APTITUDE HEALTH®

EPICS

Conference Coverage: EHA 2025 – Focus on Multiple Myeloma (MM)

June 20, 2025

The medical opinions expressed in this report reflect those of the expert panel and EHA presenters

Report Contents

EPICS

Content	Link
Meeting Snapshot	
Faculty Panel	
Meeting Agenda	
Newly Diagnosed Multiple Myeloma: Transplant Eligible	
Newly Diagnosed Multiple Myeloma: Transplant Ineligible	
Maintenance and Monitoring	
Relapsed/Refractory Multiple Myeloma: Small Molecules and Classical Antibodies	
Relapsed/Refractory Multiple Myeloma: ADCs and Multispecifics	
Relapsed/Refractory Multiple Myeloma: CAR Ts	

Meeting Snapshot: EHA 2025 – Focus on Multiple Myeloma

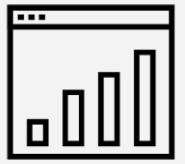
EPICS

A closed-door roundtable discussion focused on MM was held on **June 20, 2025**

MM-specific discussions on latest research updates, therapeutic advances, and their application in clinical decision-making were led by **Rafael Fonseca**, **MD,** from the Mayo Clinic in Scottsdale, AZ

The panel consisted of 7 key experts in MM

- 2 from Europe
- 5 from North America



Insights report includes postmeeting analyses and actionable recommendations

Panel Consisting of 5 North American and 2 European MM Experts

EPICS

Keith Stewart, MB, ChB, FRCP
University of Toronto

Faith Davies, MD
Perlmutter Cancer Center at
New York University Langone

Ajai Chari, MD
University of California –
San Francisco

CHAIR:
Rafael Fonseca, MD
Mayo Clinic

Hermann Einsele, MD, FRCP
University Hospital Würzburg

Sagar Lonial, MD, FACP
Emory University's Winship
Cancer Institute

Bruno Paiva, PharmD, PhD
University of Navarra

APTITUDE HEALTH®

Meeting Agenda

EPICS

Time (MT/CEST)	Topic	Speaker/Moderator
8.15 AM – 8.20 AM/16.15 – 16.20 (5 min)	**Welcome and Introductions**	Rafael Fonseca, MD
8.20 AM – 8.30 AM/16.20 – 16.30 (10 min)	**Newly Diagnosed Multiple Myeloma: Transplant Eligible**	Sagar Lonial, MD, FACP
8.30 AM – 8.50 AM/16.30 – 16.50 (20 min)	Discussion and Key Takeaways	Moderator: Rafael Fonseca, MD
8.50 AM – 9.00 AM/16.50 – 17.00 (10 min)	**Newly Diagnosed Multiple Myeloma: Transplant Ineligible**	Keith Stewart, MB, ChB, FRCP
9.00 AM – 9.25 AM/17.00 – 17.25 (25 min)	Discussion and Key Takeaways	Moderator: Rafael Fonseca, MD
9.25 AM – 9.35 AM/17.25 – 17.35 (10 min)	**Maintenance and Monitoring**	Rafael Fonseca, MD
9.35 AM – 9.55 AM/17.35 – 17.55 (20 min)	Discussion and Key Takeaways	Moderator: Rafael Fonseca, MD
9.55 AM – 10.05 AM/17.55 – 18.05 (10 min)	***BREAK***	
10.05 AM – 10.15 AM/18.05 – 18.15 (10 min)	**Relapsed/Refractory Multiple Myeloma: Small Molecules and Classical Antibodies**	Faith Davies, MD
10.15 AM – 10.35 AM/18.15 – 18.35 (20 min)	Discussion and Key Takeaways	Moderator: Rafael Fonseca, MD
10.35 AM – 10.45 AM/18.35 – 18.45 (10 min)	**Relapsed/Refractory Multiple Myeloma: ADCs and Multispecifics**	Ajai Chari, MD
10.45 AM – 11.10 AM/18.45 – 19.10 (25 min)	Discussion and Key Takeaways	Moderator: Rafael Fonseca, MD
11.10 AM – 11.20 AM/19.10 – 19.20 (10 min)	**Relapsed/Refractory Multiple Myeloma: CAR Ts**	Hermann Einsele, MD, FRCP
11.20 AM – 11.40 AM/19.20 – 19.40 (20 min)	Discussion and Key Takeaways	Moderator: Rafael Fonseca, MD
11.40 AM – 11.45 AM/19.40 – 19.45 (5 min)	**Summary and Closing Remarks**	Rafael Fonseca, MD

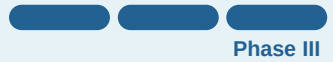
APTITUDE HEALTH®

EPICS

Newly Diagnosed Multiple Myeloma: Transplant Eligible

Abstract Selection

EPICS

Abstract	Phase
Abstract S199: Circulating Tumor Cells for the Staging of MM: A European Pooled Analysis of 2446 Newly Diagnosed Patients. (Bertamini L, et al)	Observational
Abstract S205: Minimal Residual Disease-Driven Strategy Following Isatuximab-Carfilzomib-Lenalidomide-Dexamethasone Induction in Transplant-Eligible Newly Diagnosed Multiple Myeloma: Primary Endpoints of the Phase 3 MIDAS Trial. (Perrot A, et al)	 Phase III
Abstract S208: Analysis of Sustained MRD Negativity in Patients With Newly Diagnosed Multiple Myeloma Treated With Carfilzomib-Lenalidomide-Dexamethasone With or Without Isatuximab. (Phase III ISKIA Trial) (Gay F, et al)	 Phase III
Abstract S209: Isatuximab, Carfilzomib, Lenalidomide, and Dexamethasone (Isa-KRd) for High-Risk (HR) Newly Diagnosed Multiple Myeloma (NDMM): First-Time Report of the Full Cohort of Transplant-Eligible (TE) Patients in the GMMG-CONCEPT Trial. (Leypoldt L, et al)	 Phase II
Abstract PS1712: Daratumumab + Bortezomib/Lenalidomide/Dexamethasone in Transplant-Eligible Newly Diagnosed Multiple Myeloma: Analysis of Sustained Minimal Residual Disease Negativity in the Phase 3 PERSEUS Trial. (Moreau P, et al)	 Phase III

MRD-Driven Strategy Following Isa-KRd Induction in the MIDAS Phase III Study in TE Patients With NDMM

Perrot A, et al. EHA 2025. Abstract S205

EPICS

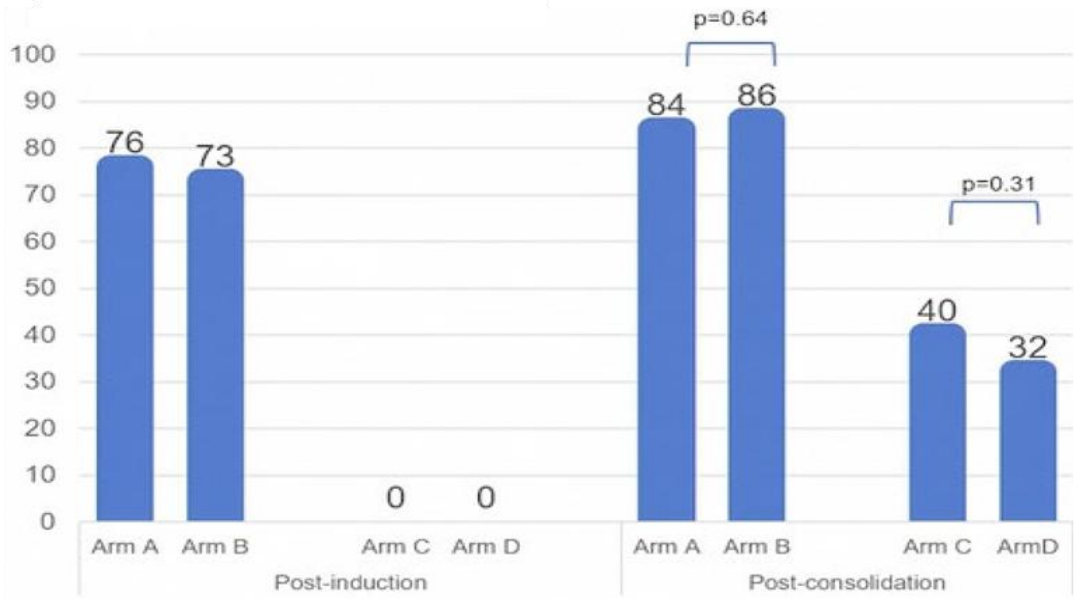
Study Design and Patients

- Phase III study of MRD-driven (10^{-6}) consolidation and maintenance strategy following induction with Isa-KRd in transplant-eligible NDMM (n=499 with standard risk [postinduction MRD negativity]; n=252 with high risk [postinduction MRD positivity])
- Standard-risk pts were randomized to Isa-KRd consolidation alone (A) or with ASCT (B)
- High-risk pts were randomized to ASCT + consolidation (C) or tandem ASCT (D)

Outcomes

- Postconsolidation MRD negativity was similar in A (76%) and B (73%), and no pts in C or D were MRD negative after induction
- Pts with t(11:14) had higher MRD-negative rates after induction, whereas those with t(4:14) had lower rates of MRD negativity
- Rates of G3 AEs were higher for D vs C
- Longer follow-up is needed to assess potential PFS/OS benefit
- Cytogenetics and MRD-based data appear to correlate with risk stratification

MRD-Negativity (10^{-6}, NGS) in ITT



Author Conclusions

- In MRD-negative pts following Isa-KRd induction, ASCT consolidation did not improve MRD-negativity rate vs continued Isa-KRd
- In MRD-positive pts, tandem ASCT did not provide additional benefit in terms of MRD negativity vs single ASCT

APTITUDE HEALTH®

Sustained MRD-Negativity Results From the Phase III IsKia Study of Isa-KRd vs KRd in TE NDMM

Gay F, et al. EHA 2025. Abstract S208

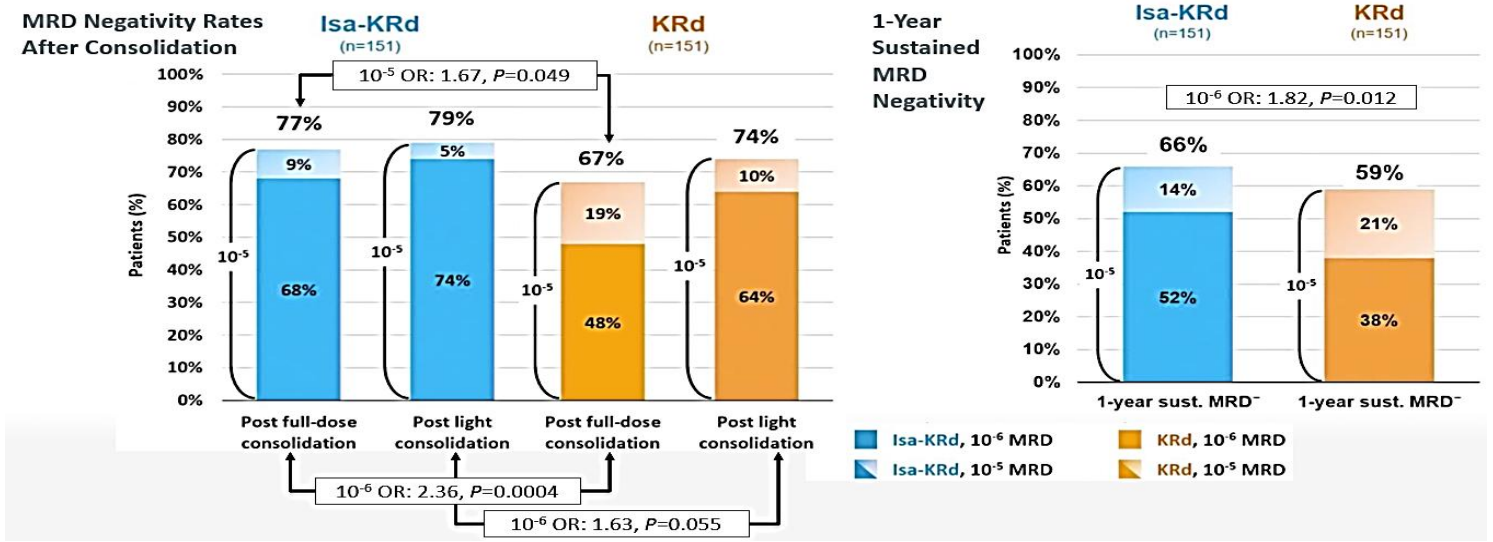
EPICS

Study Design and Patients

- Phase III trial in transplant-eligible pts with NDMM comparing induction and post-ASCT consolidation followed by a lower-dose “light consolidation” with Isa-KRd vs KRd alone
- 151 pts were enrolled in each arm; pts who completed “light consolidation” and consolidation: Isa-KRd, 83% and 90%; KRd, 90% and 94%

Outcomes

- MRD negativity after consolidation for Isa-KRd vs KRd
  - At 10^{-5}: 77% vs 67% (HR 1.67; *P*=.047)
  - At 10^{-6}: 68% vs 48% (HR 2.36; *P*=.0004)
- MRD negativity after “light consolidation” for Isa-KRd vs KRd
  - At 10^{-5}: 79% vs 74%
  - At 10^{-6}: 74% vs 64% (HR 1.63; *P*=.055)
- AEs were generally similar but diarrhea and low-grade respiratory infections were more common with Isa



Author Conclusions

- Isa-KRd significantly increased the rate of 10^{-6} 1-year sustained MRD negativity compared with KRd, even among high-risk and very-high-risk pts. The rate of early relapse was low in both arms, supporting the effectiveness of the second-generation PI carfilzomib in this setting
- ISA-KRd treatment was tolerable, with no increased toxicity compared with prolonged therapy with KRd without Isa
- When comparing highly effective regimens, the 10^{-6} MRD negativity cutoff was more informative than the 10^{-5} cutoff negativity cutoff

Isa-KRd for High-Risk (HR) Newly Diagnosed Multiple Myeloma (NDMM): First-Time Report of the Full Cohort of TE Patients in the GMMG-CONCEPT Trial

