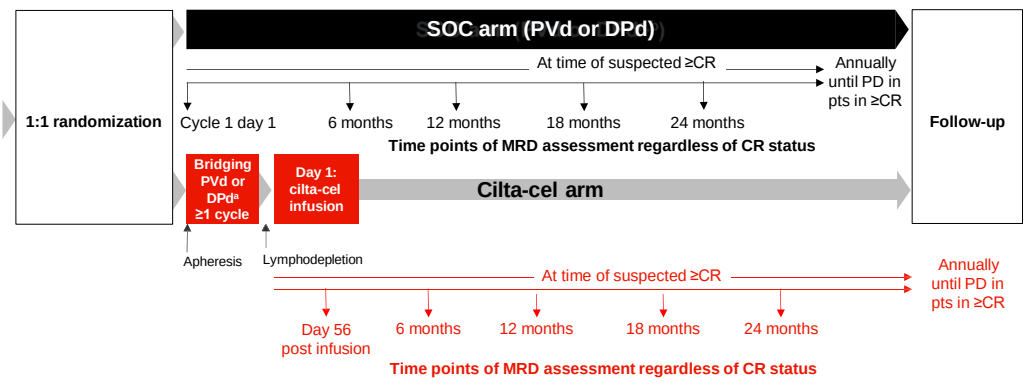
CARTITUDE-IV Update: Cilta-Cel vs SoC, 1-3 Prior Lines

Screening

Key inclusion criteria:

- Age ≥18
- 1–3 prior LOT (incl. PI + IMiD)
- Len refractory
- ECOG PS ≤1



Popat et al, Blood. 2024;144 (Supplement 1): 1032

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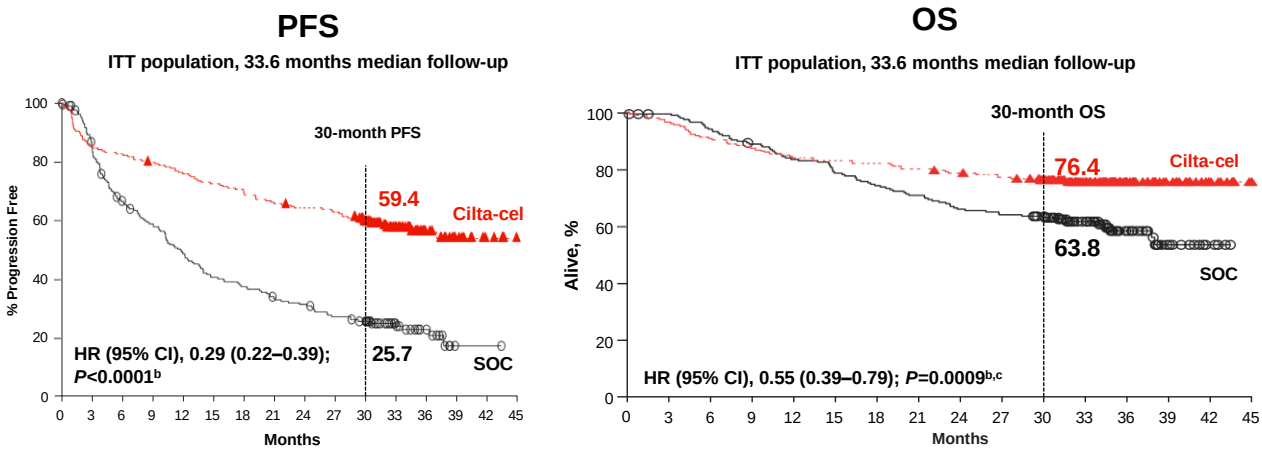
CARTITUDE-IV: PFS and OS



Popat et al, Blood. 2024;144 (Supplement 1): 1032

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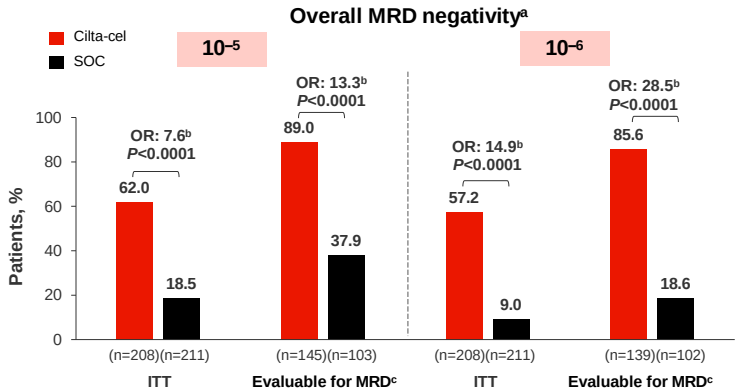
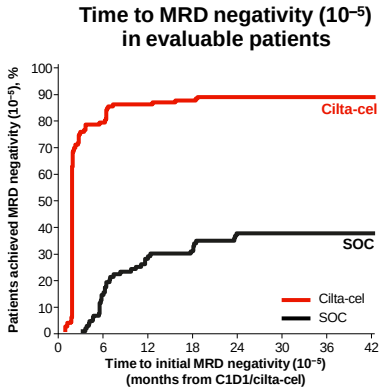
CARTITUDE-IV: Rapid MRD-Negativity





- 69% of evaluable patients achieved MRD negativity (10^{-5}) by day 56 (ITT, 48%), rising to 86% (ITT, 60%) by 6 months post cilta-cel infusion

High rates of overall MRD negativity are rapidly achieved with cilta-cel, and almost all cilta-cel patients negative at 10^{-5} were also negative at 10^{-6}

Popat et al, Blood. 2024;144 (Supplement 1): 1032

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AL Amyloidosis

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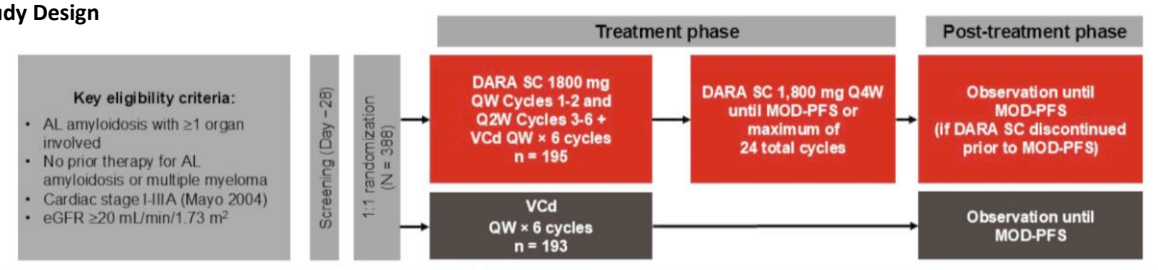
ANDROMEDA: Final Analysis, MOD-PFS and OS (Median f/u 5y)

Study Design



Background

Phase 3 ANDROMEDA study primary analysis (median follow-up: 11.4 months)[6] showed the addition of subcutaneous daratumumab (DARA) to VCd (D-VCd) resulted in:

- Significant increase in HemCR rate (53.3% vs 18.1%; *P* <0.0001)
- Prolonged major organ deterioration (MOD)–PFS (HR, 0.58; 95% CI, 0.36-0.93; *P* = 0.02)

Kastritis et al, Blood. 2024;144 (Supplement 1): 891

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ANDROMEDA: Baseline Characteristics

Baseline disease characteristics

Characteristic	D-VCd (n = 195)	VCd (n = 193)
Involved organs		
Median (range)	2 (1-5)	2 (1-6)
Distribution, n (%)		
Heart	140 (71.8)	137 (71.0)
Kidney	115 (59.0)	114 (59.1)
Liver	15 (7.7)	16 (8.3)
Other[d]	127 (65.1)	124 (64.2)
Cardiac stage, n (%)[e]		
I	47 (24.1)	43 (22.3)
II	76 (39.0)	80 (41.5)
IIIA	70 (35.9)	64 (33.2)
IIIB[f]	2 (1.0)	6 (3.1)
Renal stage, n/total n (%)[g]		
I	107/193 (55.4)	101/193 (52.3)
II	67/193 (34.7)	74/193 (38.3)
III	19/193 (9.8)	18/193 (9.3)

Subsequent therapy received:

- **D-VCd**: 25.9% (50/193) of patients
- **VCd**: 61.2% (115/188) of patients
  → ***71.3% (82/115) in VCd group who received subsequent therapy got DARA-based treatment***

Kastritis et al, Blood. 2024;144 (Supplement 1): 891

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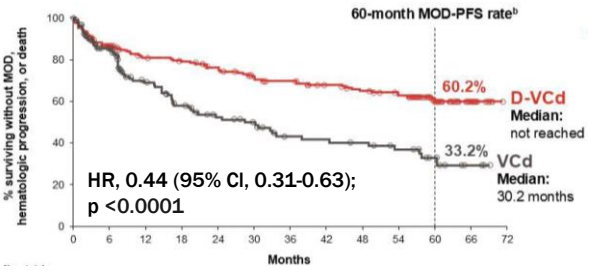
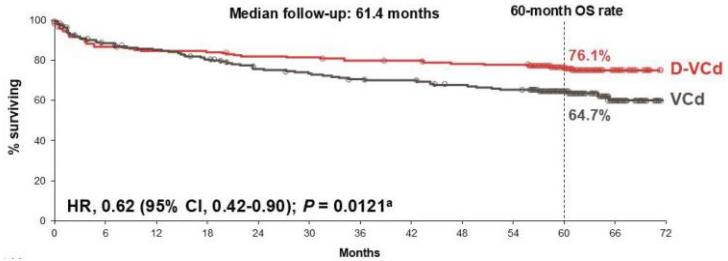
ANDROMEDA: MOD-PFS and OS

MOD-PFS



Median follow-up 61.4 months

OS



Addition of DARA to VCd significantly improved MOD-PFS and OS despite cross-over in >70% of VCd pts who received DARA as subsequent treatment.