Leypoldt L, et al. EHA 2025. Abstract S209

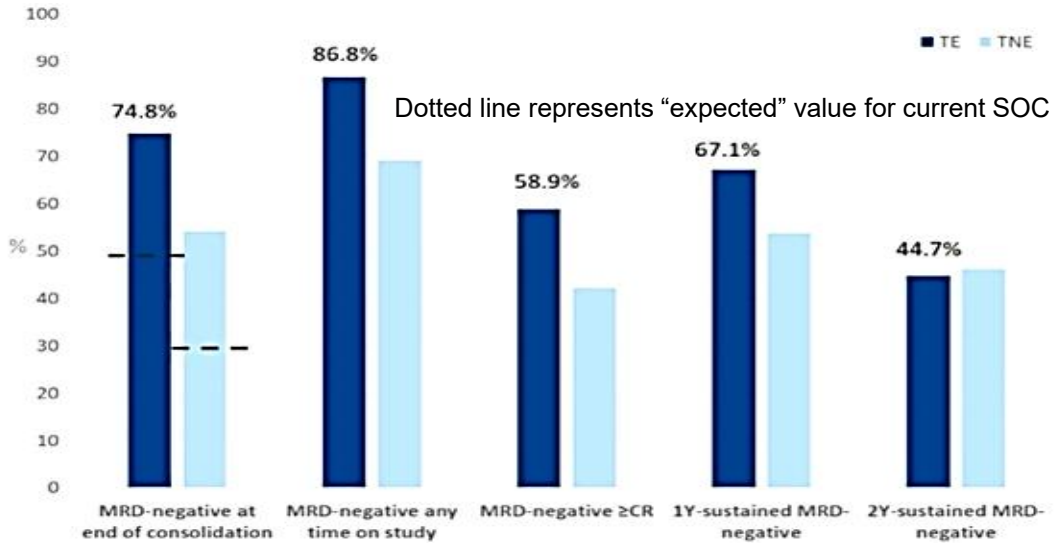
EPICS

Study Design and Patients

- Prospective, multicenter trial of intensified 1L treatment with Isa-KRd in adult pts with NDMM and poor prognosis due to high-risk cytogenetic abnormalities (transplant-eligible [TE], 219; transplant-ineligible [TNE], 26)
- Pts underwent induction with Isa-KRd, followed by further Isa-KRd cycles

Outcomes

- 54.2% of 19 evaluable TNE pts were MRD negative (10^{-5}) at the end of consolidation and 69.2% at any time
  - The proportion of pts who had a CR and MRD negativity was 42.3%
- In TE pts, sustained MRD negativity was 53.8% at 1 yr and 46.2% at 2 yr
- Reaching and remaining in MRD-negative state led to a significant PFS benefit (HR 0.16 [95% CI: 0.08–0.32])



Author Conclusions

- CONCEPT has the largest prospective trial cohort of pts purely with HR NDMM reported so far
- Isa-KRd resulted in high rates of MRD negativity, 1-yr and 2-yr sustained MRD negativity, and OS, supporting the use of Isa-KRd as an SOC in the hard-to-treat HR NDMM
- Carfilzomib once-weekly dosing with 56 mg/m^2 leads to more dose reduction but less dose discontinuation and should be preferred in this setting over twice-weekly dosing

Daratumumab + Bortezomib/Lenalidomide/Dexamethasone in Transplant-Eligible NDMM: Analysis of Sustained MRD Negativity in the Phase III PERSEUS Trial

EPICS

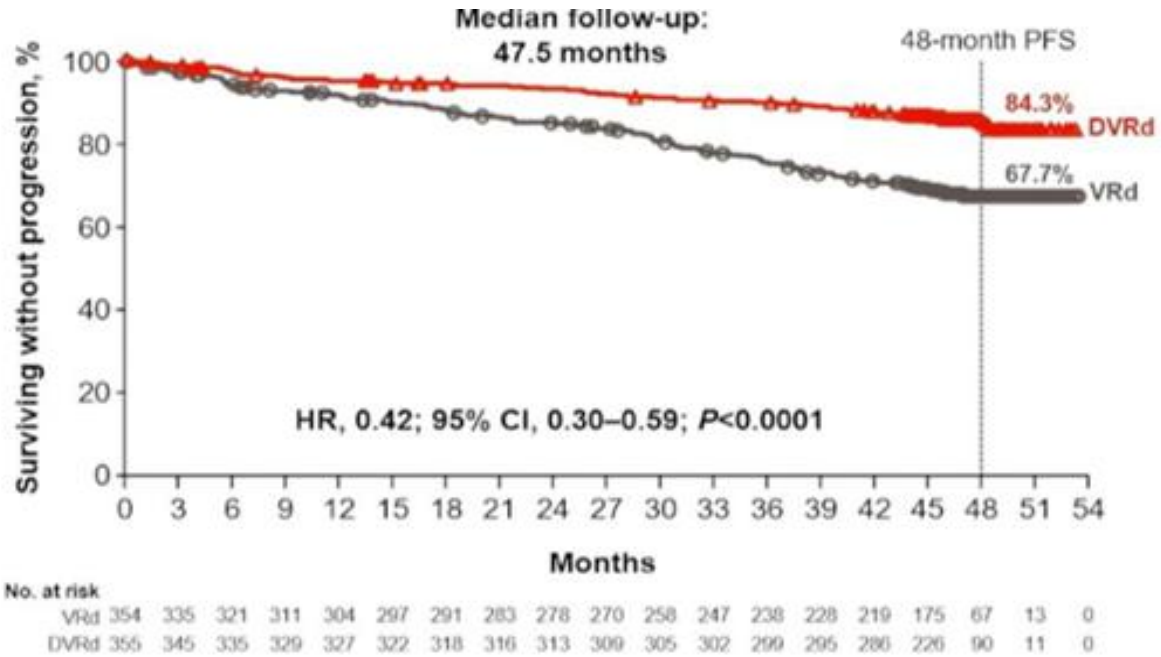
Moreau P, et al. EHA 2025. Abstract PS1712

Study Design and Patients

- Randomized trial of DVRd vs VRd, both as induction and post-HSCT consolidation (with DR maintenance in the DVRd arm)
- In transplant-eligible adult pts with NDMM and ECOG PS ≤2: DVRd n=355; VRd n=354; median f/u 47.5 mo

Outcomes

- DVRd reduced the rate of relapse/PD within 18 mo of therapy initiation (functionally high risk) vs VRd: 3.1% vs 6.8%
- 4-yr PFS significantly increased for DVRd (84.3%) vs VRd (67.7%); HR 0.42; *P*<.0001
- MRD-negative CR rates were higher with DVRd vs VRd at 12 mo (odds ratio 4.42; *P*<.0001) and 24 mo (odds ratio 4.26; *P*<.0001)
- Benefits in MRD-negative CR were seen across all subgroups analyzed



Author Conclusions

- In this post hoc analysis, DVRd + DR maintenance
  - Reduced the rates of relapse/PD for functionally high-risk pts
  - Led to higher rates of sustained MRD negativity (10^{-5}) ≥CR that was associated with a PFS benefit

APTITUDE HEALTH®

EPICS

Newly Diagnosed Multiple Myeloma: Transplant Eligible

Discussion

Update on NDMM: Transplant Eligible (1/3)

EPICS

General

- Frontline treatment regimen
  - Experts almost exclusively use quadruplet regimens to treat transplant-eligible MM at this point but questioned whether this is effective enough to replace transplant
    - They agreed that all high-risk patients should receive transplant on the basis of the current data
  - MRD negativity alone should not necessarily be used to make decisions regarding transplant, particularly if MRD is only read at a single time point
  - Maintenance selection is variable on the basis of prior treatment, risk status, and posttransplant MRD status

- Managing care for patients with low-level MRD positivity
  - Experts were split on the best strategy for patients who continue to have low-level MRD-positive status after transplant and maintenance
    - Some indicated this would be a great population to consider bispecifics
    - Others feel that if the patient has already received a sufficiently intensive treatment regimen, then observation on single-agent lenalidomide maintenance is appropriate, as many will convert to MRD negative on their own

Update on NDMM: Transplant Eligible (2/3)

EPICS

Abstract S205: Minimal Residual Disease-Driven Strategy Following Isatuximab-Carfilzomib-Lenalidomide-Dexamethasone Induction in Transplant-Eligible Newly Diagnosed Multiple Myeloma: Primary Endpoints of the Phase 3 MIDAS Trial (Perrot A, et al)

- While MRD is an effective tool for driving treatment decisions in the frontline setting, the experts stressed that MRD persistence and reproducibility are more important and useful than a single MRD reading
- The experts are not certain that MRD alone after induction can be used to make a decision about transplant, but indicated that it could be used to rule out tandem transplant on the basis of these data
  - One expert highlighted that if patients do not receive transplant because of MRD negativity, they should receive an intensive maintenance regimen to ensure MRD negativity is maintained

Update on NDMM: Transplant Eligible (3/3)

EPICS

Abstract S209: Isatuximab, Carfilzomib, Lenalidomide, and Dexamethasone (Isa-KRd) for High-Risk (HR) Newly Diagnosed Multiple Myeloma (NDMM): First-Time Report of the Full Cohort of Transplant-Eligible (TE) Patients in the GMMG-CONCEPT Trial (Leypoldt L, et al)

- Experts agreed that the strategy evaluated in this trial, where intensified maintenance and consolidation is used in high risk and ultrahigh risk, is potentially the best method to control disease
- For standard-risk patients, 2 consecutive MRD-negative tests would be sufficient to discontinue maintenance

Abstract PS1712: Daratumumab + Bortezomib/Lenalidomide/Dexamethasone in Transplant-Eligible Newly Diagnosed Multiple Myeloma: Analysis of Sustained Minimal Residual Disease Negativity in the Phase 3 PERSEUS Trial (Moreau P, et al)

- Experts were impressed with the MRD-negativity results, which they indicated are better than those seen in low-risk DLBCL
- They consider this an indicator of how effective frontline myeloma treatment has become
- Consistent with the data from CONCEPT, this study provides further support that for standard-risk patients, 2 consecutive MRD-negative tests would be sufficient to discontinue maintenance

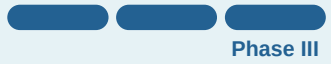
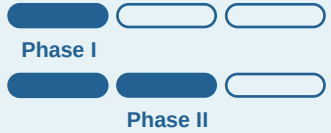
APTITUDE HEALTH®

EPICS

Newly Diagnosed Multiple Myeloma: Transplant Ineligible

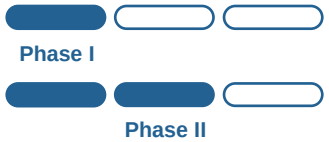
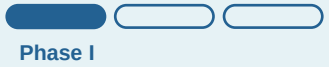
Abstract Selection (1/2)

EPICS

Abstract	Phase
Abstract PS1738: Retrospective Real-World Treatment Patterns and Outcomes in European Patients With Newly Diagnosed Multiple Myeloma Not Receiving Stem Cell Transplantation. (Garg M, et al)	Observational
Abstract S206: Elranatamab in Combination With Daratumumab and Lenalidomide (EDR) in Patients With Newly Diagnosed Multiple Myeloma (NDMM) Not Eligible for Transplant: Initial Results From MagnetisMM-6 Part 1. (Dimopoulos M, et al)	
Abstract PS1730: Daratumumab Plus Bortezomib, Lenalidomide, and Dexamethasone in Patients With Newly Diagnosed Multiple Myeloma: Subgroup Analysis of Transplant-Ineligible Patients in the Phase 3 CEPHEUS Study. (Facon T, et al)	
Abstract PF733: Extended Dosing Schedule of Belantamab Mafodotin in Combination With Daratumumab, Lenalidomide and Dexamethasone in Patients With Newly Diagnosed Multiple Myeloma: The Phase 1/2 BELADRD Study. (Terpos E, et al)	
Abstract PF729: Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone (ISA-VRd) in Newly Diagnosed Multiple Myeloma (NDMM): Outcomes in Patients With 1q21+ Status in the Phase 3 IMROZ Study. (Dimopoulos M, et al)	

Abstract Selection (2/2)

EPICS

Abstract	Phase
Abstract PF727: Isa-VRd Improves Outcomes In High-Risk (HR) Newly Diagnosed Transplant-Ineligible Multiple Myeloma (NDMM TI) Using the IMS/IMWG Consensus HR Definition. Results From the BENEFIT Phase 3 Trial (IFM 2020-05). (Corre J, et al)	
Abstract PS1746: Multicenter Phase 2 Study of Subcutaneous Isatuximab Plus Bortezomib, Lenalidomide, and Dexamethasone (ISA SC-VRd) in Newly Diagnosed Transplant-Ineligible Multiple Myeloma (NDMM TI): Results From ISASOCUT (IFM 2022-05). (Bobin A, et al)	
Abstract PS1784: Iberdomide and Dexamethasone in Elderly Patients With Newly Diagnosed Multiple Myeloma. (Puig N, et al)	
Abstract PF737: Iberdomide, Bortezomib, and Dexamethasone (IBERVd) in Transplant-Ineligible (TNE) Newly Diagnosed Multiple Myeloma: Updated Results From the CC-220-MM-001 Trial. (White D, et al)	

Retrospective Real-World Treatment Patterns and Outcomes in European Patients With NDMM Not Receiving SCT

Garg M, et al. EHA 2025. Abstract PS1738

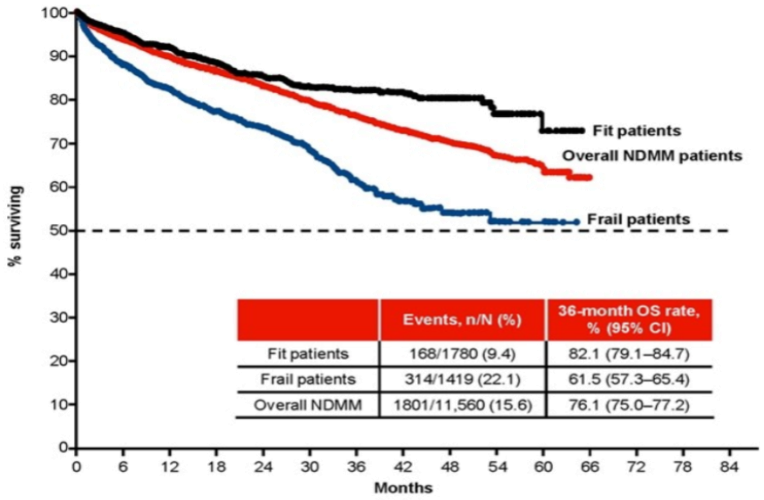
EPICS

Study Design and Patients

- RWE from 4 EU MM registries collected for adult pts with NDMM who started 1L treatment between Jan 2019 and Nov 2024 and did not receive ASCT
- TTNT and OS were analyzed