Kastritis et al, Blood. 2024;144 (Supplement 1): 891

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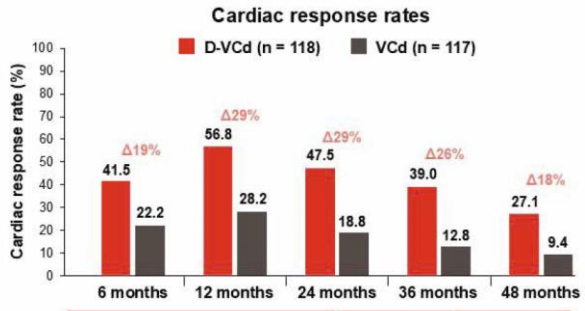
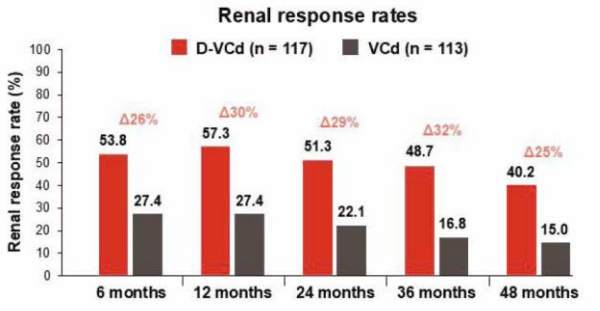
ANDROMEDA: Cardiac, Renal Response



Graded response, %	D-VCd	VCd
Cardiac CR	40.7	13.7
Cardiac ≥VGPR	64.4	31.6



Addition of DARA to VCd leads to 2-3 times higher cardiac and renal response rates across study timepoints

Kastritis et al, Blood. 2024;144 (Supplement 1): 891

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Emerging Therapies

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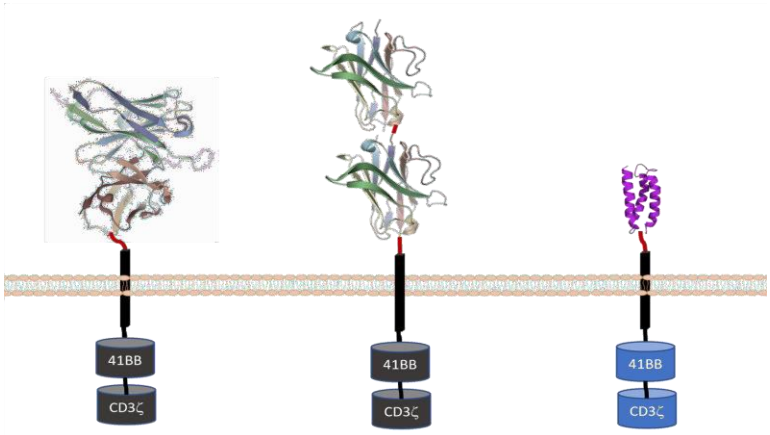
IMMagine-1: Anitocabtagene Autoleucel (anito-cel), BCMA CAR-T, Novel D-domain



scFv (~25 kDa) | Bivalent camelid VHH (~30 kDa) | **D-Domain (~8 kDa)**

D-Domain Attributes:
Non-Antibody Derived Synthetic Protein[1,2]

Size	Small D-Domain construct facilitates high transduction efficiency and CAR positivity[2-4] resulting in a low total cell dose
Structure & Stability	D-Domain CARs are stable and lack tonic signaling[4,6] due to the rapid folding, lack of disulfide bonds, and hydrophobic core[5,6] of the D-Domain
Binding	The D-Domain binder has a fast off-rate[4] and high CAR surface expression[4]. This combination may allow optimal tumor cell killing without prolonged inflammation

[1]Rotte, et al. Immuno-Oncology Insights 2022; 3(1), 13–24; [2]Frigault, et al. Blood Adv. 2023; 7(5):768-777; [3]Cante-Barrett, et al. BMC Res. Notes 2016; 9:13; [4]Buonato, et al. Mol. Cancer Ther. 2022; 21(7):1171-1183; [5]Zhu, et al. Proc. Nat. Acad. Sci. 2003; 100(26): 15486-15491; [6]Qin, et al. Mol. Ther. 2019; 27(7): 1262-1274.

Freeman et al, Blood. 2024;144 (Supplement 1): 1031

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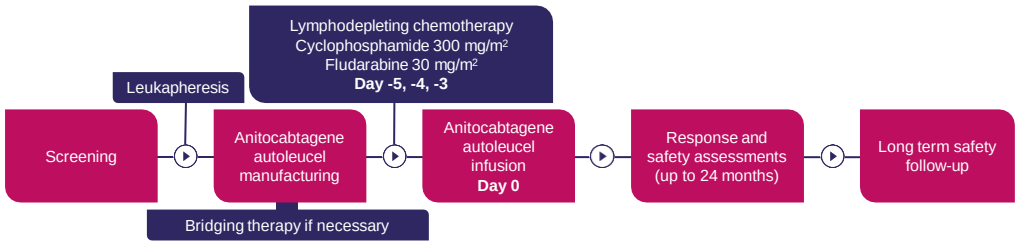
IMMagine-1: Phase 2 Registrational Study of Anito-cel



Key Eligibility Criteria

- Prior IMiD, PI, and CD38-targeted therapy
- Received ≥3 prior lines of therapy
- Refractory to the last line of therapy
- ECOG PS of 0 or 1
- Evidence of measurable disease

Primary Endpoint:

- ORR, per 2016 IMWG criteria

Key Secondary Endpoints:

- sCR/CR rate, per 2016 IMWG criteria
- ORR in patients limited to 3 prior LoT, per 2016 IMWG criteria

Target Dose of 115 x 10^6 CAR+ T cells

Primary and key secondary endpoints to be assessed per Independent Review Committee (IRC); Investigator assessment of response per IMWG also permitted per protocol.
CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; LoT, line of therapy; ORR, overall response rate; PI, proteosome inhibitor; sCR,

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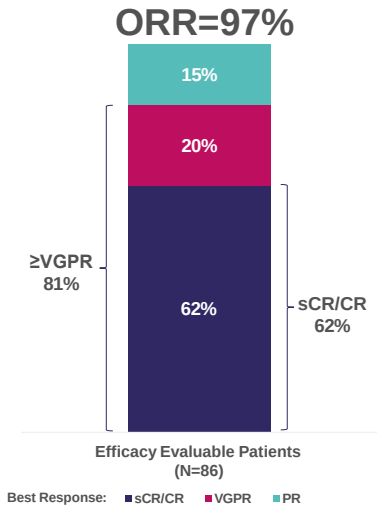
IMMagine-1: ORR, PFS, OS

Efficacy Evaluable Patients (N=86)



	PFS Rate (%) (95% CI)	OS Rate (%) (95% CI)
6-Month	93.3% (84.4%, 97.2%)	96.5% (89.6%, 98.9%)
12-Month	78.5% (63.5%, 87.9%)	96.5% (89.6%, 98.9%)

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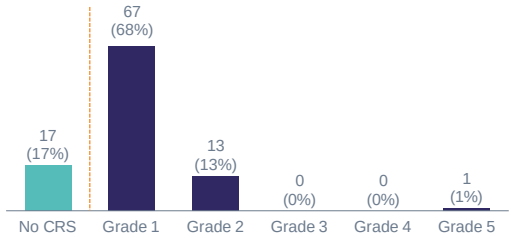
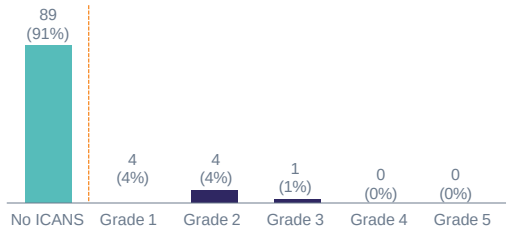
IMMagine-1: CRS, ICANS

Maximum CRS Grade (N=98)



- 83% (81/98) any Grade CRS; median onset 4 days
- 86% (84/98) Grade ≤1 CRS, including 17% (17/98) with no CRS
- % of patients with either no CRS or CRS that resolved by:
  - ≤7 days of anito-cel infusion: 63% (62/98)
  - ≤10 days of anito-cel infusion: 92% (90/98)
  - ≤14 days of anito-cel infusion: 98% (96/98)

Maximum ICANS Grade (N=98)



- 9% (9/98) any grade ICANS; all cases resolved
- **No delayed or non-ICANS neurotoxicities in this study or in prior Phase 1 study (n=38, median f/u 38 mo):**
  - **no parkinsonism**
  - **no cranial nerve palsies**
  - **no Guillain-Barré syndrome**

Freeman et al, Blood. 2024;144 (Supplement 1): 1031

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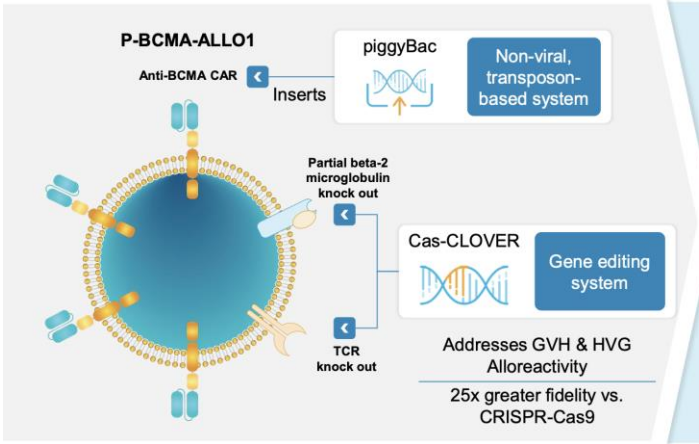
P-BCMA-ALLO1: Phase 1 Study of Non-Viral, Allogeneic BCMA CAR-T



Proprietary technologies used to create P-BCMA-ALLO1 with high percentage of stem cell memory T cell (T_{scm})

- T_{scm} have a less differentiated phenotype, which is associated with prolonged persistence and improved antitumor reactivity and expansion

Drug resistance gene permits positive selection

- ~100% of T cells in final product express the CAR

Incorporates proprietary safety switch

- Rapid, dose-dependent elimination of engineered T cells if necessary in case of severe toxicity

Dholaria et al., IMS 2024

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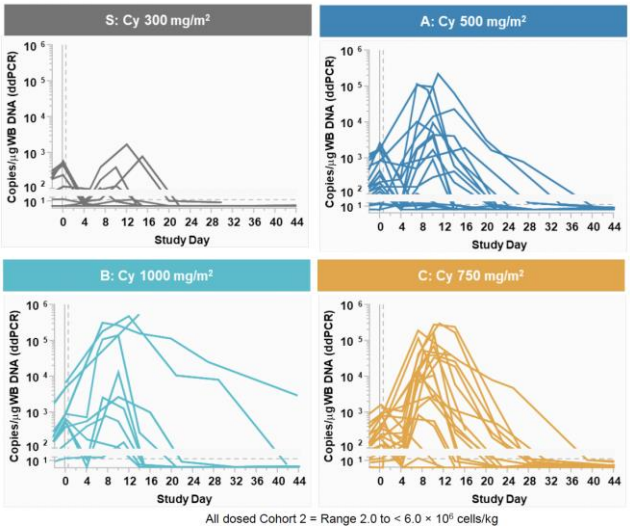
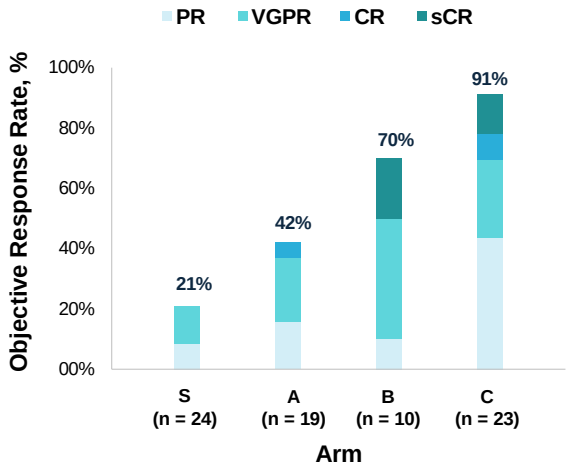
P-BCMA-ALLO1: LD Intensity Impacts CAR-T Expansion and Persistence



All dosed Cohort 2 = Range 2.0 to < 6.0 × 10^6 cells/kg



Dholaria et al., IMS 2024

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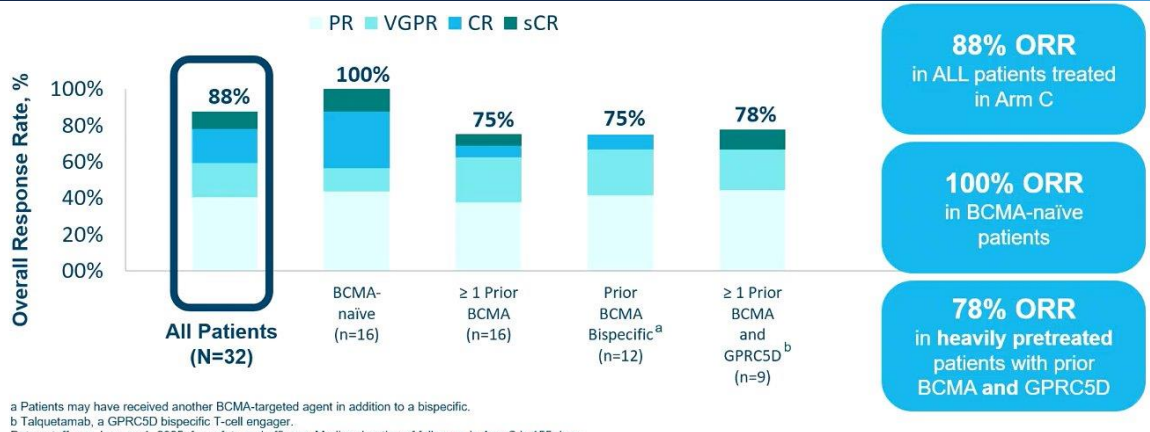
P-BCMA-ALLO1: Outcomes for Arm C Cyclophosphamide 750 mg/m²



a Patients may have received another BCMA-targeted agent in addition to a bispecific.
b Talquetamab, a GPRC5D bispecific T-cell engager.
Data cutoff was January 1, 2025, for safety and efficacy. Median duration of follow-up in Arm C is 155 days.
ORR = sCR, CR, VGPR, or PR, including confirmed and unconfirmed responses. Evaluable patients: Obtained first response assessment by IMWG M-protein criteria or PD/death and completed Week 4 visit.
Patients received cell doses ranging from 1.57 to 6 x10^6 cells/kg.
BCMA, B-cell maturation antigen; CR, complete response; GPRC5D, G protein-coupled receptor class C group 5 member D; IMWG, International Myeloma Working Group; ORR, objective response rate; PD, progressive disease; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Dholaria B, Cruz JC, Costello C. A Phase 1 Study of P-BCMA-ALLO1, a Non-Viral, Allogeneic BCMA Directed CAR-T in Relapsed/Refractory Multiple Myeloma (RRMM): Results from Optimized Lymphodepletion Cohort (Arm C). Presented at: 2025 Transplantation and Cellular Therapy Meetings; February 12-15, 2025; Honolulu, HI. Abstract 48.

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P-BCMA-ALLO1: Safety Profile

- TEAEs in ≥20% of all patients treated in Arm C **(N=36)**

Adverse Event	Any Grade	Grade ≥3	Related[b] Grade ≥3
	n (%)	n (%)	n (%)
Patients with TEAEs	36 (100)	32 (89)	27 (75)
Neutropenia	**24 (67)**	**24 (67)**	**18 (50)**
Leukopenia	**24 (67)**	**24 (67)**	**16 (44)**
Thrombocytopenia	**24 (67)**	**19 (53)**	**13 (36)**
Anemia	**21 (58)**	**19 (53)**	**14 (39)**
CRS	**15 (42)**	–	–
Hypocalcemia	13 (36)	2 (6)	–
Hypotension	11 (31)	1 (3)	1 (3)
Febrile neutropenia	9 (25)	7 (19)	1 (8)
Fatigue	9 (25)	2 (6)	1 (3)
Lymphopenia	8 (22)	7 (19)	2 (6)
Pyrexia	8 (22)	–	–

[a] Retreated subjects are re-enrolled and receive a unique study ID; therefore, they are included in safety analysis.
[b] Related is defined as TEAEs (from the start of P-BCMA-ALLO1) for which the investigator assessed there was a reasonable possibility that P-BCMA-ALLO1 caused the adverse event.
Data cutoff was January 1, 2025, for safety and efficacy. Median duration of follow-up in Arm C is 155 days.
CRS, cytokine release syndrome; TEAEs, treatment-emergent adverse events.

Dholaria B, Cruz JC, Costello C. A Phase 1 Study of P-BCMA-ALLO1, a Non-Viral, Allogeneic BCMA Directed CAR-T in Relapsed/Refractory Multiple Myeloma (RRMM): Results from Optimized Lymphodepletion Cohort (Arm C). Presented at: 2025 Transplantation and Cellular Therapy Meetings; February 12-15, 2025; Honolulu, HI. Abstract 48.

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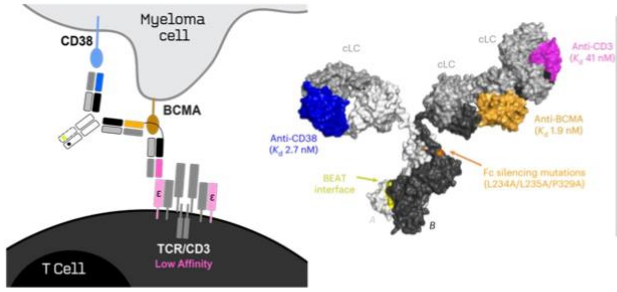
ISB-2001-101

ISB 2001 (BCMAxCD38xCD3): First TREAT™ Trispecific Antibody for Relapsed/Refractory Multiple Myeloma



Key Attributes

- Generated using IGI's proprietary BEAT® protein platform
- Enhanced avidity-based binding to myeloma cells with both BCMA and CD38 Fab domains
- CD38 Fab domain targets non-overlapping epitopes with Daratumumab
- Tuned BCMA>CD38>CD3 binding affinity and distal positioning of the CD38 vs CD3 binders drive potent tumor killing while minimizing CD38-related off-tumor adverse events

Quach et al, Blood. 2024;144 (Supplement 1): 1026

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ISB-2001-101: Safety

Drug-Related Hematologic TEAEs (N=20)

AEs, n (%)	All	Grade 3	Grade 4
Any Related Hematologic TEAEs	12 (60)	6 (30)	3 (15)
Anaemia	1 (5)	1 (5)	0
Lymphocyte count decreased	2 (10)	1 (5)	0
Neutropenia	7 (35)	3 (15)	3 (15)
Thrombocytopenia	8 (40)	2 (10)	0

Non-Hematologic Drug-Related TEAEs (≥ 15%, N=20)

AEs, n (%)	All	Grade 3	Grade 4
Any Related Non-Hematologic TEAEs	20 (100)	3 (15)	0
Cytokine release syndrome	15 (75)	0	0
Injection site reaction	12 (60)	0	0
Alanine aminotransferase increased	5 (25)	0	0
Aspartate aminotransferase increased	4 (20)	1 (5)	0
Fatigue	3 (15)	0	0
Gamma-glutamyltransferase increased	3 (15)	0	0
Nausea	3 (15)	0	0

Quach et al, Blood. 2024;144 (Supplement 1): 1026

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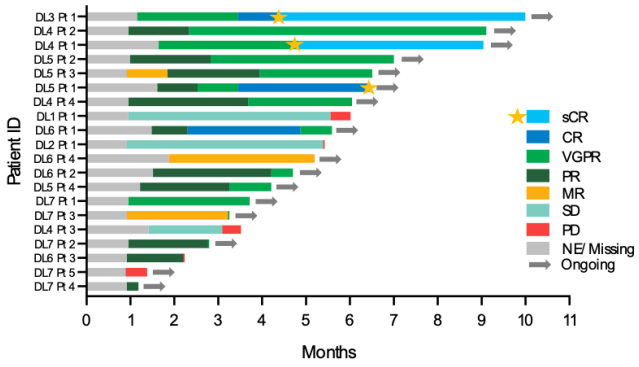
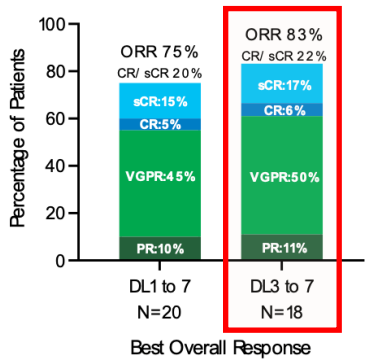
ISB-2001-101: Responses





Median follow up 6 months (range: 2-10)

First objective response observed at DL3 (sCR, MRD negative at 10^{-5} level)

Median time to first response was 36 days (range: 29-57)

Quach et al, Blood. 2024;144 (Supplement 1): 1026

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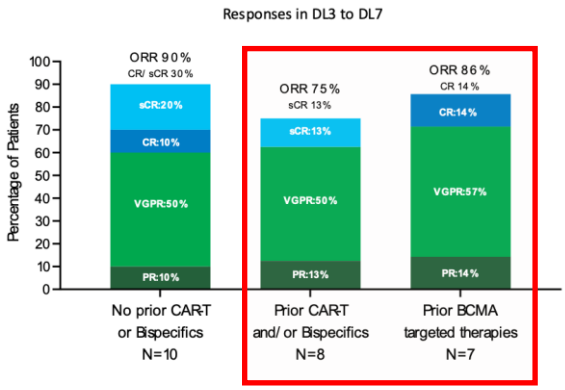
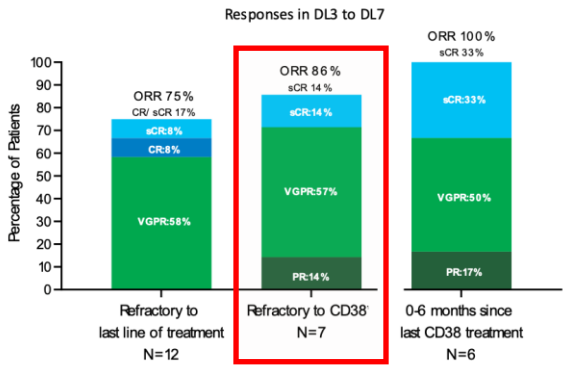
ISB-2001-101: Responses in BCMA- and CD38-Refractory Patients





Quach et al, Blood. 2024;144 (Supplement 1): 1026

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Disparities in the Diagnosis and Treatment of MM

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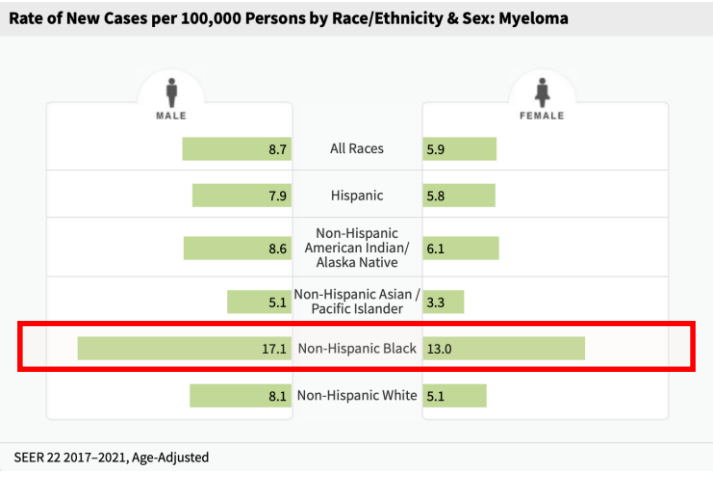
Disparities in MM incidence and Outcomes



- Compared to non-Hispanic White (NHW) pts, **median age of onset 4-5y earlier** for Black pts
- Among pts under 50, incidence vs NWH pts:
  - **2.6x higher in Black men**
  - **3.3x higher in Black women**
- **Black MM pts**:
  - More indolent disease biology, lower incidence of HRCAs, similar/better MM-specific and overall survival
  - **Have not experienced similar survival benefits from recent tx advances.**
- **Many factors:** systemic racism, socioeconomic disparities, delay in diagnosis, disparities in access to quality care, and disparities in access to clinical trials.