Outcomes

- SOC backbone therapy evolved from mostly bortezomib (71.5%) in 2019 to dara (60.8%) in 2023, which was consistent across subgroups
- 36-mo OS: 76.1%; OS rates improved from 2019: 24 mo 83.1% (to 85.3% in 2022); 36-mo OS: 73.9% (to 80.3% in 2021); TTNT: 19.7 mo in 2019 vs 26.4 mo in 2022
- For bort/dara backbones: 48-mo OS was 68.0%/78.2%, respectively



	Events, n/N (%)	36-month OS rate, % (95% CI)
Fit patients	168/1780 (9.4)	82.1 (79.1–84.7)
Frail patients	314/1419 (22.1)	61.5 (57.3–65.4)
Overall NDMM	1801/11,560 (15.6)	76.1 (75.0–77.2)

Number at risk

Overall NDMM patients	11560	8126	6526	5218	4189	3178	2320	1552	1003	487	166	0	0	0	0
Fit patients	1780	1042	793	598	469	353	258	180	126	56	16	0	0	0	0
Frail patients	1419	894	684	502	383	267	171	89	42	19	7	0	0	0	0

Author Conclusions

- This real-world study shows the diverse pt characteristics, age, and frailty status among nontransplanted pts with NDMM, emphasizing the need for personalized treatment approaches
- The population recruited in this study reflects the heterogeneity of nontransplanted pts in the real world compared with clinical trials, with more than one-third ≥75 years old
- These data highlight the positive impact of dara-containing regimens on the OS of frontline nontransplanted pts with MM vs bortezomib- and lenalidomide-backbone treatments
- Frail pts showed worse TTNT and OS outcomes, highlighting the importance of developing tailored treatment options for these pts

Elranatamab in Combination With Daratumumab and Lenalidomide (EDR) in Patients With NDMM Not Eligible for Transplant: Initial Results From MagnetisMM-6 Part 1

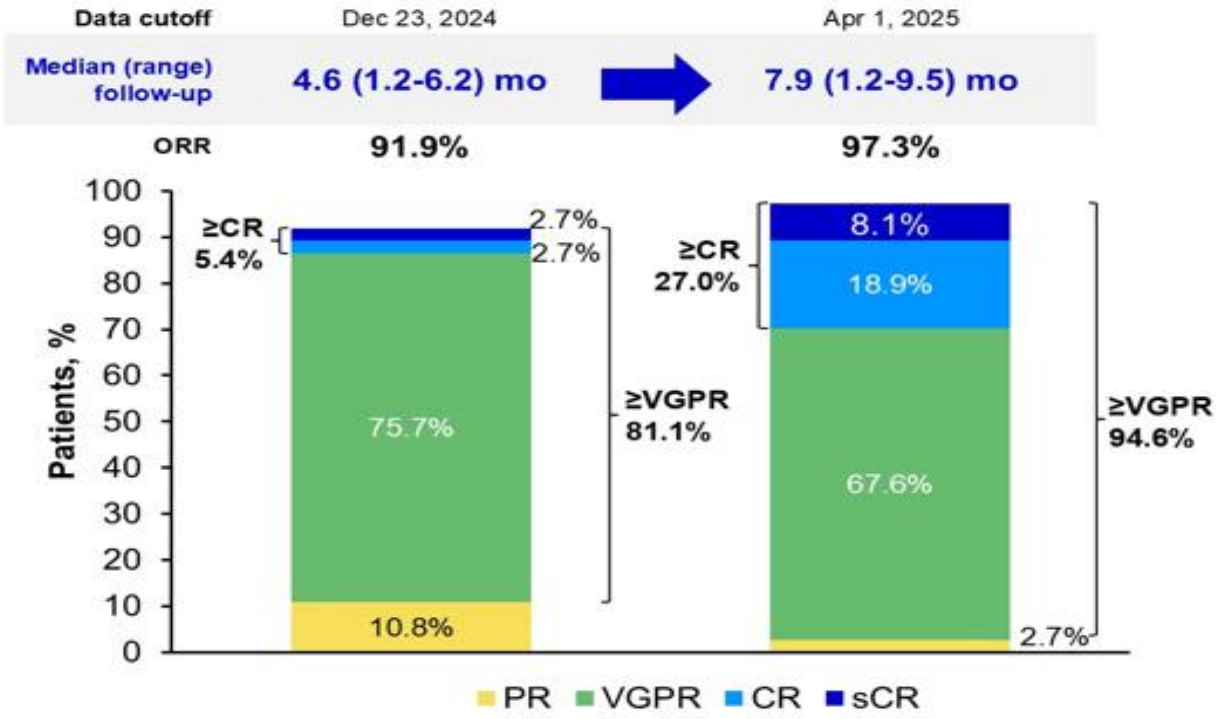
Dimopoulos M, et al. EHA 2025. Abstract S206

Study Design and Patients

- MagnetisMM-6 Part 1 dose level G is evaluating elranatamab, SC dara, and lenalidomide in pts with transplant-ineligible (TI) NDMM (N=37)

Outcomes

- Anti-infective prophylaxis was given, and 34 pts received IVIg
- Most frequent TEAEs (overall/grade 3 or 4): hematologic (83.8%/78.4%); infections* (70.3%/18.9%), CRS (62.2%/0)
  - *One grade 5 case of *Candida* pneumonia
- One grade 2 ICANS
- Confirmed ORR 97.3%; 94.6% ≥VGPR; 27% ≥CR
- Time to response median 1.5 (0.3-4.2 mo)



Author Conclusions

- EDR demonstrated a manageable safety profile in pts with TI NDMM, along with a high response rate and early responses

Daratumumab Plus Bortezomib, Lenalidomide, and Dexamethasone in Patients With NDMM: Subgroup Analysis of Transplant-Ineligible Patients in the Phase III CEPHEUS Study

EPICS

Facon T, et al. EHA 2025. Abstract PS1730

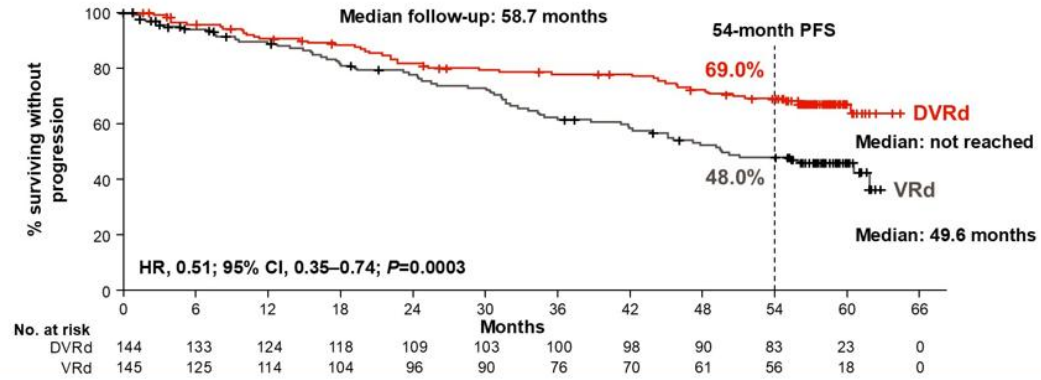
Study Design and Patients

- Randomized phase III trial of DVRd induction with DRd maintenance vs VRd/Rd in NDMM (transplant ineligible [TNE] or deferred) with ECOG PS 0-2 and IMWG frailty score 0–1 (N=395)
- Post hoc analysis of only TNE subgroup (~75%)

Outcomes

- Among TNE pts, adding dara to VRd significantly improved 54-mo PFS (69% vs 48%; HR 0.51; *P*=.0003)
- OS trended favorably for the DVRd arm and was significant when censoring for death due to COVID-19; OS HR for dara arm vs no dara improved in the TNE subgroup vs ITT
- DVRd showed no additional safety concerns in this older, frailer TNE subgroup vs the ITT population
- Pts with high-risk cytogenetics had worse PFS and OS vs those with standard cytogenetics in both treatment arms in the ITT and the TNE subset

CEPHEUS TIE Subgroup: Progression-Free Survival



DVRd significantly improved PFS, with a 49% reduction in the risk of disease progression or death – greater than the ITT population (43% reduction in risk with DVRd vs VRd)[1]

Author Conclusions

- Results of this post hoc CEPHEUS TIE subgroup analysis reinforce DVRd as SOC for TIE NDMM
- DVRd improved depth and duration of response in CEPHEUS pts with TNE NDMM
- Risk of disease progression or death was 49% lower for DVRd vs VRd, with more pts alive and progression free at 4.5 yr
- There were trends toward OS improvement, especially when censoring for COVID-19 death
- No additional safety concerns vs ITT population in this older TNE subgroup

Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone (ISA-VRd) in NDMM: Outcomes in Patients With 1q21-Positive Status in the Phase III IMROZ Study

EPICS

Dimopoulos M, et al. EHA 2025. Abstract PF729

Study Design and Patients

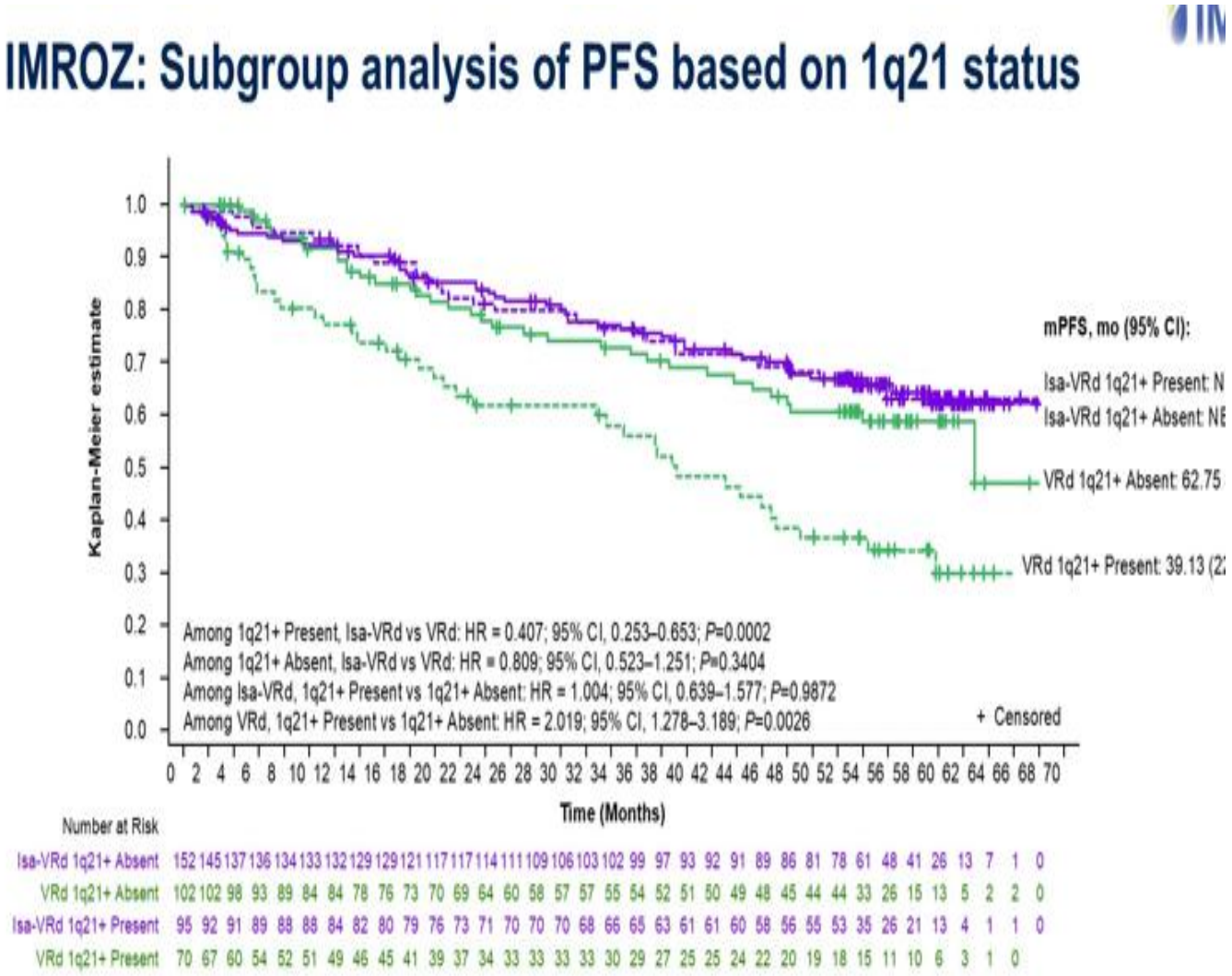
- IMROZ compared Isa-VRd initiation with Isa + Rd maintenance vs VRd initiation with Rd maintenance (with allowed crossover to Isa + Rd for PD) in transplant-ineligible pts ≤80 yr with NDMM
- Subset analyses performed on the basis of 1q21 mutation status

Outcomes

- mPFS not reached for Isa-VRd in both 1q21 negative and positive; for VRd: 62.75 for 1q21 negative and 39.13 mo for 1q21 positive

Author Conclusions

- Isa-VRd improved PFS vs VRd regardless of 1q21 status and demonstrated a significant PFS benefit vs VRd in the 1q21-positive subgroup



APTITUDE HEALTH®

Isa-VRd Improves Outcomes in High-Risk TI NDMM Using the IMS/IMWG Consensus HR Definition: Results From the BENEFIT Phase III Trial (IFM 2020-05)

EPICS

Corre J, et al. EHA 2025. Abstract PF727

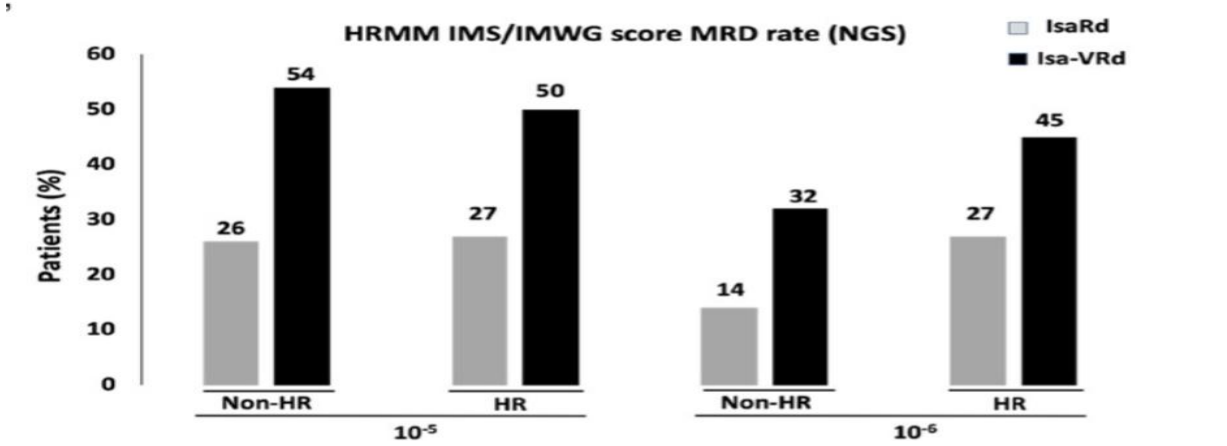
Study Design and Patients

- Open-label, multicenter, parallel-arm phase III trial
- Pts with NDMM (N=135) randomized to Isa-Rd vs Isa-VRd; analyses performed only in IMWG high-risk pts

Outcomes

- High-risk status originally assigned in 42 (31%) Isa-VRd and 30 (22%) Isa-Rd; overall 49/247 (18%) pts were increased to high-risk status when applying IMS criteria instead
- 18-mo MRD negativity (10^{-5}): 50% Isa-VRd vs 27% Isa-Rd; OR 2.75
- Data were similar at 10^{-6} sensitivity: OR 2.27
- Higher MRD negativity for Isa-VRd vs Isa-Rd at 12 and 24 mo for both 10^{-5} and 10^{-6} thresholds
- In HR pts, sustained MRD-negativity rates 31% for Isa-VRd vs 13% for Isa-Rd (OR 2.91; *P*=.091)
- OS data are immature
- In the HR population, the safety profile was no different between treatment arms

Table 1. MRD negativity rates according to treatments' arms at 10^{-5} and 10^{-6} thresholds at different timepoints from 12 to 24 months in ITT analysis.