Bhutani et al., Blood Cancer J. 13, 189 (2023); https://seer.cancer.gov/

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Ongoing Disparities in Clinical Trial Participation

- In the US, 20% of NDMM pts are Black, expected be 24% within next decade (approx. 14% of US population is Black). Incidence among Hispanic populations in the US is estimated to be similar to non-Hispanic Whites.
- Significant underrepresentation of Black patients in most pivotal trials – recent examples:
  AQUILA (2.8%), **PERSEUS** (1.3%), **MAIA** (4.5%), **CEPHEUS** (4.8%), **IMROZ** (0.9%), **IKEMA** (3%), **CANDOR** (1.9%), **DREAMM-7** (4%), **DREAMM-8** (0%), **CARTITUDE-4** (5.1%), **MonumenTAL-1** (10%), **MajesTEC-1** (12.7%)
- Some studies have been more successful: **MASTER** (20%), **DETERMINATION** (19%)
- In general, ongoing **inadequate representation of minority groups** among US participants in MM trials.
- **FDA draft guidance** released 6/2024 (to take effect 6/2025), mandated **diversity action plans (DAPs)** with IND submissions, detailing enrollment goals by race, ethnicity, sex, and age group.
  - Guidance removed 1/2025, re-posted 2/2025 (with disclaimer, per court order)

Bhutani et al., Blood Cancer J. 13, 189 (2023)

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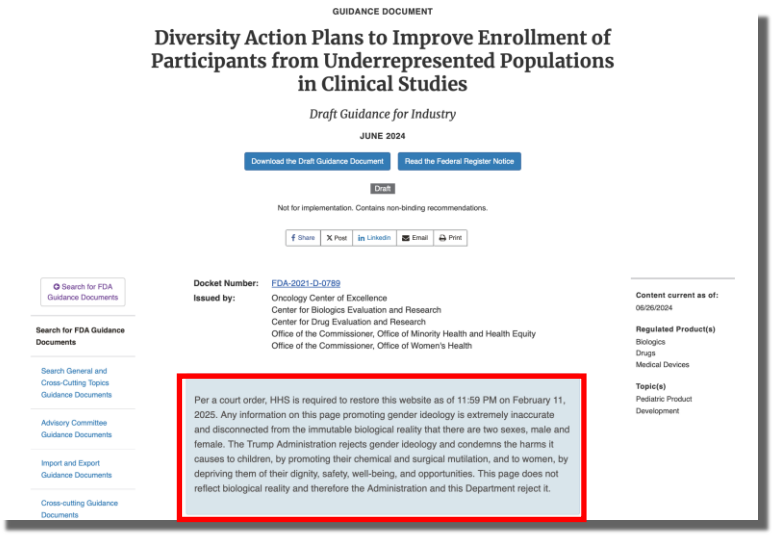
FDA Diversity Action Plan Requirement


GUIDANCE DOCUMENT

Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies

Draft Guidance for Industry

JUNE 2024

Download the Draft Guidance Document | Read the Federal Register Notice

Draft

Not for implementation. Contains non-binding recommendations.

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Cross-cutting Guidance Documents

Docket Number: FDA-2021-D-0789

Issued by: Oncology Center of Excellence
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Office of the Commissioner, Office of Minority Health and Health Equity
Office of the Commissioner, Office of Women's Health

Per a court order, HHS is required to restore this website as of 11:59 PM on February 11, 2025. Any information on this page promoting gender ideology is extremely inaccurate and disconnected from the immutable biological reality that there are two sexes, male and female. The Trump Administration rejects gender ideology and condemns the harms it causes to children, by promoting their chemical and surgical mutilation, and to women, by depriving them of their dignity, safety, well-being, and opportunities. This page does not reflect biological reality and therefore the Administration and this Department reject it.

Content current as of: 06/26/2024

Regulated Product(s)
Biologics
Drugs
Medical Devices

Topic(s)
Pediatric Product Development

From: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diversity-action-plans-improve-enrollment-participants-underrepresented-populations-clinical-studies

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Conclusions

- **AQUILA**: survival benefit for dara in HR-SMM
- **IMROZ, CEPHEUS, BENEFIT**: quadruplets SoC for TI-NDMM and TD-NDMM
- **MajesTEC-4,-5**: early/deep responses with tec-based induction, maintenance
- **DREAMM-7, CARTITUDE-IV**: promising outcomes of BCMA-therapy vs SoC in early relapsed myeloma
- **ANDROMEDA:** DARA added to VCd significantly improves OS and MOD-PFS in AL amyloidosis despite high cross-over rates
- **IMMagine-1**: encouraging efficacy of anito-cel (BCMA CAR-T) with favorable toxicity profile and lack of non-ICANS neurotox.
- **Promising new drugs:** allo BCMA-CAR-T, BCMAxCD38xCD3 trispecific Ab

- ***Ongoing disparities in access to these novel therapies and clinical trials***

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The Future is Now: Bispecific Antibodies and the Shift to Community Practice

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BSABS

- Improved efficacy in RRMM compared to non-T cell redirecting therapies in late relapse
- Off-the-shelf treatment compared to CAR-T
- Less short-term toxicity compared to CAR-T

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ASH 2024

- A retrospective observational study in 2024 highlighted the rapid adoption of BsAbs in community oncology settings
- In 2023, approximately 44.7% of evaluable RRMM received a BsAb, increasing to 54.3% in the first half of 2024
- This trend indicates growing confidence and reliance on BsAbs among community practitioners

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Herms et al. ASH Annual Meeting 2024

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Questions

- What were the biggest **logistical or administrative challenges** in getting BsAbs approved for use at your institution?
- Are BsAb **widely accepted** at your practice or do you find there is hesitation among your colleagues?
- How does your practice determine which patients are appropriate candidates for BsAb therapy?
  - Is there a particular patient population that you would be hesitant?

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Case: Mr. S

- **Age:** 71M
- **Co-morbidities:** CKD III, HFpEF, hx prostate cancer, COPD (ex-smoker)
- **Diagnosis:** RRMM, standard risk
- **Prior Treatments**
  - 1st line: Dara-Rd – achieved a VGPR
  - 2nd line: KPd – responded but relapsed after 9 months
  - 3rd line: PCd – minimal response and now with PD

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Mr. S: Current Status

- ECOG 1-2
- Rising M spike on a monthly basis (0.5 → 0.8→ 1.2g/dL)
- Mild cytopenias (Hb 9, WBC 2, ANC 0.8, plts 100K)
- Lives **2 hours** away from nearest academic center
- Son has limited ability to drive pt due to work commitments
- Receives care at community oncology practice

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Question

Given the barriers, would you still pursue BsAb therapy or should Mr. S be placed on another triplet regimen
(ex. Isa or Selinexor-based therapy)?

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Considerations

- Reimbursement
- SUD/Monitoring requirements
- Long term toxicity

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Oupt Drug Acquisition - 340B Pricing

- 340B medications are **outpatient drugs** that pharmaceutical manufacturers sell at discounted prices to certain health care organizations
  - % underserved population
- Created in 1992 to help hospitals and clinics treat low-income and uninsured patients

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Inpt -Disease Related Group (DRG) Pricing

- A system where hospitals are paid a **predetermined amount** for a patient's hospital stay based on their assigned DRG code (according to their diagnosis and procedures), rather than billing for each individual service provided
- Insufficient reimbursement if Tec/Tal are given as inpt → rolled into DRG pricing
- Anything given within the prior 72h of an inpatient admission also gets rolled into DRG unless admitted under "**OBSERVATION**"

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Moral of the Story…

Using expected Medicare reimbursement rates and wholesale acquisition costs while **excluding** DRG reimbursement → **total net revenue** for shifting use of Tec/Tal to OP care exclusively is in the 5-digit $ range **per dose**

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BsAb is a More Feasible OP Model

- BsAbs have much lower rates of high-grade CRS compared to CAR-T
  - 72% of pts experience CRS but nearly ALL cases are **grade 1-2**
  - Only 2% of pts experience grade 3 or higher compared to 20-30% in CAR-T recipients
  - Resolution is rapid- typically within **24-48h**
- Rates of ICANS are exceedingly low

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Considerations

- Reimbursement
- SUD/Monitoring requirements
- Long term toxicity

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SUD/Monitoring

- Due to reimbursement hurdles, patient would need frequent back and forth visits after each 48-h admission due to dosing schema
- Pt may need to stay local after each discharge and prior to next SUD – financial toxicity
- Caregiver required – work conflicts
- Outpatient monitoring capabilities?

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Remote Patient Monitoring

Patient Factors

- Patient adherence
- 24/7 caregiver
- Adequate equipment for vitals
- Tylenol/Dexamethasone
- Proximity to a site experienced in BsAbs

Institutional Factors

- Access to Toci
- Access to telehealth/virtual visits
- An **escalation plan**
  - Rapid admission protocol in place

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RPM Strategies

Mayo Clinic

- Outpatient transplant program
- Wearable to monitor heart rate, temperature, blood pressure and oxygen saturation
  - iPad Mini, Bluetooth-enabled devices
  - Telemetry automatically sends data to nurse who can intervene
- Daily assessment face-to-face
- Must stay within 15-20 min of the facility for the first week
- Any evidence of CRS, pt easily admitted

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LCI: Hospital At Home (HaH)

- HaH is an established program equipped with a **home monitoring** kit:
  - Electronic tablet
  - Wearable patch (RR, HR)
  - Blood pressure cuff
  - Pulse oximeter
  - Thermometer
- 24/7 access to a trained nurse
- Patients have **in-person** visits from an EMS in conjunction with a **video visit** with a HaH internist between SUDs
- The EMS conducts the **ICE score** daily

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HaH – Eligibility Criteria for Outpt Monitoring

- Within **1 hour** from CMC Main
- 24/7 caregiver
- Pt should **NOT** have a large tumor burden
- Pt should **NOT** have an elevated Ferritin at baseline
- Pt should **NOT** have neutropenia at baseline

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HaH- SOP

- Patients take **prophylactic dexamethasone** 8mg on the day after each SUD
- Pt is told to take Tylenol for grade 1 CRS
  - For persistent fever, can take Dex 4-8mg q 8h if needed
- For G2 or persistent G1 CRS, pts are to present to ED
- For severe CRS or ICANS, caregiver to call 911