Author Conclusions

- Results from BENEFIT demonstrated meaningful advantage of the quadruplet-based Isa-VRd regimen vs Isa-Rd in HR NDMM, as reflected in improved MRD-negativity rates, including sustained MRD negativity
- These data continue to support Isa-VRd as the new SOC for transplant-ineligible pts with HR NDMM aged 65–79, replacing the current triplet-based SOC

Multicenter Phase II Study of Subcutaneous Isatuximab + Bortezomib, Lenalidomide, and Dexamethasone (ISA SC-VRd) in NDMM TI: Results From ISASOCUT (IFM 2022-05)

Bobin A, et al. EHA 2025. Abstract PS1746

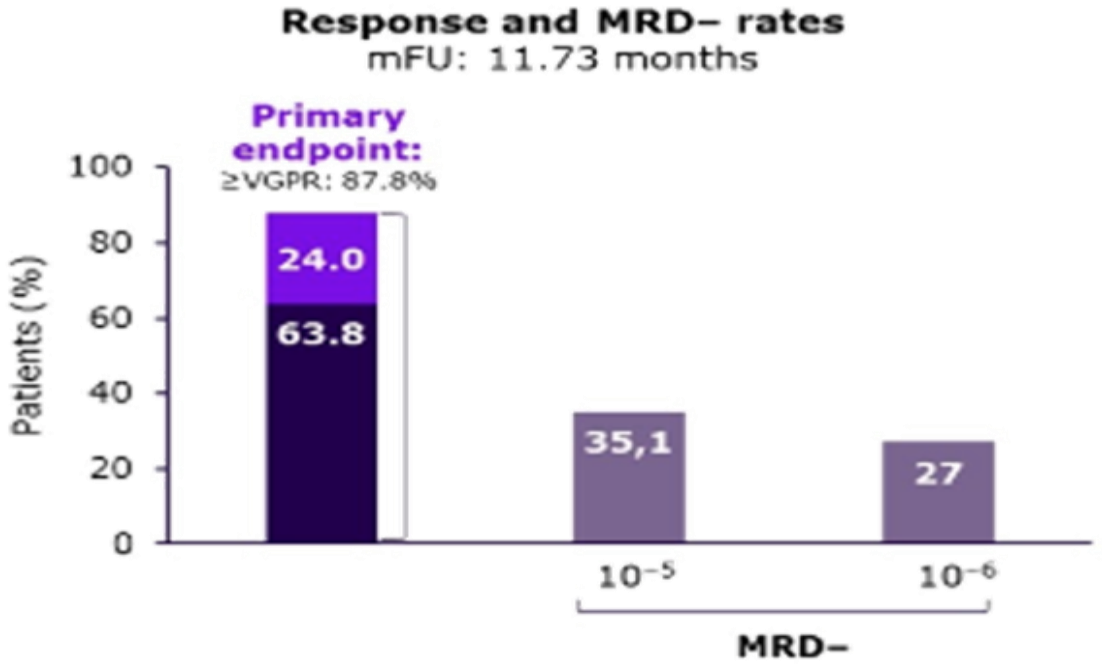
EPICS

Study Design and Patients

- Open-label phase II study evaluating SC isatuximab (Isa-SC) in combination with VRd in TI NDMM
- N=74

Outcomes

- At median follow-up of 17.3 mo
  - ≥VGPR rate: 87.8%
  - ≥CR rate: 24%
  - MRD-negativity rates: 35.1% (10^{-5}) and 27% (10^{-6})
  - 4 pts discontinued therapy and 2 pts had died
  - No instances of PD
- Infusion-related reactions in 9.5%, mostly G1
- Injection site reactions in 27%, majority G1



Author Conclusions

- The ISASOCUT trial demonstrated the consistent efficacy of Isa in TI NDMM regardless of route of administration
- Supports Isa SC-VRd as a new SOC

Iberdomide and Dexamethasone in Elderly Patients With NDMM

Puig N, et al. EHA 2025. Abstract PS1784

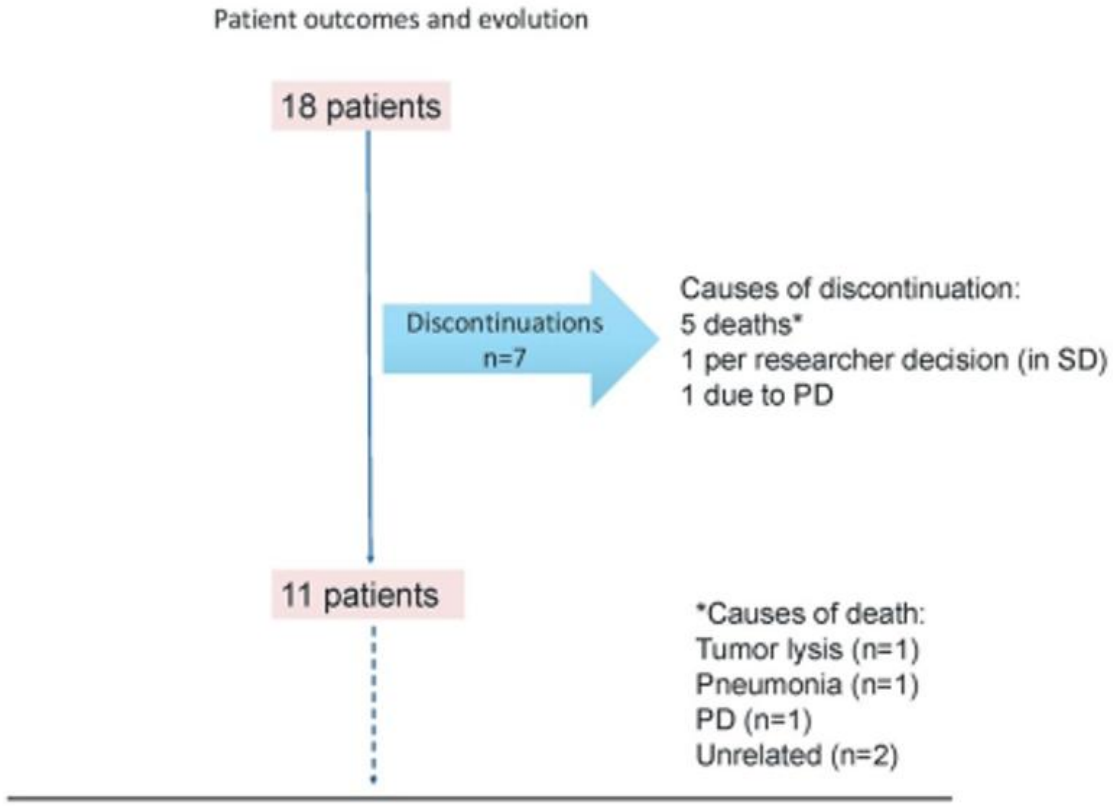
EPICS

Study Design and Patients

- Phase I/II study evaluating the combination of iberdomide, a novel CELMoD, with dexamethasone (IberDex) alone or in combination with daratumumab in TI NDMM
- Results from 18 pts in the IberDex arm

Outcomes

- ORR: 82%
  - CR/sCR: 47%
  - ≥VGPR: 71%
- Most common AEs: neutropenia, infections, thrombocytopenia, anemia, rash, and diarrhea
- 7 pts experienced G3/4 infections, all pneumonia



Author Conclusions

- In this frail, elderly MM cohort, IberDex showed notable and sustained efficacy and manageable toxicity

APTITUDE HEALTH®

Iberdomide, Bortezomib, and Dexamethasone (IBERVd) in Transplant-Ineligible (TNE) NDMM: Updated Results From the CC-220-MM-001 Trial

White D, et al. EHA 2025. Abstract PF737

EPICS

Study Design and Patients

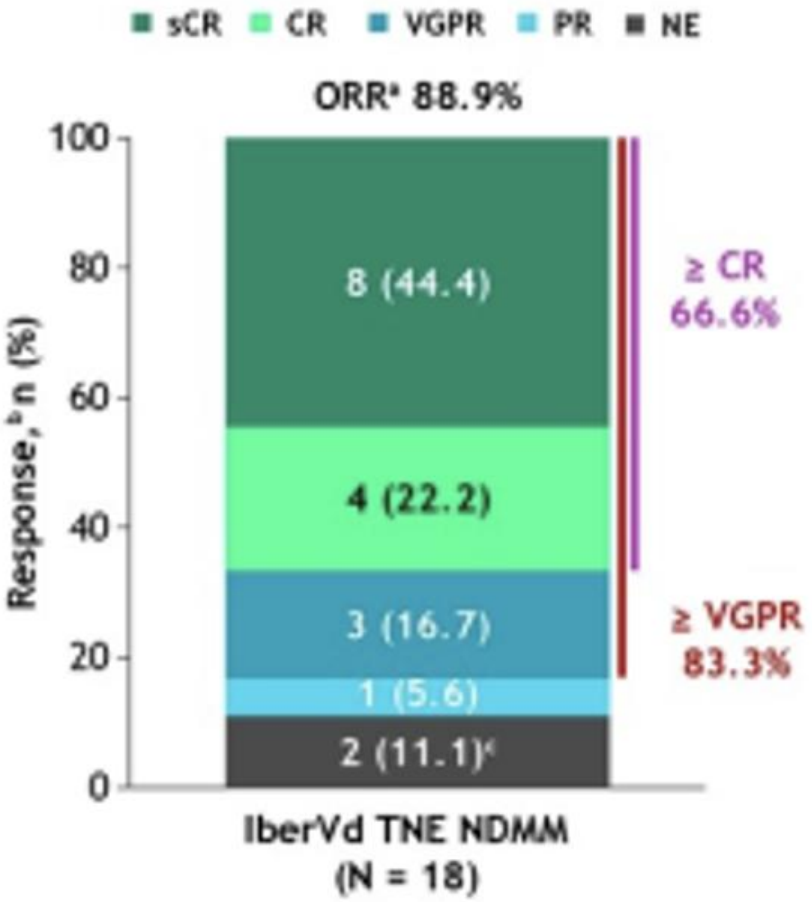
- Phase I/II study evaluated iberdomide with different treatment combinations in pts with MM
- This analysis evaluated iberdomide + bortezomib and dexamethasone (IberVd) in 18 elderly pts with TI NDMM

Outcomes

- ORR: 88.9%; CR: 66.6%
- MRD negativity at 10^{-5} in 44.4% of pts
- 82.4% of pts experienced G3/4 TEAEs
  - Infections were the most common (47.1%)
- Most common TEAE leading to dose reduction were peripheral neuropathy (23.5%), neutropenia (11.8%), and thrombocytopenia (11.8%)

Author Conclusions

- In mostly older pts with TI NDMM, treatment with IberVd is associated with deep, durable responses
- Iber was well tolerated with no new safety signals with continued treatment



APTITUDE HEALTH®

APTITUDE HEALTH®

EPICS

Newly Diagnosed Multiple Myeloma: Transplant Ineligible

Discussion

Update on NDMM: Transplant Ineligible (1/3)

EPICS

General

- Changing SOC in older but fit patients
  - The experts are beginning to use quadruplet regimens in their patients who are transplant ineligible due to age only and are otherwise in good shape
    - A criticism of these quadruplet regimens was that twice-weekly bortezomib is not a realistic treatment option and once-weekly dosing is what is used in real-world clinical practices because of similar efficacy and reduced toxicity vs twice weekly
  - This may be a challenge in the future, since most ongoing trials in this population use the MAIA regimen as a control arm, which is no longer the standard of care
  - While bispecifics are intriguing in this population, better control of infection is needed to ensure patients do not have diminished quality of life or early death

- Treatment of truly frail patients
  - While novel quadruplet regimens have shown good responses in more-fit patients who are transplant ineligible, the best regimen for the truly frail patient remains the MAIA regimen of daratumumab, lenalidomide, and dexamethasone
  - Some of the novel treatment regimens may change this in the future, but only if toxicities can be minimized in this patient population
  - The experts are not enthusiastic about bispecific antibodies in truly frail, elderly patients because of the high risks of infection

Update on NDMM: Transplant Ineligible (2/3)

EPICS

Abstract PS1730: Daratumumab Plus Bortezomib, Lenalidomide, and Dexamethasone in Patients With Newly Diagnosed Multiple Myeloma: Subgroup Analysis of Transplant-Ineligible Patients in the Phase 3 CEPHEUS Study (Facon T, et al)

- The experts were very critical of the way the overall survival analysis of this study was handled
  - Patients who died from COVID-19 infection while on daratumumab were excluded from the OS analysis, which caused the OS benefit to become significant (from nonsignificant when COVID deaths were included)
  - Experts noted that the increased rate of COVID-19 could possibly have been due to the daratumumab, thus making the OS analysis inaccurate
  - They indicated this sort of statistical analysis might not be appropriate in trials of frontline bispecifics, where infection has a major impact on survival outcomes