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HaH vs. SOC

	HaH cohort (n = 32)	SOC cohort (n = 24)
Max CRS, n (%)		
None	13 (40.6)	11 (45.8)
Any	19 (59.4)	13 (54.2)
G1	13 (40.6)	8 (33.3)
G2	6 (18.8)	3 (12.5)
G3	0 (0.0)	1 (4.2)
G4	0 (0.0)	1 (4.2)
Recurrent CRS, n (%)	6 (31.6)	6 (46.2)
ICANS, n (%)	2 (6.3)	4 (16.7)
Dose delay, n (%)	9 (28.1)	7 (29.2)
Tocilizumab use, n (%)	4 (12.5)	10 (41.7)
Dex dose (mg), mean (range)	28.9 (8-48)	3.3 (0-40)
Pts admitted, n (%)	15 (46.9)	24 (100.0)
Inpatient days/patient, mean (range)	1.3 (0-8)	7.7 (5-11)
Total inpatient days	42	185

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Ferreri et al. Submitted to ASCO

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Expansion to LCI Regional Sites

- Pt referred to LCI Main to **ensure eligibility** and establish care with MM specialist
- Pt receives SUD at pt's local infusion center
- HaH monitors these patients at their home
- For any urgent issues, HaH will reach out to LCI Main oncologist during daytime hours or BMT attending after hours
- If G2 or persistent G1 CRS, pt sent to our **outpt cellular therapy** program and oncologist notified

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Outpatient Cellular Therapy Program

- Dedicated APP trained in CRS, ICANS (7am-7pm)
- Lead physician/BMT attending available on-call daily for escalation of patient care
- Trained pharmacist
- Infusion center nurses with expertise
- On-site Toci at all times
- Same-day lab monitoring
- Imaging capabilities
- ATBx and growth factor available
- Designated inpt back-up unit with rapid admission protocol in place

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Candidate for In-Patient Care?

- No caregiver
- No transportation
- Far distance/no local housing
- Poor adherence

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Considerations

- Reimbursement
- SUD/Monitoring requirements
- Long term toxicity

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Long Term Toxicity

Teclistamab

Infections
- Approximately 80%
- Gr 3/4 55%, most within the first 2 months
  - COVID, URTI, PJP

Talquetamab

Infections
- 58-70% across different dosing cohorts
- Gr 3/4 15-26%

On-target/Off-tumor
- Dysgeusia
- Skin-related events
- Nail disorders
- Cerebellar toxicity**

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Questions

- Once a patient has completed SUD and has returned to your practice, how are you monitoring for ongoing side effects?
- For talquetamab, have you seen significant issues with dysgeusia, skin or nail changes? How do you counsel patients on these side effects?
- For Teclistamab, infection risk has been a major concern. How are you handling infection ppx?

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Key Takeaway Points

- If CRS is predictable, mild and easily managed, why keep therapies confined to academic centers?
- SUD protocols are already showing feasibility for outpt models in leading academic centers
- Community centers with proper education and telemedicine support can integrate BsAb safety, bringing cutting-edge therapy closer to patients

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Strategies for Community Practice

Develop outpt protocols

Remote monitoring

Academic-Community Partnership

Collaboration between academic centers and community hospitals can facilitate knowledge transfer, training and share resources

Telemedicine integration

Remote consultations and **monitoring** can extend the reach of specialized care into community settings ensuring pts receive expert oversight

"buddy system"

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Smoldering Multiple Myeloma and the AQUILA Study

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DukeHealth

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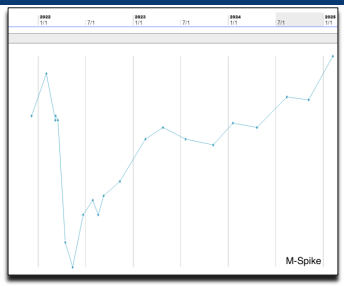
Starting with a Case

Our patient is an 83-year-old female with a past medical history of a chronic DVT who follows with myeloma clinic for follow up of Intermediate-risk IgA lambda SMM.

Smoldering Multiple Myeloma History

- Diagnosed in 2021 during PCP w/u of neuropathy revealed a M spike of 2.0 and IFE demonstrated monoclonal IgA lambda.
- Lambda: 52.5, Kappa: 9, K/L = 0.17
- Bone survey: no lesions, osteopenia.
- BMBx with Plasma cell myeloma and a 30% cellular marrow with trilineage hematopoiesis and 19% atypical monoclonal lambda plasma cells; FISH: Deletion of 13q, Gain of two copies of 1q21, Loss of FGFR3/4p



Most Recent Data

- Serum free light chains: K 0.62 L 10.85, K/L 0.06
- SPEP: M spike 2.33
- Whole body MR: Nonspecific marrow enhancement.

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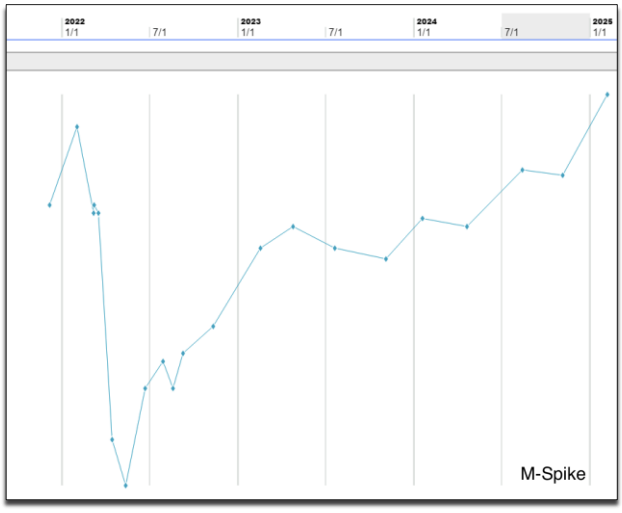
M-Spike Trend



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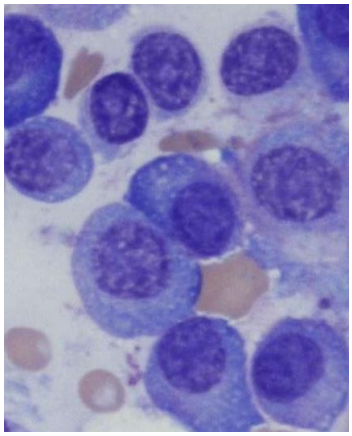
Continuing with Our Case

Assessment: A well 83 YOF with intermediate risk (20/2/20) SMM and up-trending monoclonal protein presents for routine monitoring.

- Bone Marrow Biopsy is pending.
- Patient asks about her risk of progressing to MM.
- Patient asks about how her risk of progression can be lowered.



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The AQUILA Trial

- A phase 3 trial, in which patients with high-risk smoldering multiple myeloma were randomly assigned to receive either subcutaneous daratumumab monotherapy or active monitoring
- In this study, high risk SMM was defined as at least 10% clonal BM plasma cells and another risk factor (IgA isotype, M protein >30 g/L, immunoparesis, SFLC ratio 8-100 or >50% to <60% clonal bone marrow plasma cells.
- Treatment was continued for 39 cycles, for 36 months, or until confirmation of disease progression, whichever occurred first.
- A total of 390 enrolled patients, 194 were assigned to the daratumumab group and 196 to the active-monitoring group.
- The median follow up time was 65.2 months.

PMID: 39652675

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Highlights from the Demographics Table

Characteristic	Daratumumab (N=194)	Active Monitoring (N=196)
Age		
Median (range) — yr	63.0 (31–86)	64.5 (36–83)
Distribution — no. (%)		
18 to <65 yr	106 (54.6)	98 (50.0)
65 to <75 yr	67 (34.5)	74 (37.8)
≥75 yr	21 (10.8)	24 (12.2)
Cytogenetic risk profile — no./total no. (%)¶		
≥1 High-risk cytogenetic abnormality	29/167 (17.4)	22/170 (12.9)
del(17p)	3/166 (1.8)	8/166 (4.8)
t(4;14)	19/151 (12.6)	11/157 (7.0)
t(14;16)	7/146 (4.8)	3/145 (2.1)

PMID: 39652675

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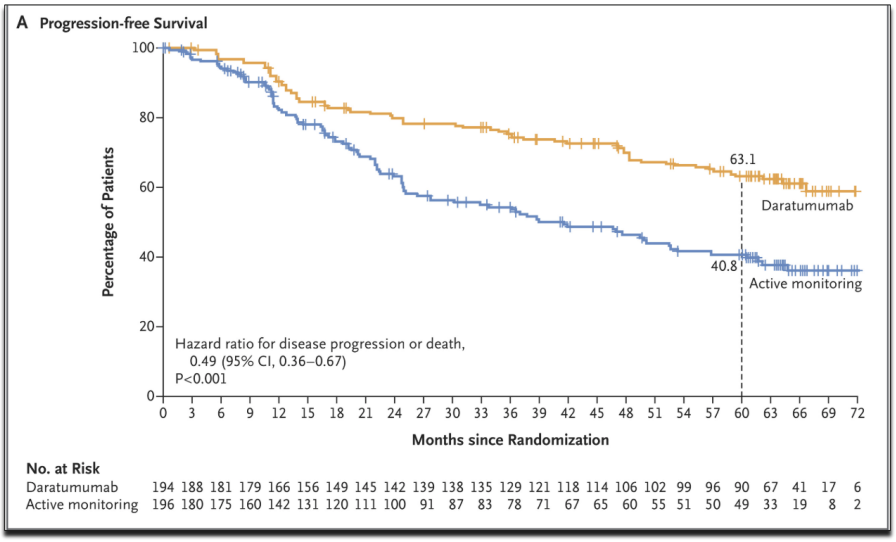
Highlights from the Demographics Table

Cytogenetic risk profile — no./total no. (%)¶		
≥1 High-risk cytogenetic abnormality	29/167 (17.4)	22/170 (12.9)
del(17p)	3/166 (1.8)	8/166 (4.8)
t(4;14)	19/151 (12.6)	11/157 (7.0)
t(14;16)	7/146 (4.8)	3/145 (2.1)
Risk of progression according to Mayo 2018 risk criteria‖		
Low	45 (23.2)	34 (17.3)
Intermediate	77 (39.7)	76 (38.8)
High	72 (37.1)	86 (43.9)
Median time from diagnosis of smoldering multiple myeloma to randomization (range) — yr	0.80 (0–4.7)	0.67 (0–5.0)

PMID: 39652675

104

Progression-Free Survival (PFS)



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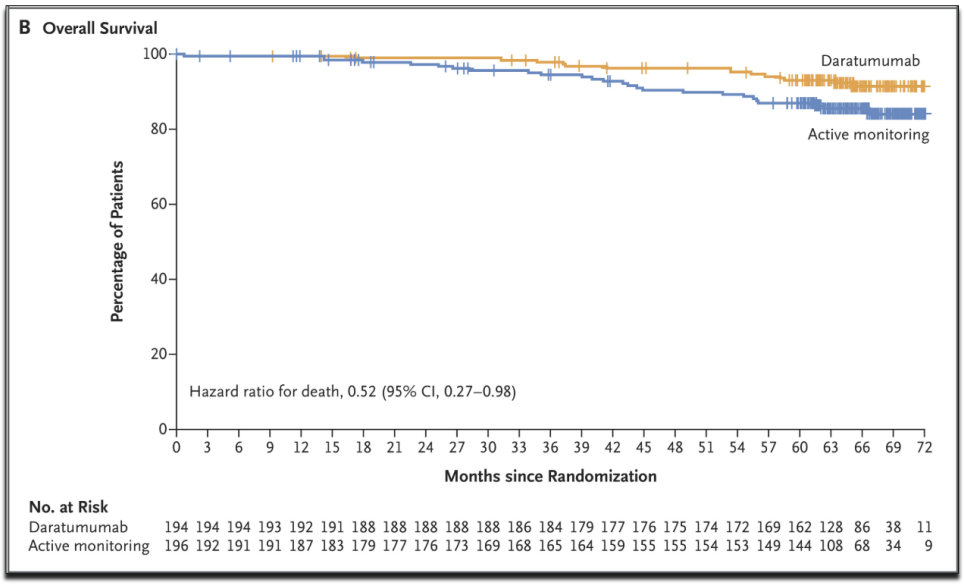
105

Overall Survival (OS)



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Discussion Slides

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Inclusion Criteria

- High risk SMM was defined as at least 10% clonal BM plasma cells and another risk factor (IgA isotype, M protein >30 g/L, immunoparesis, SFLC ratio 8-100 or >50% to <60% clonal bone marrow plasma cells.
- 41% of the study patients met criteria for high-risk disease by the 20/2/20 rule.

PMID: 39652675

108

Previous Studies: Lonial et al.

- Single agent lenalidomide was given to 182 patients with high or intermediate risk SMM.
- Median follow up was 35 months.
- Lenalidomide improved PFS in the entire study population (93 versus 76 percent at two years; HR 0.28, 95% CI 0.12-0.62). In the lenalidomide arm, there were fewer progression events due to end-organ damage, including fewer cases of kidney failure (0 versus 3 events) and bone lesions (3 versus 11 events).
- On subgroup analysis, the PFS benefit was clear in patients with high-risk SMM (HR 0.09, 95% CI 0.02-0.44) but did not reach statistical significance in those with intermediate-risk SMM (HR 0.52, 95% CI 0.15-1.85).
- Approximately 20 percent of patients stopped lenalidomide early due to toxicities.

PMID: 31652094

109

Previous Studies: Mateos et al.

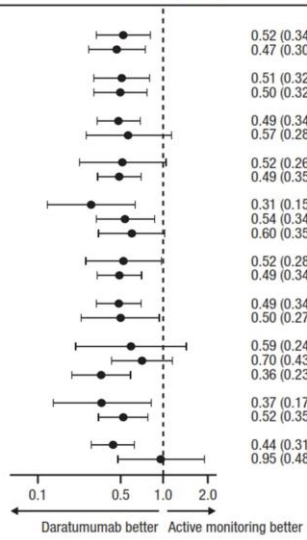
- 119 patients with high risk SMM treated with lenalidomide and dexamethasone for 9 cycles then single agent lenalidomide for up to two years or until progression. This study used a different definition of high risk SMM.
  - At least 95% phenotypically aberrant plasma cells in the bone marrow as determined by flow cytometry and immunoparesis
- Treatment with Rd resulted in improved PFS (median of 9.5 years vs. 2.1 years) and OS (median not reached after 12 years versus 8.5 years).
- One treatment-related death (a respiratory infection). Severe (grade 3/4) toxicities included infection (6 percent), asthenia (6 percent), neutropenia (5 percent), rash (3 percent), and more second primary malignancies (6 versus 1).

PMID: 36067617

110

Subgroup Analyses

Subgroup	Disease progression or death: Daratumumab (No. of events/total no. of patients)	Disease progression or death: Active monitoring (No. of events/total no. of patients)	Hazard ratio for disease progression or death (95% CI)
Sex			
Male	37/95	48/93	0.52 (0.34–0.80)
Female	30/99	51/103	0.47 (0.30–0.74)
Age			
<65 years	34/106	45/98	0.51 (0.32–0.79)
≥65 years	33/88	54/98	0.50 (0.32–0.77)
Race			
White	53/161	79/162	0.49 (0.34–0.69)
Non-White	14/33	20/34	0.57 (0.28–1.12)
Region			
Western EU+US	13/48	20/52	0.52 (0.26–1.04)
Other	54/146	79/144	0.49 (0.35–0.69)
Weight			
≤65 kg	11/43	26/46	0.31 (0.15–0.63)
>65–85 kg	33/96	39/84	0.54 (0.34–0.86)
>85 kg	23/55	34/64	0.60 (0.35–1.02)
Baseline renal function			
Normal	17/54	27/58	0.52 (0.28–0.96)
Abnormal	50/140	72/138	0.49 (0.34–0.70)
Risk factors			
<3	49/154	77/156	0.49 (0.34–0.70)
≥3	18/40	22/40	0.50 (0.27–0.94)
Mayo 2018 risk criteria			
Low	9/45	10/34	0.59 (0.24–1.45)
Intermediate	31/77	35/76	0.70 (0.43–1.14)
High	27/72	54/86	0.36 (0.23–0.58)
Cytogenetic risk at study entry			
Yes	13/29	14/22	0.37 (0.17–0.82)
No	39/116	59/118	0.52 (0.35–0.78)
Baseline ECOG performance status			
0	53/165	80/160	0.44 (0.31–0.63)
1	14/29	19/36	0.95 (0.48–1.91)



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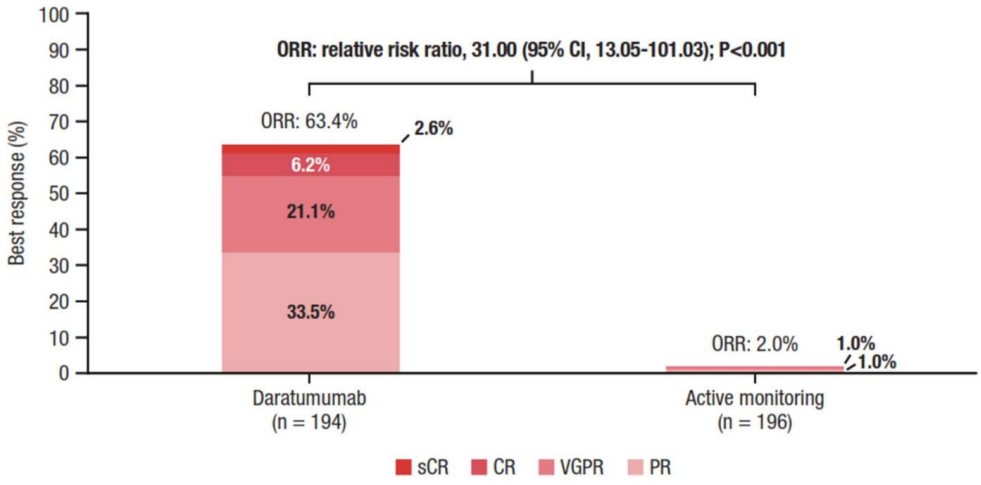
Overall Response Rates



PMID: 39652675

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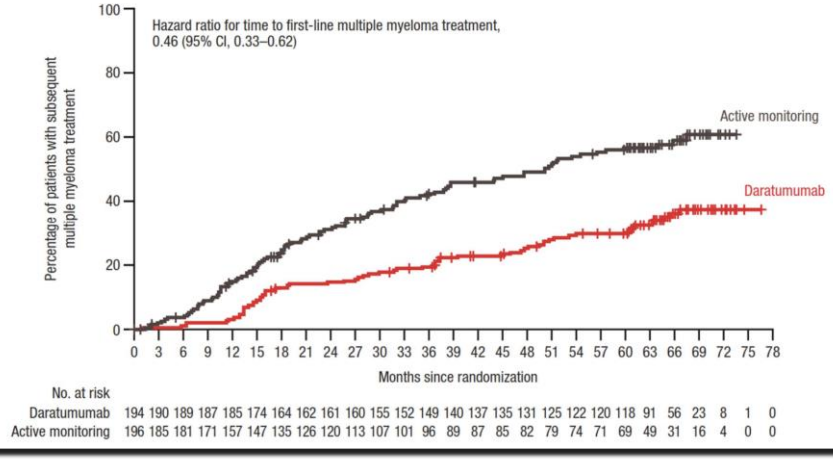
Time to First MM Treatment

Figure S5. Time to First-line Multiple Myeloma Treatment.

Shown are the results of the Kaplan–Meier estimates of time to first-line multiple myeloma treatment among patients in the intention-to-treat population, defined as all randomized patients. CI denotes confidence interval.



PMID: 39652675

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Questions?
Kimberly.Burcher@duke.edu

Thank you for your time!

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Maintenance Therapy in Transplant Eligible

John McKay, DO
Assistant Professor
Wake Forest Baptist
Atrium Health
Winston-Salem, NC

Sean Ormond, MD
Internal Medicine Residency, PGY-2
Wake Forrest Baptist
Atrium Health
Winston-Salem, NC

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Case

65 yo M presents for evaluation of multiple myeloma and consideration for maintenance. Patient initially presented with multiple lytic lesions, anemia. Marrow with 40% Karyotype was wnl. FISH with del13. LDH and B2M WNL. Underwent 4 cycles with D-RVd, was in CR. MRD was + at 0.5%. Underwent ASCT with mel 200. Day 100 marrow showing sCR, MRD + at 0.001%. No neuropathy from induction.

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What Would your Recommendation be for Maintenance?

A. Lenalidomide monotherapy
B. Lenalidomide + bortezemib
C. Lenalidomide + daratumamab
D. Second transplant
E. Other

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What if Patient were MRD (-) After Transplant?

A. Lenalidomide monotherapy
B. Lenalidomide + bortezemib
C. Lenalidomide + daratumamab
D. Second transplant
E. Other

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What if Patient Was MRD (-) and Had t(4:14)?