Abstract PS1746: Multicenter Phase 2 Study of Subcutaneous Isatuximab Plus Bortezomib, Lenalidomide, and Dexamethasone (ISA SC-VRd) in Newly Diagnosed Transplant-Ineligible Multiple Myeloma (NDMM TI): Results From ISASOCUT (IFM 2022-05) (Bobin A, et al)

- Experts are enthusiastic about this new method of subcutaneous treatment delivery and indicated this approach will increase usage of isatuximab, which was previously low due to the availability of subcutaneous daratumumab
  - One small potential challenge is the effort it will take to train nurses on how to use the novel drug-delivery system

Update on NDMM: Transplant Ineligible (3/3)

Abstract PF737: Iberdomide, Bortezomib, and Dexamethasone (IBERVd) in Transplant-Ineligible (TNE) Newly Diagnosed Multiple Myeloma (NDMM): Updated Results From the CC-220-MM-001 Trial (White D, et al)

- The experts were intrigued by these data and generally like this combination, particularly for truly frail patients

Abstract S206: Elranatamab in Combination With Daratumumab and Lenalidomide (EDR) in Patients With Newly Diagnosed Multiple Myeloma (NDMM) Not Eligible for Transplant: Initial Results From MagnetisMM-6 Part 1 (Dimopoulos M, et al)

- Controlling the infection rate associated with elranatamab (and bispecifics in general) was a major focus of discussion
- Experts are not currently comfortable with using agents with high rates of infection in elderly and frail populations
- Developing strategies to minimize the risk of infection should be a major focus of bispecific antibody development in this setting

APTITUDE HEALTH®

EPICS

Maintenance and Monitoring

Abstract Selection

EPICS

Abstract	Phase
Abstract PF795: Relapse From Measurable Disease Negativity as Indication for Treatment in Multiple Myeloma: The Phase 3 REMNANT Study. (Bugge Askeland F, et al)	Phase III
Abstract PS1719: Impact of Mass Spectrometry on the Evaluation of Maintenance Treatment in Patients With Myeloma Enrolled in the GEM2014MAIN Trial: Insights Into Treatment Response and Disease Progression. (Puig N, et al)	Phase III
Abstract PF754: Interim Analysis of MRD-Guided Maintenance Therapy With Belantamab Mafodotin and Lenalidomide After Auto-HCT in Newly Diagnosed Multiple Myeloma. (Aljawai Y, et al)	Phase II
Abstract S204: Daratumumab or Observation for Minimal Residual Disease Reappearance in Multiple Myeloma: Results From the PREDATOR-MRD Randomized Trial. (Jamroziak K, et al)	Phase III
Abstract S193: Carfilzomib, Lenalidomide, and Dexamethasone (KRd) as Maintenance Therapy After Autologous Stem-Cell Transplantation (ASCT) in Patients With Newly Diagnosed Multiple Myeloma (NDMM). (Dytfeld D, et al)	Phase II
Abstract S194: Carfilzomib Induction, Consolidation, and Maintenance With or Without Autologous Stem-Cell Transplant: Long-Term Follow-Up of the Randomised, Phase 2 FORTE Trial. (Gay F, et al)	Phase II

Relapse From Measurable Disease Negativity as Indication for Treatment in MM: The Phase III REMNANT Study

Bugge Askeland F, et al. EHA 2025. Abstract PF795

Study Design and Patients

- Multicenter phase II/III trial
- Newly diagnosed TE pts with MM (N=383) received Norwegian SOC 1L therapy; those with MRD-negative CR were randomized to an MRD-guided or PD-guided arms
- 2L therapy initiated at either MRD relapse or PD, on the basis of cohort

Outcomes

- ORR on 1L therapy: 94%
- 57% of pts completing 1L treatment had MRD-negative CR
- 30% of pts discontinued 1L treatment, primarily due to PD, death, pt choice, or AEs
- At median follow-up of 22.7 mo, 28 pts had started 2L treatment
- 3 pts had experienced progression on 2L treatment: 1 in the MRD-guided cohort and 2 in the PD-guided cohort

Author Conclusions

- SOC Norwegian treatment in TE NDMM resulted in an ORR of 94%, with 57% of pts who started maintenance therapy demonstrating MRD-negative CR
- Trial is ongoing to evaluate results of MRD-guided treatment vs PD-guided treatment

Impact of Mass Spectrometry on the Evaluation of Maintenance Treatment in Patients With Myeloma Enrolled in the GEM2014MAIN Trial: Insights Into Treatment Response and Disease Progression

EPICS

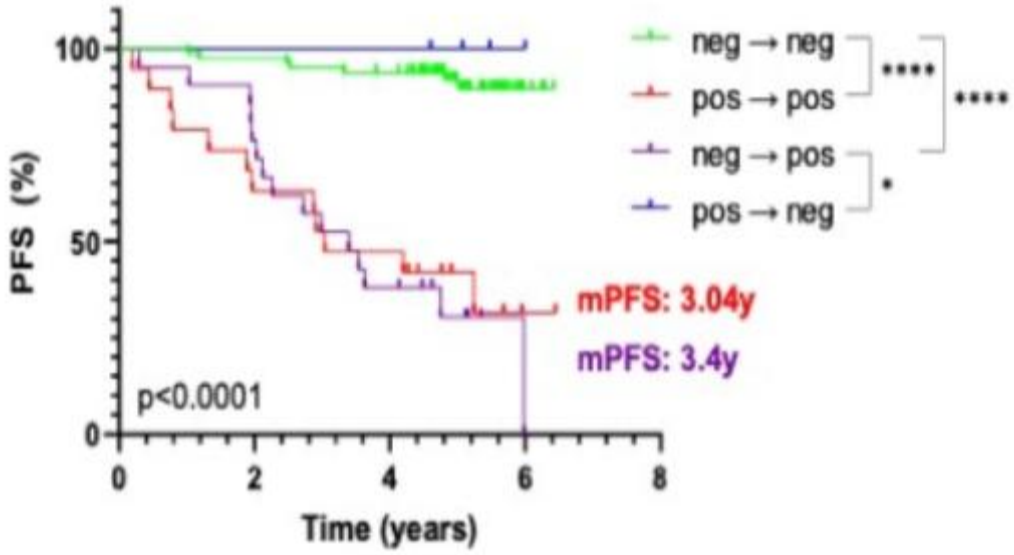
Puig N, et al. EHA 2025. Abstract PS1719

Study Design and Patients

- The phase III GEM2014MAIN trial evaluated maintenance therapy with ixazomib + lenalidomide and dexamethasone (IRd) vs Rd alone in pts with TE NDMM
- This analysis is examining the potential for mass spectrometry (MS) as a method to evaluate treatment response in 124 pts

Outcomes

- Pts who were disease negative by MS (MS neg) had improved outcomes compared with those who were MS pos
  - mPFS not reached vs 5.24 yr (HR 0.331; *P*=.0013)
- Duration of MS negativity was important
  - In the entire cohort of MS neg, the 6-yr relapse rate was 22%
  - Among pts who remained MS neg for 4.87 yr, only 8.45% had relapse by yr 6
- Conversion from MS pos to MS neg was associated with improved outcomes (figure)



Author Conclusions

- MS is a valuable tool for monitoring residual disease and detecting early relapse in MM
- MS could be incorporated into myeloma management to determine the optimal duration of maintenance therapy

Interim Analysis of MRD-Guided Maintenance Therapy With Belantamab Mafodotin and Lenalidomide After Auto-HCT in NDMM

Aljawai Y, et al. EHA 2025. Abstract PF754

EPICS

Study Design and Patients

- Phase II study evaluating belantamab mafodotin and lenalidomide maintenance guided by MRD outcomes in TE NDMM
- Pts in CR with sustained MRD negativity are allowed to stop treatment after 2 yr
- Presented was an interim analysis of the first 12 enrolled pts (median follow-up 4.7 mo)

Outcomes

- Responses prior to maintenance therapy: 33% sCR/CR, 42% VGPR, and 25% PR
- Best response on maintenance therapy: 58% sCR/CR, 33% VGPR, and 8% PR
- TRAEs occurred in 83% of pts, with 50% experiencing G3/4 hematologic AEs
- 33% developed G2 keratopathy, with symptom resolution in 3/4 pts

Author Conclusions

- Early data suggest that maintenance with belantamab and lenalidomide is feasible, with manageable toxicity

Daratumumab or Observation for MRD Reappearance in MM: Results From the PREDATOR-MRD Randomized Trial

Jamroziak K, et al. EHA 2025. Abstract S204

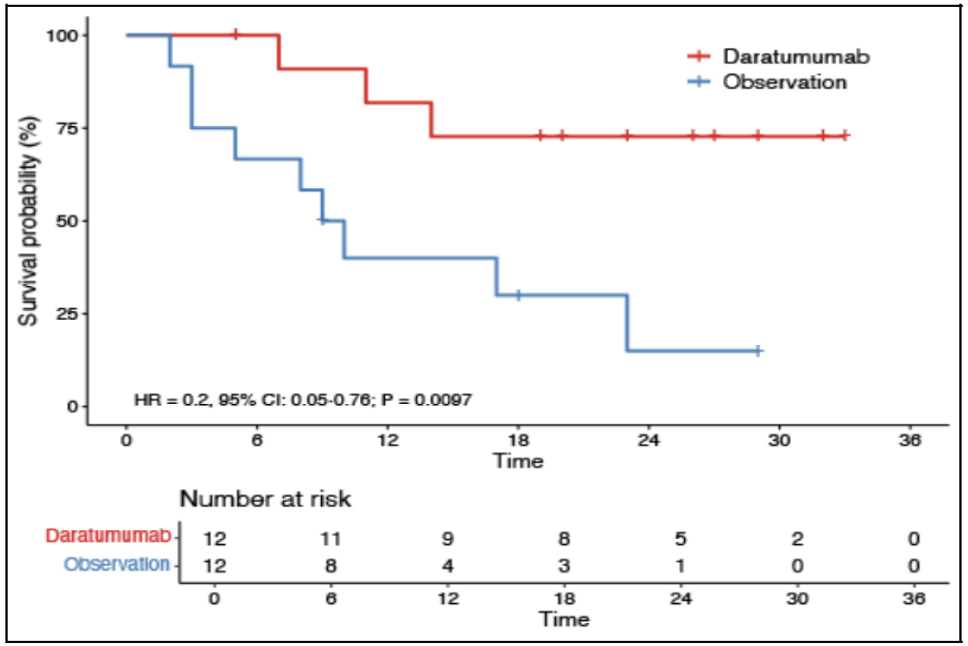
EPICS

Study Design and Patients

- Randomized, open-label, phase II study in pts with MM who had CR with MRD negativity on their most recent treatment
- Pts were observed for 24 mo with MRD testing every 4 mo
- At MRD reappearance, pts without symptomatic progression were randomized to a daratumumab or observation
- N=24 randomized 1:1 to treatment vs observation

Outcomes

- Primary endpoint of event-free survival (EFS) after randomization (median follow-up: 17.9 mo)
  - mEFS not reached with daratumumab vs 9.5 mo for observation (HR 0.20; *P*=.0097)
- 75% of pts in the daratumumab treatment arm again demonstrated MRD negativity
- No G≥3 AEs in treatment arm vs 2 in observation arm (abscess and cholangitis)



Author Conclusions

- MRD monitoring every 4 mo allows detection of biochemical progression
- Preemptive treatment with daratumumab restores MRD negativity in most pts with no negative impact on patient QOL

APTITUDE HEALTH®

Carfilzomib, Lenalidomide, and Dexamethasone (KRd) as Maintenance Therapy After ASCT in Patients With NDMM

EPICS

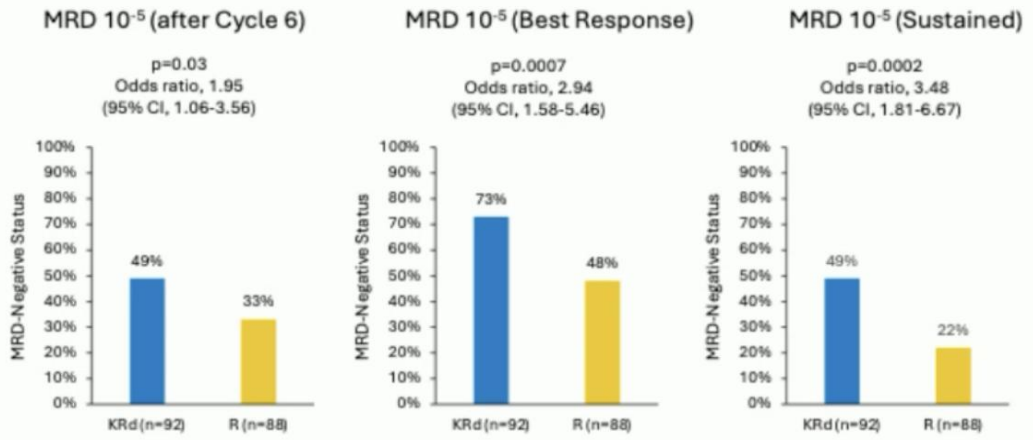
Dytfeld D, et al. EHA 2025. Abstract S193

Study Design and Patients

- Phase II trial comparing carfilzomib, lenalidomide, and dexamethasone (KRd) to R alone as maintenance therapy in TE NDMM
- N=180; median follow-up 5.7 yr

Outcomes

- Median PFS 72.8 mo vs 37.3 mo for R alone (HR 0.46; *P*=.0002)
- PFS benefit of KRd over R maintained in key subgroups
  - High-risk cytogenetics: HR 0.51
  - MRD negative at randomization: HR 0.49
  - MRD positive at randomization: HR 0.30
- Median OS not reached vs 82.2 mo for R alone (HR 0.49; *P*=.02)
- 12-mo sustained MRD negativity in 49% KRd and 22% R-only pts (figure)
- Most common serious AEs of any grade
  - KRd: lung infection (11%), upper respiratory infection (5.5%), urinary tract infection (3.3%)
  - R: lung infection (4.6%), upper respiratory infection (3.4%)
  - No differences in cardiac toxicity



Author Conclusions

- KRd was associated with an improvement in PFS and OS compared with R for maintenance therapy, with greater depth of response and higher rates of sustained MRD
- KRd may be considered a new option for maintenance therapy in TE NDMM

Carfilzomib Induction, Consolidation, and Maintenance With or Without ASCT: Long-Term Follow-Up of the Randomized, Phase II FORTE Trial

Gay F, et al. EHA 2025. Abstract S194

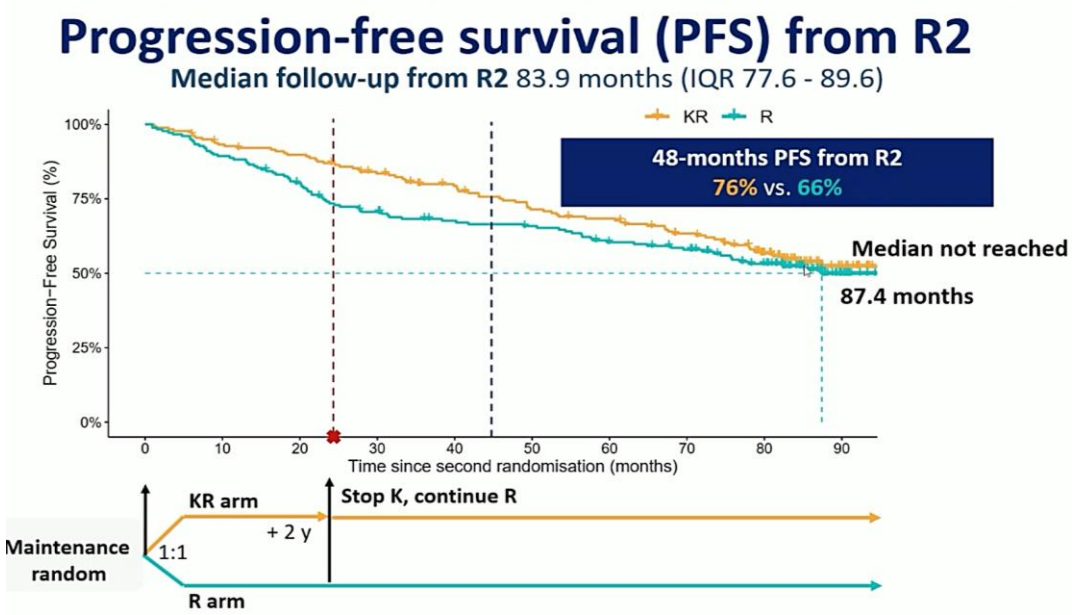
EPICS

Study Design and Patients

- Phase II trial evaluating the role of carfilzomib in induction, consolidation, and maintenance for TE NDMM
- Pts (N=474) randomized (R1) to receive 1 of 3 carfilzomib-based induction and consolidation regimens before being randomized (R2) to receive either KR or R maintenance

Outcomes

- KRd-ASCT induction significantly prolonged PFS from R1 compared with KRd alone (HR 0.69; *P*=.019) or KCd-ASCT (HR 0.63; *P*=.003)
- OS and TTNT also favored KRd-ASCT
- Median PFS from R2 favored KR maintenance over R alone (not reached vs 87.4 mo)
- Benefit of KR maintenance was seen in all pts, including those who were MRD negative before maintenance



Author Conclusions

- KRd-ASCT significantly prolonged PFS vs KRd with no ASCT
- Maintenance with K for 2 yr and R until PD significantly prolonged PFS vs R alone

APTITUDE HEALTH®

APTITUDE HEALTH®

EPICS

Maintenance and Monitoring

Discussion

Update on Maintenance and Monitoring (1/2)

EPICS

General

- Decreasing toxicity of maintenance
  - Patients have already received intensive therapy by the time they reach maintenance therapy, so minimizing toxicity should be a major goal in maintenance therapy
  - Early discontinuation of maintenance should be prioritized in standard-risk patients, particularly if they are receiving a more intensive, multidrug maintenance regimen
    - Experts believe maintenance therapy can be stopped in patients who have stringent MRD negativity after 2 years of maintenance
  - The continued role of PIs in maintenance therapy is doubtful for patients with standard-risk disease, but experts indicated there is still a role for these agents in high-risk disease

- Impact of induction vs maintenance
  - Most experts agreed that a strong induction regimen has a much greater impact on outcomes than maintenance therapy
    - Their general experience has been that when patients receive a strong induction regimen, they have outcomes superior to patients receiving a weaker induction regimen, regardless of the maintenance regimen (if any) they receive

Update on Maintenance and Monitoring (2/2)

Abstract S194: Carfilzomib Induction, Consolidation, and Maintenance With or Without Autologous Stem-Cell Transplant: Long-Term Follow-Up of the Randomised, Phase 2 FORTE Trial (Gay F, et al)

- While some experts expressed doubt that PIs should be included in maintenance regimens, others pointed to the FORTE trial as an example of the importance of PIs in improving disease control, particularly in patients with high-risk disease

Abstract PF795: Relapse From Measurable Disease Negativity as Indication for Treatment in Multiple Myeloma: The Phase 3 REMNANT Study (Bugge Askeland F, et al)

and

Abstract S204: Daratumumab or Observation for Minimal Residual Disease Reappearance in Multiple Myeloma: Results From the PREDATOR-MRD Randomized Trial (Jamroziak K, et al)

- These 2 studies highlight that not all MRD relapses after frontline therapy are the same
  - Some patients experience progression very quickly after relapse, while others will remain asymptomatic long-term after becoming MRD positive
  - Additional research into biomarkers differentiating these 2 subsets is needed
  - One expert suggested that using ctDNA for this form of monitoring is the best option, as many patients have long-term remission and repeated bone marrow aspirates can become cumbersome and expensive

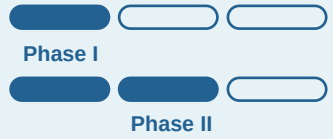
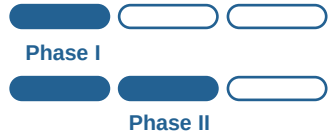
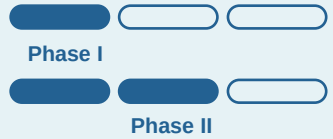
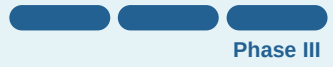
APTITUDE HEALTH®

EPICS

Relapsed/Refractory Multiple Myeloma: Small Molecules and Classical Antibodies

Abstract Selection

EPICS

Abstract	Phase
Abstract PF791: The Treatment of Patients Progressing After Lenalidomide Maintenance: An Italian Real-Life Study of 284 Cases. (Barilà G, et al)	Observational
Abstract PS1727: Mezigdomide (MEZI) in Novel Combinations for Relapsed or Refractory Multiple Myeloma (RRMM): Updated Results From the CA057-003 Trial. (Schjesvold F, et al)	
Abstract PF723: Mezigdomide (MEZI) Plus Dexamethasone (DEX) and Bortezomib (BORT) or Carfilzomib (CFZ) in Patients With Relapsed/Refractory Multiple Myeloma (RRMM): Updated Results From the CC-92480-MM-002 Trial. (Sandhu I, et al)	
Abstract PF721: Updated Interim Results of Sonrotoclax + Dexamethasone in Patients With T(11;14)-Positive Relapsed/Refractory Multiple Myeloma: An All-Oral Treatment. (Dhakal B, et al)	
Abstract PF751: Safety And Efficacy of Ixazomib, Pomalidomide and Dexamethasone as 2nd or 3rd Line Treatment for Triple Exposed Multiple Myeloma Patients: A Phase II Multi-Center Trial (IPoD-790). (Shragai T, et al)	
Abstract S203: Isatuximab Subcutaneous via an On-Body Delivery System Versus Isatuximab Intravenous, Plus Pomalidomide and Dexamethasone, in Relapsed/Refractory Multiple Myeloma: The Randomized Phase 3 IRAKLIA Study. (Leleu X, et al)	

The Treatment of Patients Progressing After Lenalidomide Maintenance: An Italian Real-Life Study of 284 Cases

Barila G, et al. EHA 2025. Abstract PF791

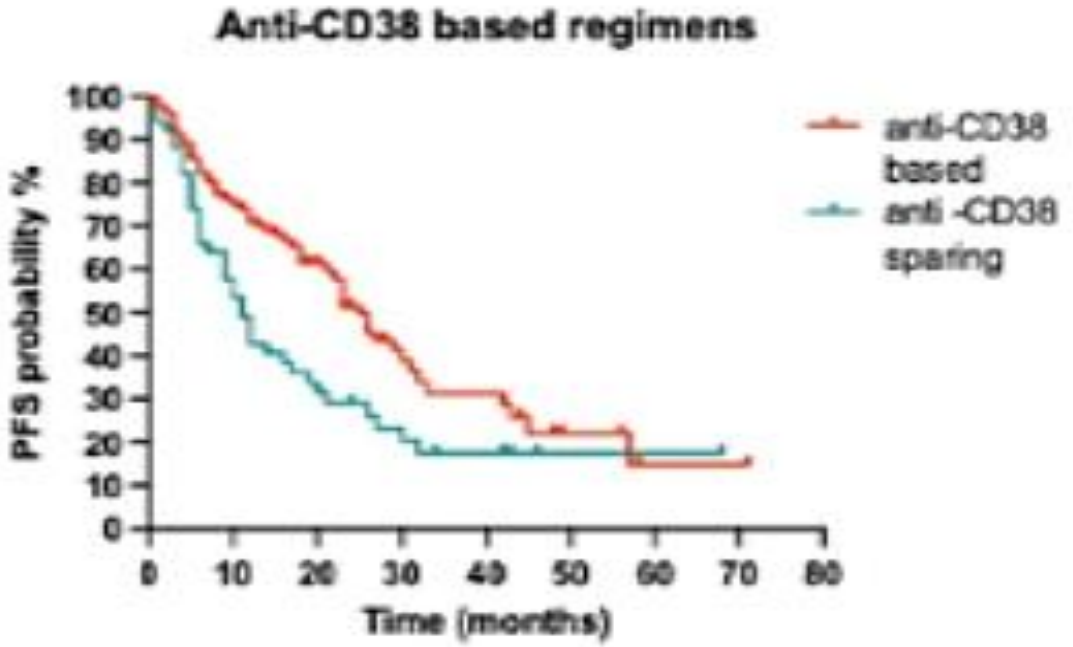
EPICS

Study Design and Patients

- Italian real-world study of treatment patterns of pts with lenalidomide-refractory MM (N=284)
- Only 5.6% of pts had received anti-CD38 therapy
- Median follow-up: 17 mo

Outcomes

- Median PFS: 22.0 mo; median OS: not reached
- Clinical and biological high-risk factors predicted for poorer outcomes
- Treatment at biochemical relapse resulted in improved PFS compared with treatment at clinical relapse (24 mo vs 17 mo; *P*=.0049)
- Use of anti-CD38 regimens resulted in superior PFS compared with no anti-CD38 therapy (PFS: 23 mo vs 11 mo; *P*=.0044)



Author Conclusions

- In pts experiencing progression on R maintenance, anti-CD38–based combinations granted superior outcomes, with Isa-KD showing the longest PFS

APTITUDE HEALTH®

Mezigdomide (MEZI) in Novel Combinations for RRMM): Updated Results From the CA057-003 Trial

Schjesvold F, et al. EHA 2025. Abstract PS1727

EPICS

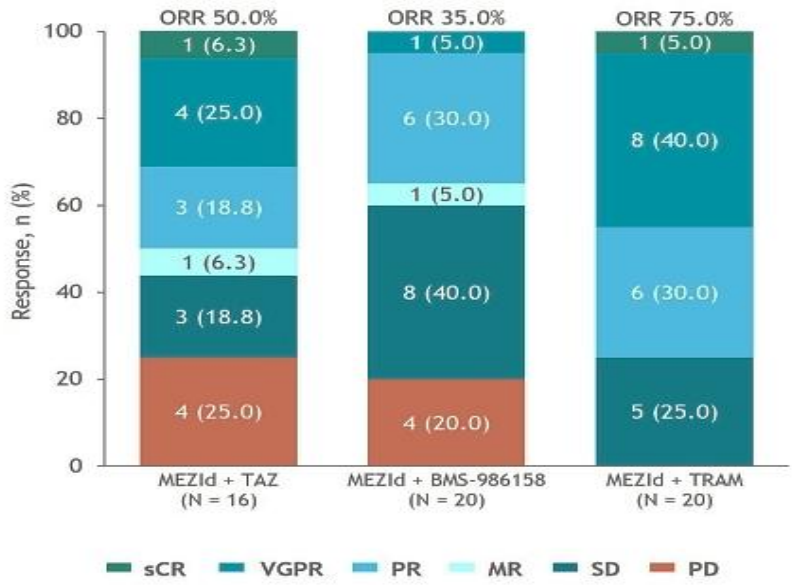
Study Design and Patients

- Phase I/II trial evaluating the novel CELMoD mezigdomide + dexamethasone in RRMM in combination with either the EZH2 inhibitor tazemetostat, the BET inhibitor BMS-986158, or the MEK inhibitor trametinib
- 16 pts received MEZId + TAZ, 20 MEZId + BMS, and 20 MEZId + TRAM

Outcomes

- Median follow-up between 4.2 mo and 5.7 mo
- Response rates
  - MEZId + TAZ: 50%
  - MEZId + BMS: 35%
  - MEZId + TRAM: 75%
- There were no drug-drug interactions noted between MEZId and the novel agents
- G3/4 neutropenia was seen in 62.5%–85.0% of pts
- 8 pts had DLT: 1 with MEZId + TAZ, 5 with MEZId + BMS, 2 with MEZId + TRAM

Figure. Overall response rate



Author Conclusions

- MEZId combined with the novel therapeutic agents TAZ, BMS-986158, or TRAM showed promising efficacy and safety in RRMM
- These results provide a rationale for further exploration of these novel all-oral combinations

APTITUDE HEALTH®

Mezigdomide (MEZI) + Dexamethasone (DEX) and Bortezomib (BORT) or Carfilzomib (CFZ) in Patients With RRMM: Updated Results From the CC-92480-MM-002 Trial

Sandhu I, et al. EHA 2025. Abstract PF723

EPICS

Study Design and Patients

- Phase I/II trial evaluating MEZI + either bortezomib and dexamethasone (MeziVd) or carfilzomib and dexamethasone (MeziKd) in RRMM
- N=104

Outcomes

- Dose-escalation cohort outcomes
  - ORR: 75.0% MeziVd and 85.2% MeziKd
  - Median DOR: 10.9 mo and 11.9 mo
  - Median PFS: 12.3 mo and 13.5 mo
- G3/4 TEAEs
  - MeziVd: neutropenia (35.7%), thrombocytopenia (21.4%), and infections (17.9%)
  - MeziKd: neutropenia (44.4%) and infection (33.3%)
- MeziVd dose-expansion cohort
  - ORR 85.7%; mDOR 19.4 mo; mPFS 17.5 mo
  - G3/4 TEAEs: neutropenia (63.3%), infections (32.7%), thrombocytopenia (26.5%)