A. Lenalidomide monotherapy
B. Lenalidomide + bortezemib
C. Lenalidomide + daratumamab
D. Second transplant
E. Other

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What if Patient were MRD (-) and del17p in 25% of Cells

A. Lenalidomide monotherapy
B. Lenalidomide + bortezemib
C. Lenalidomide + daratumamab
D. Second transplant
E. Other

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Objectives

- Review current guidelines
- Brief review of current literature on maintenance in myeloma
- Discuss changes to myeloma risk stratification and current trial landscape in myeloma maintenance

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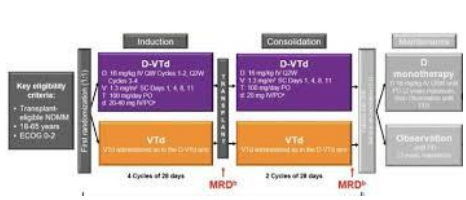
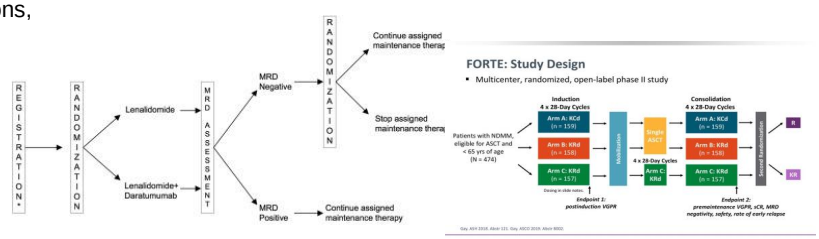
Is Lenalidomide a solo act or does it need a dance partner? Maintenance considerations in 2025

122

Maintenance in Myeloma

- Lenalidomide cornerstone of maintenance and only FDA approved therapy
- For many patient's indefinite
- Recent trials questioning combinations, durations, selection of patients





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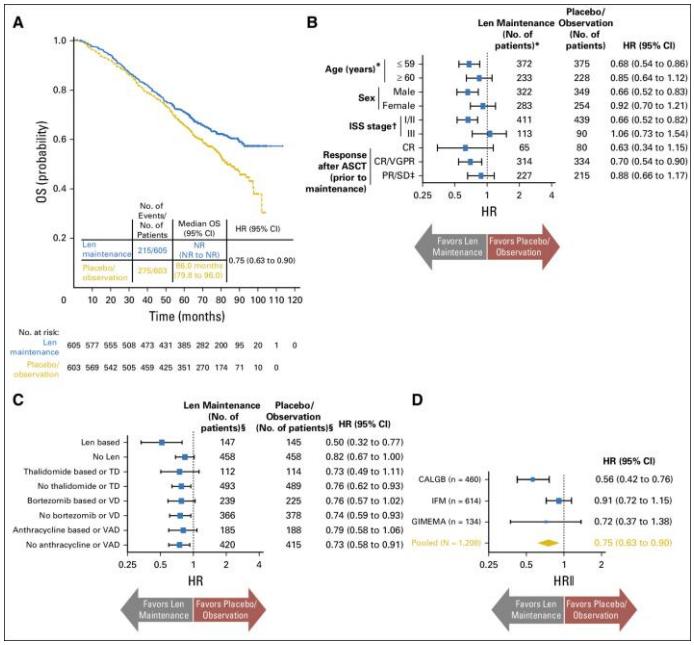

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McCarthy et al, JCO 2017

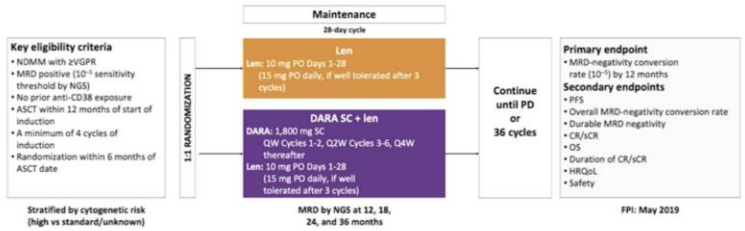
124

CLINICAL TRIALS AND OBSERVATIONS

Daratumumab with lenalidomide as maintenance after transplant in newly diagnosed multiple myeloma: the AURIGA study

Ashraf Badros,[1] Laahn Foster,[2] Larry D. Anderson Jr,[3] Chakra P. Chaulagain,[4] Erin Pettijohn,[5] Andrew J. Cowan,[6] Caitlin Costello,[7] Sarah Larson,[8] Douglas W. Sborov,[9] Kenneth H. Shain,[10] Rebecca Silbermann,[11] Nina Shah,[12] Alfred Chung,[12] Maria Krevvata,[13] Huiling Pei,[14] Sharmila Patel,[15] Vipin Khare,[15] Annelore Cortoos,[15] Robin Carson,[13] Thomas S. Lin,[15] and Peter Voorhees[16]

AURIGA study



11 @rahulbanerjeemd

UCSF

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	D-R	R
Age, y	n = 99	n = 101
Median (range)	63 (35-77)	62 (35-78)
Category, n (%)		
<65	61 (61.6)	61 (60.4)
65-70	23 (23.2)	21 (20.8)
≥70	15 (15.2)	19 (18.8)
Sex, n (%)	n = 99	n = 101
Male	61 (61.6)	58 (57.4)
Female	38 (38.4)	43 (42.6)
Race, n (%)	n = 99	n = 101
White	67 (67.7)	68 (67.3)
Black or African American	20 (20.2)	24 (23.8)
Asian	5 (5.1)	1 (1.0)
American Indian or Alaska native	0	1 (1.0)
Other*	5 (5.1)	5 (5.0)
Not reported	2 (2.0)	2 (2.0)
ECOG PS score, n (%)	n = 99	n = 101
0	45 (45.5)	55 (54.5)
1	52 (52.5)	44 (43.6)
2	2 (2.0)	2 (2.0)
ISS disease stage, n (%)	n = 91	n = 98
I	40 (44.0)	38 (38.8)
II	28 (30.8)	37 (37.8)
III	23 (25.3)	23 (23.5)
No. of induction cycles	n = 98	n = 99
Median (range)	5.0 (4.0-8.0)	5.0 (4.0-8.0)
Cytogenetic risk at diagnosis	n = 92	n = 89
Standard risk	63 (68.5)	66 (74.2)
High risk†	22 (23.9)	15 (16.9)
del(17p)	13 (14.1)	3 (3.4)
t(4;14)	10 (10.9)	12 (13.5)
t(14;16)	6 (6.5)	7 (7.9)
Unknown	7 (7.6)	8 (9.0)
Revised cytogenetic risk at diagnosis	n = 93	n = 89
Standard risk	52 (55.9)	53 (59.6)
High risk‡	32 (34.4)	30 (33.7)
del(17p)	13 (14.0)	3 (3.4)
t(4;14)	10 (10.8)	12 (13.5)
t(14;16)	6 (6.5)	7 (7.9)
t(14;20)	1 (1.1)	2 (2.2)
gain/amp(1q21)	16 (17.2)	22 (24.7)
Unknown	9 (9.7)	6 (6.7)

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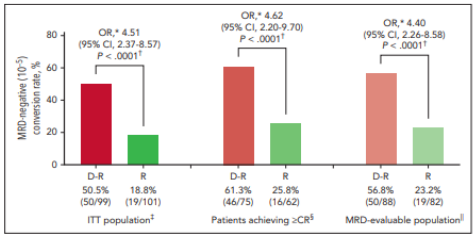

	D-R MRD-negative rate, n/N (%)	R MRD-negative rate, n/N (%)	OR (95% CI)
ITT (overall)	50/99 (50.5)	19/101 (18.8)	4.51 (2.37-8.57)
Sex			
Male	32/61 (52.5)	11/58 (19.0)	4.71 (2.06-10.78)
Female	18/38 (47.4)	8/43 (18.6)	3.94 (1.45-10.68)
Age			
<65 years	30/61 (49.2)	12/61 (19.7)	3.95 (1.76-8.85)
≥65 years	20/38 (52.6)	7/40 (17.5)	5.24 (1.86-14.74)
Race			
White	31/67 (46.3)	14/68 (20.6)	3.32 (1.55-7.10)
Black	12/20 (60.0)	4/24 (16.7)	7.50 (1.85-30.34)
Other	7/12 (58.3)	1/9 (11.1)	11.20 (1.04-120.36)
Weight			
≤70 kg	12/23 (52.2)	4/18 (22.2)	3.82 (0.96-15.18)
>70 kg	38/76 (50.0)	15/81 (18.5)	4.40 (2.14-9.03)
Baseline ECOG PS score			
0	20/45 (44.4)	9/55 (16.4)	4.09 (1.62-10.31)
≥1	30/54 (55.6)	10/46 (21.7)	4.50 (1.86-10.88)
ISS at diagnosis			
I	19/40 (47.5)	8/38 (21.1)	3.39 (1.25-9.19)
II	13/28 (46.4)	7/37 (18.9)	3.71 (1.23-11.25)
III	15/23 (65.2)	3/23 (13.0)	12.50 (2.83-55.25)
Cytogenetic risk at diagnosis			
High risk*	7/22 (31.8)	1/15 (6.7)	6.53 (0.71-60.05)
Standard risk	35/63 (55.6)	14/66 (21.2)	4.64 (2.15-10.04)
Revised cytogenetic risk at diagnosis			
High risk†	14/32 (43.8)	4/30 (13.3)	5.06 (1.43-17.88)
Standard risk	28/52 (53.8)	12/53 (22.6)	3.99 (1.72-9.26)

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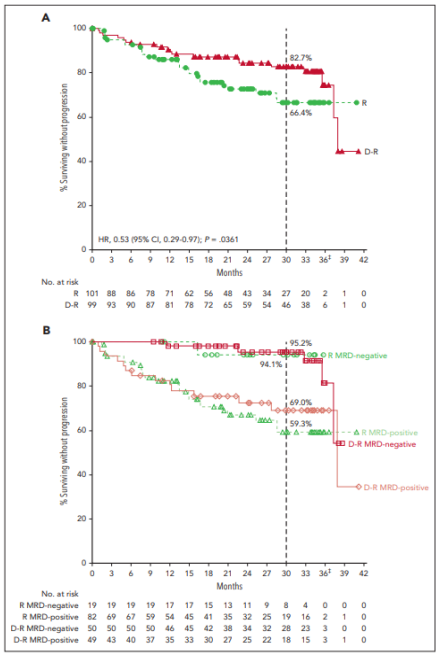
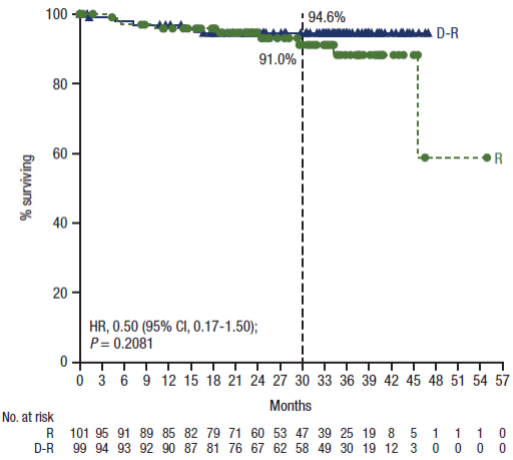


Supplementary Figure 2. OS in the ITT population.



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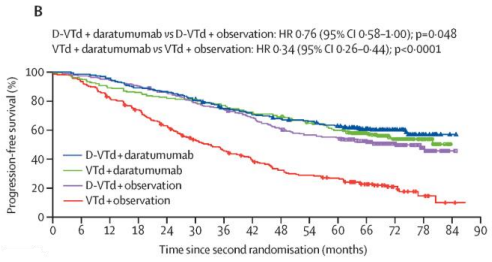
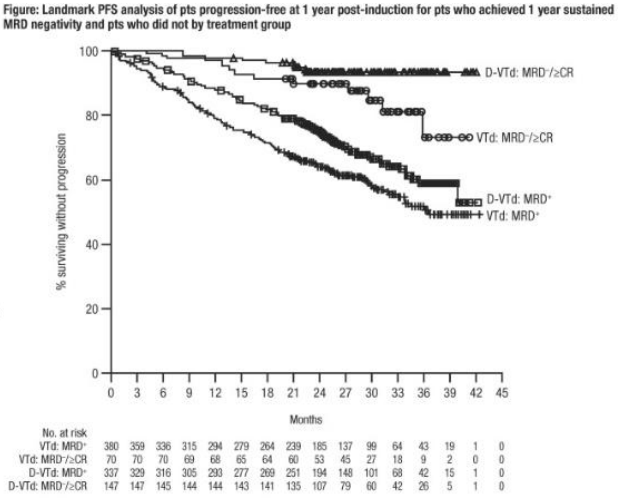
CASSIOPEIA Trial





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Moreau, P et al., Lancet 2024
Loiseau, H., et al., Blood 2022

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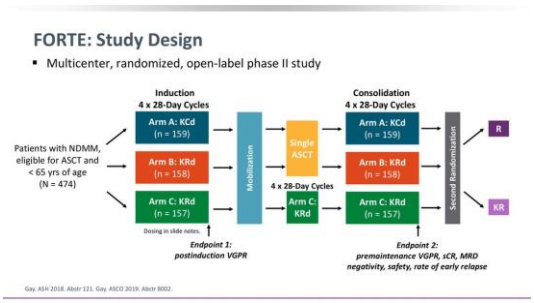
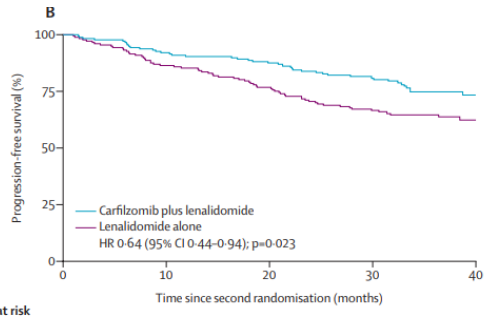
FORTE Trials





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Mina, R et al., Lancet Oncology 2023

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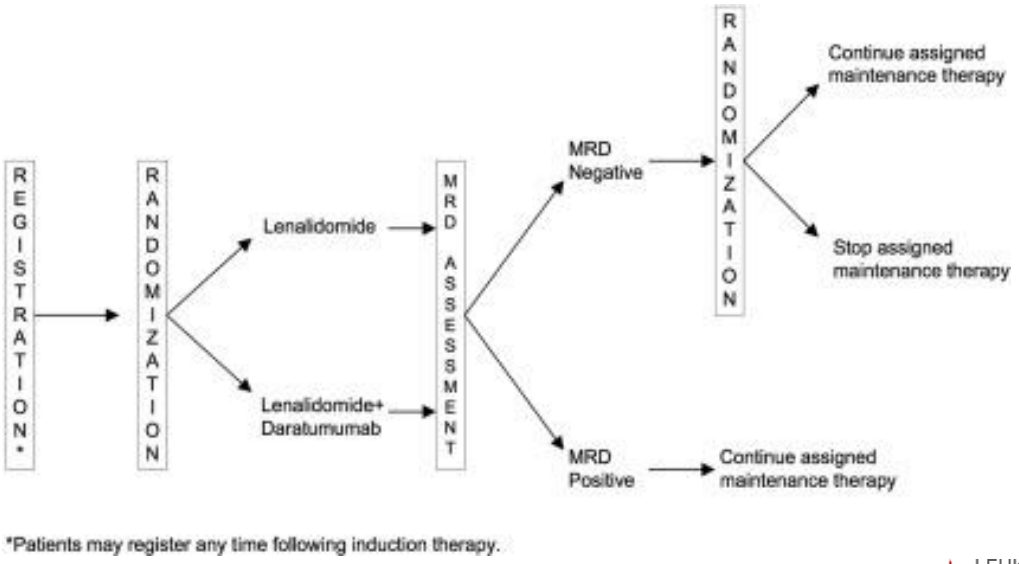
S1803



*Patients may register any time following induction therapy.

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Krishnan, A et al., Blood 2020

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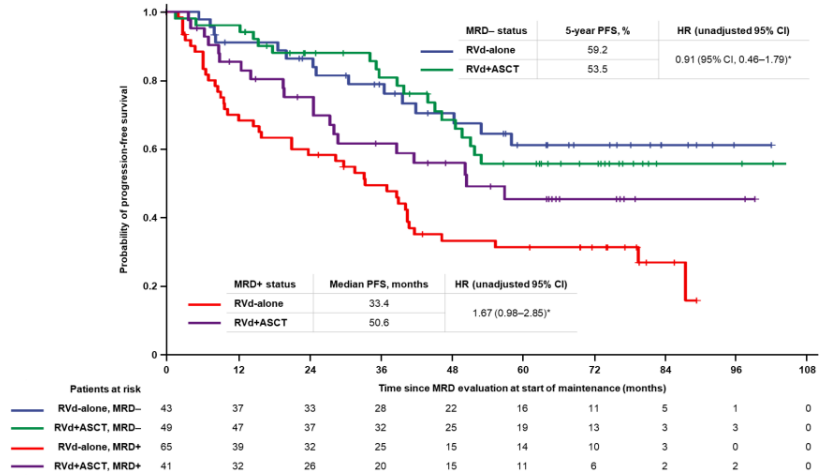
Importance of MRD in Myeloma

Figure S7: Kaplan–Meier analysis of progression-free survival by MRD status from start of maintenance therapy

ASCT, autologous stem cell transplantation. CI, confidence interval. HR, hazard ratio. MRD, minimal residual disease. PFS, progression-free survival. RVd, lenalidomide, bortezomib, dexamethasone. *The widths of the CIs have not been adjusted for multiplicity, and so the intervals should not be used in place of a hypothesis test.



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Richardson, P et al., NEJM 2022

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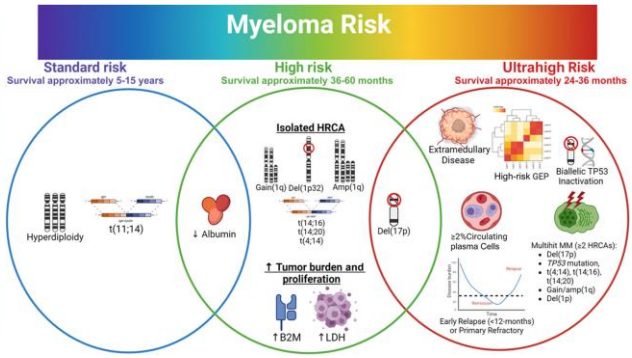
What Is High Risk?

IMS consensus on genomic definition of high risk myeloma

- **Del17p** in more than 20% of plasma cells
- **TP53 mut** (no threshold VAF)
- **Del(1p32)$^{del/del}$**
- **t(4;14)** or **t(14;16)** or **t(14;20)** + **Gain/amp 1q** or **del(1p32)$^{del/wt}$**
- **Gain/amp 1q** + **del(1p32)$^{del/wt}$**

Manuscript in prep



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Rees, M et al., Hematologic Malignancies 2024

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Current Trials

Maintenance regimens utilized

Nonrandomized studies	Total studies
Single agent maintenance	
Belantamab	1
Daratumumab	1
Iberdomide	2
Lenalidomide	1
Combination maintenance	
Belantamab + lenalidomide	2
Isatuximab + lenalidomide	2

Randomized Studies	Total studies	Control arm maintenance
Single agent maintenance: treatment arm		
Elranatamab	1	Lenalidomide
Lenalidomide	2	Lenalidomide
Combination maintenance: treatment arm		
Belantamab + lenalidomide	1	Belantamab + lenalidomide
Cellprotect[a] + isatuximab	1	Isatuximab
Daratumumab + lenalidomide	2	Lenalidomide
Daratumumab + ixazomib	1	Ixazomib
Ixazomib + lenalidomide	1	Lenalidomide
Selinexor + lenalidomide	1	Lenalidomide
Teclistamab + lenalidomide	1	Lenalidomide

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Tariq, S. et al., Clinical Hematology International, 2023

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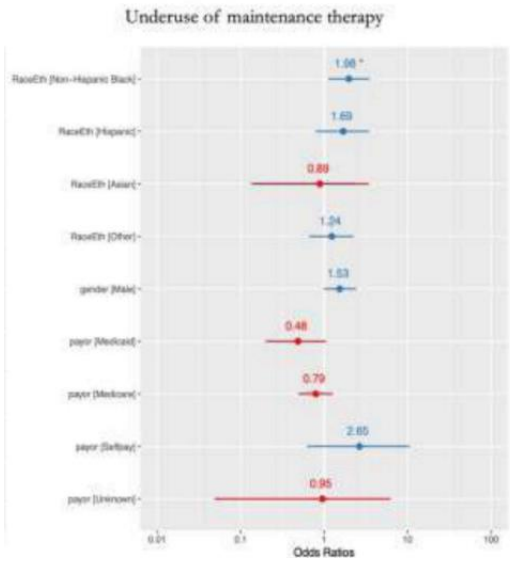
Underuse of Maintenance



Joshi, H et al., Cancer Epidemiology, 2022

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Questions to Consider

- How does MRD status effect your maintenance suggestions? Does MRD burden factor in?
- What about risk status? Does recent proposed suggestion by IMS potentially change how you approach maintenance in patients and what is considered high risk?
- Are there patients you would NOT enroll on trials that would potentially randomize to lenalidomide maintenance?

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Revisit Cases

65 yo M presents for evaluation of multiple myeloma and consideration for maintenance. Patient initially presented with multiple lytic lesions, anemia. Marrow with 40% Karyotype was wnl. FISH with del13. LDH and B2M WNL. Underwent 4 cycles with D-RVd, was in CR. MRD was + at 0.5%. Underwent ASCT with mel 200. Day 100 marrow showing sCR, MRD + at 0.001%. No neuropathy from induction. What would your recommended maintenance be?

A. Lenalidomide monotherapy
B. Lenalidomide + bortezomib
C. Lenalidomide + daratumumab
D. Second transplant
E. Other

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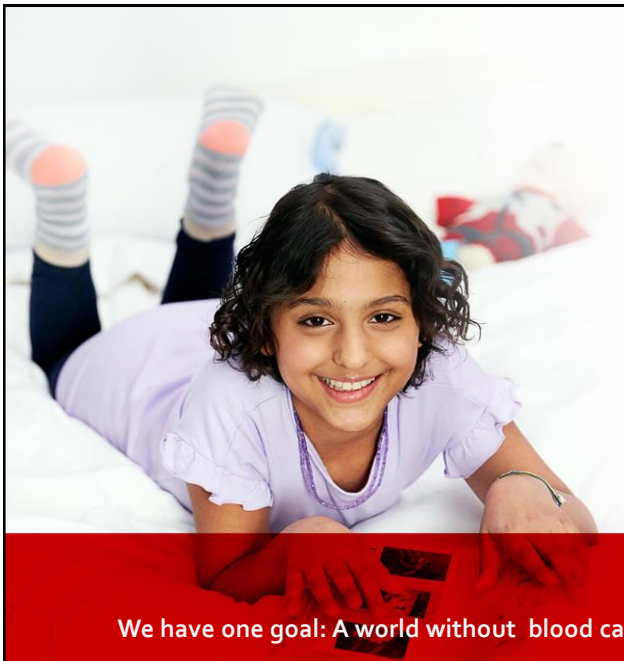

THANK YOU!

Please scan the QR Code to download a copy of the presentation slides.

We have one goal: A world without blood cancers

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