Author Conclusions

- With longer follow-up, MeziVd and MeziKd confirmed promising efficacy with sustained PFS and a manageable safety profile in RRMM
- These results informed ongoing and planned phase III trials

Updated Interim Results of Sonrotoclax + Dexamethasone in Patients With t(11;14)-Positive RRMM: An All-Oral Treatment

Dhakal B, et al. EHA 2025. Abstract PF721

EPICS

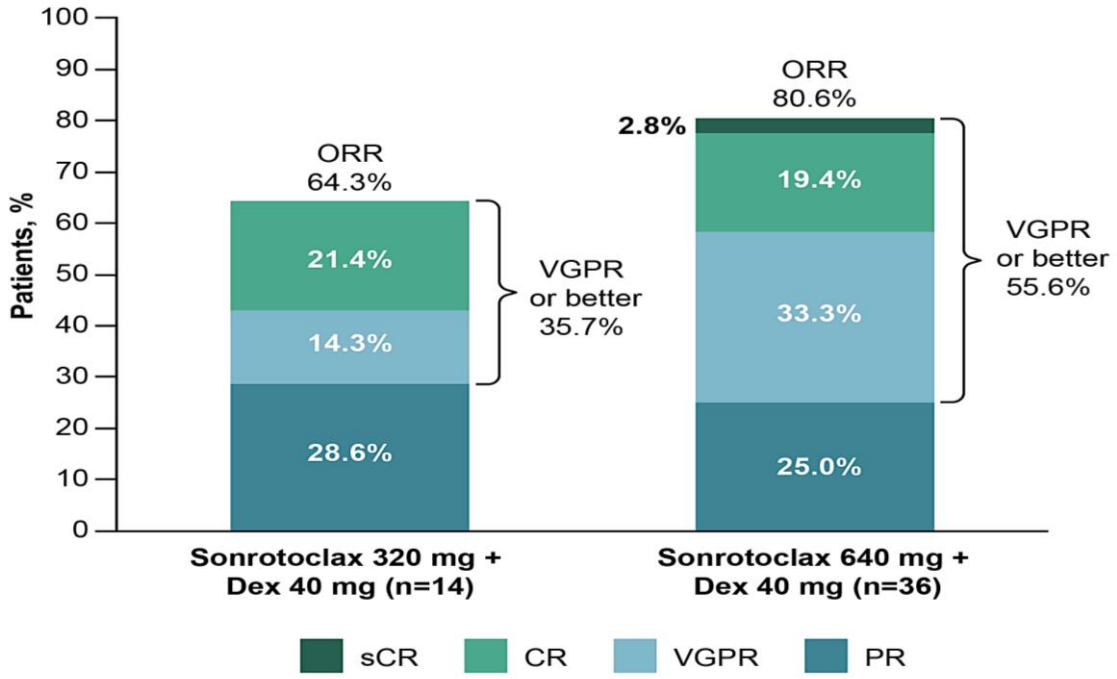
Study Design and Patients

- Phase Ib/II study of the next-generation BCL2 inhibitor sonrotoclax + dexamethasone in t(11;14)-positive RRMM
- 2 cohorts of different doses of sonrotoclax: 320 mg (n=14) and 640 mg (n=36)
- Median follow-up 6.2 mo and 12.1 mo

Outcomes

- Responses by cohort
  - 320 mg: ORR 64.3% with 21.4% CR
  - 640 mg: ORR 80.6% with 19.4% CR
- Median DOR 5.9 mo and 12.2 mo
- Median PFS 6.6 mo and 13.3 mo
- Safety profile tolerable and manageable for both cohorts
  - G≥3 TEAEs in 5 (320 mg) and 17 (640 mg) pts
  - 4 deaths due to unrelated reasons on study (2 in each cohort)
  - 4 additional deaths occurred >30 days after last 640-mg dose

Treatment response assessment in patients with t(11;14)-positive R/R MM



Author Conclusions

- The all-oral combination of sonrotoclax + dex continues to show a tolerable safety profile, with low rates of infection and heme toxicity, and promising efficacy

Safety and Efficacy of Ixazomib, Pomalidomide, and Dexamethasone as 2L or 3L Treatment for Triple-Exposed Patients With MM: A Phase II Multicenter Trial (IPoD-790)

Shragai T, et al. EHA 2025. Abstract PF751

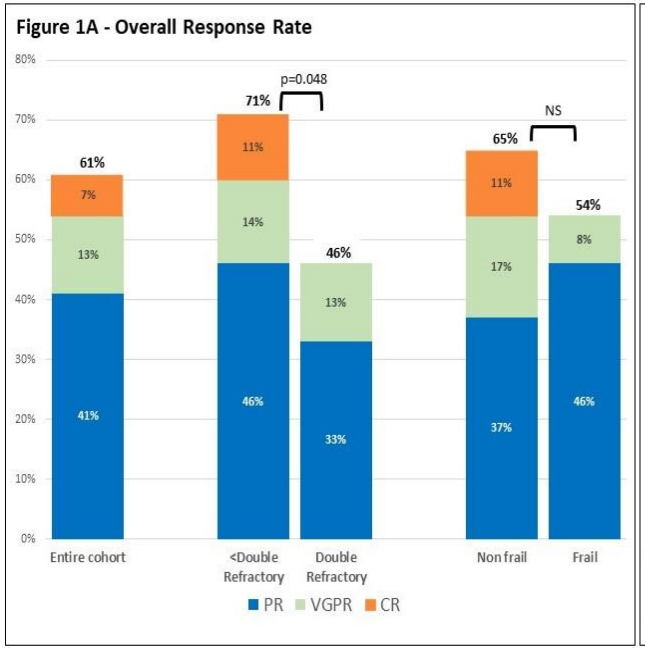
EPICS

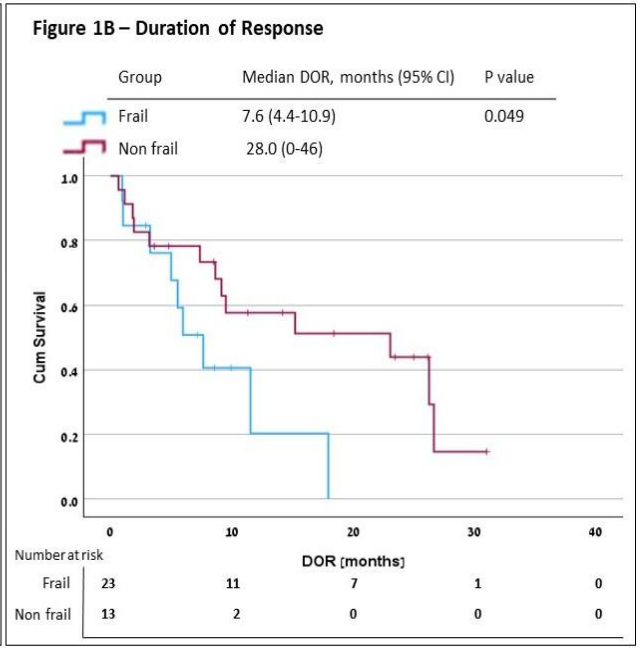
Study Design and Patients

- Phase II trial testing the all-oral combination of ixazomib, pomalidomide, and dexamethasone (IPd) in triple-class exposed (TCE) RRMM (N=61)

Outcomes

- Median follow-up: 23.9 mo
- Median PFS: 8.6 mo
- Median OS for entire cohort: 27.4 mo
  - Responders: not reached
  - Frail patients: 7.6 mo
- Most common TEAEs included neutropenia (34%), thrombocytopenia (30%), anemia (21%), diarrhea (21%), pneumonia (20%), and edema (20%)
- Rates of G≥3 TEAEs was not increased in frail vs nonfrail pts





Author Conclusions

- This all-oral IPd regimen for pts with TCE RRMM showed high response rates with durable remissions and a manageable safety profile, including in elderly and frail pts

APTITUDE HEALTH®

Isatuximab Subcutaneous Via an On-Body Delivery System vs Isatuximab IV, + Pomalidomide and Dexamethasone, in RRMM: The Randomized Phase III IRAKLIA Study

EPICS

Leleu X, et al. EHA 2025. Abstract S203

Study Design and Patients

- Phase III trial evaluating delivery of isatuximab SC via an on-body delivery system (OBDS) in combination with pomalidomide and dexamethasone (Pd) in RRMM (N=531)
- Noninferiority comparison to Isa IV

Outcomes

- Co-primary endpoints can be seen in the table
  - ORR: 71.1% OBDS vs 70.5% IV
- No notable difference in pharmacokinetics
- G≥3 TEAEs in 81.7% OBDS and 76.1% IV
  - All-grade infusion reactions: 1.5% OBDS vs 25.0% IV
- 99% of OBDS injections completed without interruption

Table. Co-primary and key secondary endpoints

	Isa SC OBDS + Pd	Isa IV + Pd
Efficacy, %	**N=263**	**N=268**
ORR	71.1	70.5
≥VGPR	46.4	45.9
PK*, µg/mL	**N=131/121**	**N=126/121**
Geometric mean Isa C_{trough} at C2D1 / C6D1	360/426	277/278
Safety, %	**N=263**	**N=264**
All grade IR	1.5	25.0
Patient satisfaction with injection method at C5D15, %	70.0	53.4

Author Conclusions

- IRAKLIA met its co-primary endpoints, showing efficacy and pharmacokinetic noninferiority of Isa SC OBDS compared with Isa IV + Pd, supporting delivery through OBDS to improve pt experiences

APTITUDE HEALTH®

APTITUDE HEALTH®

EPICS

Relapsed/Refractory Multiple Myeloma: Small Molecules and Classical Antibodies

Discussion

Update on RRMM: Small Molecules and Classical Antibodies (1/2)

EPICS

General

- Role of small-molecule therapy in the era of bispecifics
  - The experts are not certain there is a clear role for some of the small-molecule therapies now that bispecific antibodies are established treatment options
  - Use will likely be limited to combination therapy or highly specific patient populations
    - CELMoDs in particular are seen as ideal combination therapy partners in multiple settings, including pre– and post–CAR T-cell therapy and as an adjunct to bispecifics to limit the duration of bispecific treatment
  - These agents may also play a role as salvage therapy after progression on a bispecific antibody
    - Experts identified post-bispecific salvage as the single greatest area of unmet need in RRMM

Update on RRMM: Small Molecules and Classical Antibodies (2/2)

EPICS

Abstract PF721: Updated Interim Results of Sonrotoclax + Dexamethasone in Patients With T(11;14)-Positive Relapsed/Refractory Multiple Myeloma: An All-Oral Treatment (Dhakal B, et al)

- The results of this study were as expected, and experts believe this agent will be approved soon
  - The experts commented on the unique biology of t(11;14) disease and how progression after BCL2 inhibitor often occurs very rapidly and aggressively; they indicated there is a need to study this progression pattern more to better understand how to treat this disease subset
  - Other studies have suggested that amplification and gain of 1q in patients with t(11;14) seems to predispose for more-aggressive relapse, and this will need to be evaluated further in the future

Abstract PF723: Mezigdomide (MEZI) Plus Dexamethasone (DEX) and Bortezomib (BORT) or Carfilzomib (CFZ) in Patients With Relapsed/Refractory Multiple Myeloma (RRMM): Updated Results From the CC-92480-MM-002 Trial (Sandhu I, et al)

- The experts believe mezigdomide is the best IMiD/CELMoD currently available and are hopeful it will find a place in the treatment algorithm
  - Use before and/or after CAR T-cell therapy or in combinations may be the best path forward for this agent
  - Some experts indicated that just using mezigdomide as a replacement for lenalidomide in currently available treatment options would be ideal

APTITUDE HEALTH®

EPICS

Relapsed/Refractory Multiple Myeloma: ADCs and Multispecifics

Abstract Selection (1/3)

EPICS

Abstract	Phase
Abstract PS178: Impact of Corticosteroids on the Efficacy and Toxicity of Bispecific Antibodies in Relapsed/Refractory Multiple Myeloma. (Gutierrez-Padilla C, et al)	Observational
Abstract PS1673: Selective Depletion of B-Cell Lineage Subsets During Treatment With Anti-BCMA vs Anti-GPRC5D Bispecific Antibodies (Bsabs) Underlies Different Risk of Infections in Patients With Multiple Myeloma (MM). (Jelinek T, et al)	Observational
Abstract PB2885: Systematic Review of Bispecific Antibodies Efficacy and Safety in Relapsed/Refractory Multiple Myeloma. (Pérez-Granado J, et al)	Systematic Review
Abstract PF798: ALTITUDE-1: Real-World Treatment Patterns Associated With Elranatamab Among Patients With Multiple Myeloma. (Banerjee R, et al)	Observational
Abstract PS1721: BCMA-Targeting T-Cell Redirecting Bispecific Antibody Therapy Post-GPRC5D-Directed Bispecific Antibody in Relapsed or Refractory Multiple Myeloma. (IFM 2024-13 BCMA POST-GPRC5D). (Hulin C, et al)	Observational
Abstract PF771: Efficacy and Safety of Less Frequent Dosing With Elranatamab (Elra) in Patients With Relapsed or Refractory Multiple Myeloma (RRMM): A US Subgroup Analysis From MAGNETISMM-3. (Raje N, et al)	 Phase III

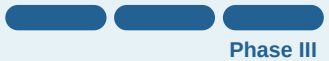
Abstract Selection (2/3)

EPICS

Abstract	Phase
Abstract S100: First-In-Human Study of JNJ-79635322 (JNJ-5322), a Novel, Next-Generation Trispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma: Initial Phase 1 Results. (Popat R, et al)	Phase I
Abstract PS1766: Real-World Analysis of Talquetamab in Heavily Pretreated and High-Risk Patients With Relapsed/Refractory Multiple Myeloma (RRMM). (Tan CR, et al)	Observational
Abstract S200: Talquetamab + Cetrelimab in Patients With Relapsed/Refractory Multiple Myeloma: Initial Safety and Efficacy Results From the Phase 1B TRIMM-3 Study. (Perrot A, et al)	Phase I
Abstract S202: Linvoseltamab + Carfilzomib in Patients With Relapsed/Refractory Multiple Myeloma: Initial Results From the LINKER-MM2 Trial. (Manier S, et al)	Phase I Phase II
Abstract PS1716: Linvoseltamab + Bortezomib in Patients With Relapsed/Refractory Multiple Myeloma: Initial Results From the LINKER-MM2 Trial. (Rodríguez-Otero P, et al)	Phase I Phase II

Abstract Selection (3/3)

EPICS

Abstract	Phase
Abstract PF728: Updated Results From Phase 3 DREAMM-8 Study of Belantamab Mafodotin Plus Pomalidomide and Dexamethasone vs Pomalidomide Plus Bortezomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma. (Dimopoulos M, et al)	 Phase III
Abstract PF739: DREAMM-7: Study of Belantamab Mafodotin + Bortezomib + Dexamethasone vs Daratumumab + Bortezomib + Dexamethasone in Relapsed/Refractory Multiple Myeloma: A High-Risk Cytogenetic Subgroup Analysis. (Mateos M, et al)	 Phase III
Abstract PS1734: DREAMM-7: Study of Belantamab Mafodotin + Bortezomib + Dexamethasone vs Daratumumab + Bortezomib + Dexamethasone in Relapsed/Refractory Multiple Myeloma: Efficacy in Patients by Subsequent Therapy. (Hungria V, et al)	 Phase III

Impact of Corticosteroids on the Efficacy and Toxicity of Bispecific Antibodies in RRMM

EPICS

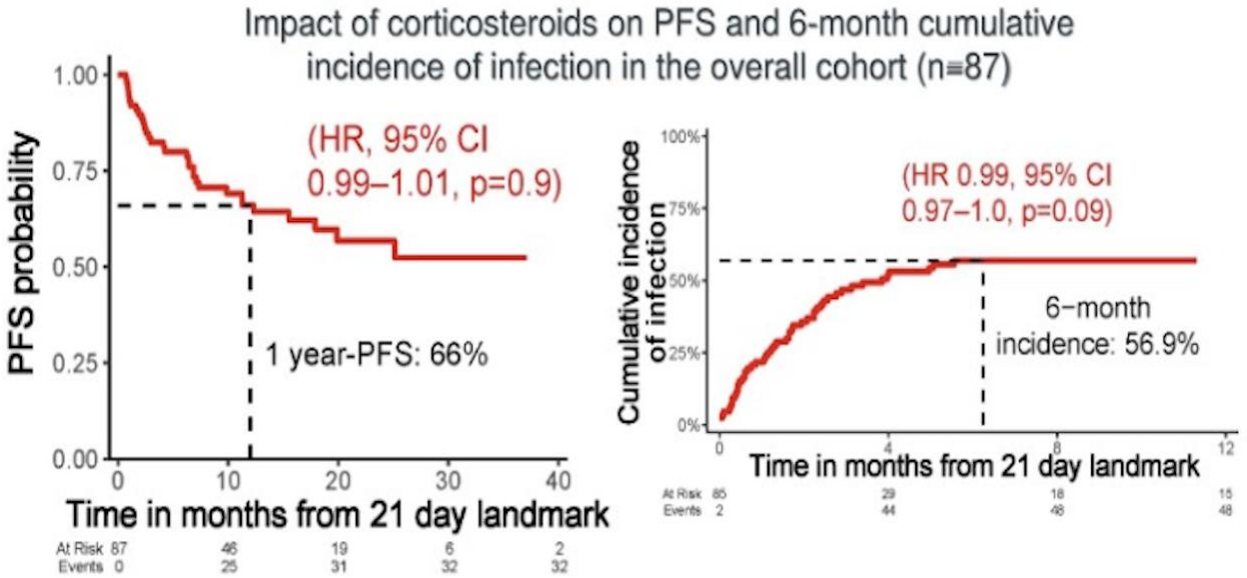
Gutierrez-Padilla C, et al. EHA 2025. Abstract PS178

Study Design and Patients

- Single-center, observational study evaluating impact of corticosteroid treatment on outcomes with bsAbs among 96 pts with RRMM
- 45.9% of pts received bsAb monotherapy

Outcomes

- 9 pts who died or had progression were excluded from the analysis
- Corticosteroid use did not appear to impact PFS
  - Overall cohort: 1-yr PFS 66%
  - bsAb monotherapy subgroup: 1-yr PFS 36.6%
- 6-mo cumulative incidence of infection was also not impacted by corticosteroid use in either subgroup (HR 1.0)



Author Conclusions

- Exposure to steroids during early bsAb treatment does not compromise efficacy or infections-related toxicity

APTITUDE HEALTH®

Selective Depletion of B-Cell Lineage Subsets During Treatment With Anti-BCMA vs Anti-GPRC5D BsAbs Underlies Different Risk of Infections in Patients With MM

EPICS

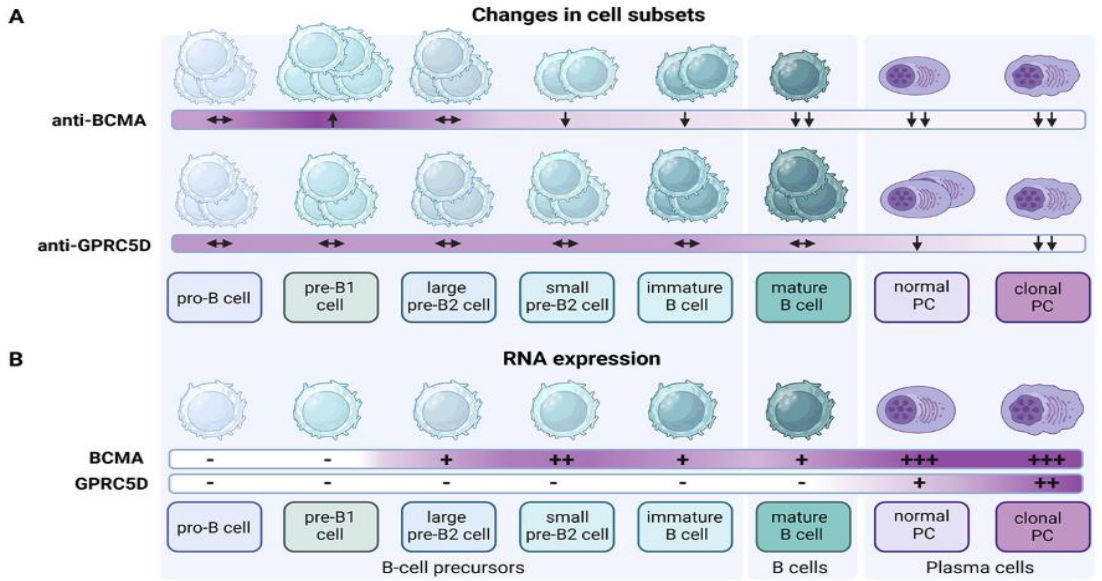
Jelinek T, et al, et al. EHA 2025. Abstract PS1673

Study Design and Patients

- Observational study examining potential mechanisms for higher infection rates with anti-BCMA antibodies
- N=75 pts treated with either BCMA- or GPRC5D-targeting bsAbs

Outcomes

- Higher infection rates and more frequent use of IVIg in pts receiving anti-BCMA bsAbs vs anti-GPRC5D
  - Infection rate: 82% vs 53%; *P*=.012
  - IVIg use: 74% vs 32%; *P*=.001
- Significant depletion of mature B cells and normal plasma cells observed in BCMA group during treatment (*P*<.001)
- Distinct patterns of BCMA and GPRC5D expression observed throughout the B-cell lineage
  - BCMA expression: plasma cells, mature B cells, B-cell precursors, and small pre-B2 cells
  - GPRC5D expression: limited to plasma cells



Author Conclusions

- Anti-BCMA bsAbs are associated with higher risk of infection and more profound and persistent hypogammaglobulinemia
- Distinct patterns of BCMA and GPRC5D expression explain different on-target, off-tumor effects

APTITUDE HEALTH®

Systematic Review of Bispecific Antibodies Efficacy and Safety in RRMM

Pérez-Granado J, et al. EHA 2025. Abstract PB2885

EPICS

Study Design and Patients

- Systematic review of outcomes from trials of bsAbs in RRMM
- Analysis included elranatamab, teclistamab, linvoseltamab, and talquetamab (TALQ)

Outcomes

- Monotherapy outcomes
  - Elranatamab: ORR 61%; mOS 24.6 mo
  - Teclistamab: ORR 63%; mOS 18.3 mo
  - Linvoseltamab: ORR 70.9%; mOS 31.4 mo
  - TALQ: ORR 69.5%; mOS 20.1 mo
- Among combination regimens, TALQ + dara had the best outcomes (ORR 77.7%; mPFS 24.9 mo)
- High rates of CRS were seen across studies, along with infection rates as high as 79%

Author Conclusions

- bsAbs are a promising advancement in the treatment of RRMM
- They are associated with safety challenges, including CRS and high rates of infection
- Combination strategies will provide opportunities to enhance outcomes and overcome resistance

ALTITUDE-1: Real-World Treatment Patterns Associated With Elranatamab Among Patients With MM

Banerjee R, et al. EHA 2025. Abstract PF798

EPICS

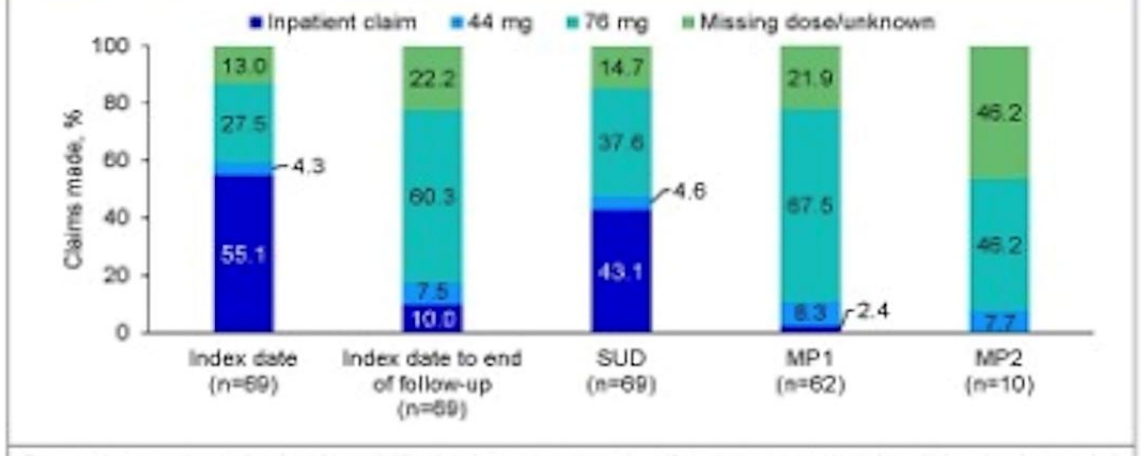
Study Design and Patients

- Real-world study evaluating treatment/dosing patterns of elranatamab
- 69 pts with RRMM included in the analysis
- Patterns for elranatamab treatment at 3 time periods: step-up dosing (SUD), days 9 to 168 (maintenance period 1; MP1), and day 169+ (maintenance period 2; MP2)

Outcomes

- Mean days between administrations
  - SUD: 5.7 days
  - MP1: 10.7 days
  - MP2: 27 days

Figure 1. Proportions of claims by vial size during step-up dosing and maintenance[a-c]



Author Conclusions

- Elranatamab was administered less frequently than label with Q2W and Q4W dosing schedules observed during maintenance periods

APTITUDE HEALTH®

Efficacy and Safety of Less Frequent Dosing With Elranatamab in Patients With RRMM: A US Subgroup Analysis From MagnetisMM-3

EPICS

Raje N, et al. EHA 2025. Abstract PF771

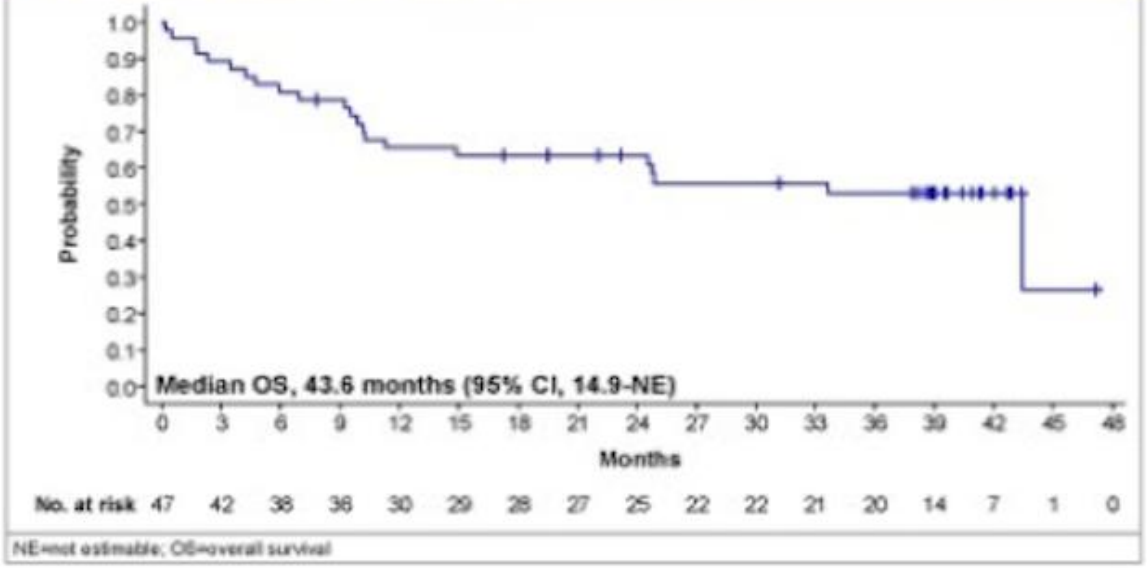
Study Design and Patients

- Subgroup analysis from the phase III MagnetisMM-3 trial evaluating elranatamab as a treatment for RRMM
- Evaluated outcomes in heavily pretreated subgroup 38 mo from last pt's first dose (median follow-up: 39.6 mo)
- N=47

Outcomes

- ORR: 66.0%, including 27.7% CR
- mPFS: 27.3 mo; mOS: 43.6 mo, but this may not be mature
- Pts who changed to Q2W or Q4W dosing
  - Q2W: 77.8% maintained or improved response
  - Q4W: 87.5% maintained or improved response
- Safety profile was consistent with the total study population, with CRS and ICANS of G1 or G2 only

Figure 3. Overall survival



Author Conclusions

- In a heavily pretreated subgroup, elranatamab was associated with deep, durable responses consistent with overall data from Cohort A of MagnetisMM-3

First-in-Human Study of JNJ-79635322 (JNJ-5322), a Novel, Next-Generation Trispecific Antibody, in Patients With RRMM: Initial Phase I Results

Popat R, et al. EHA 2025. Abstract S100

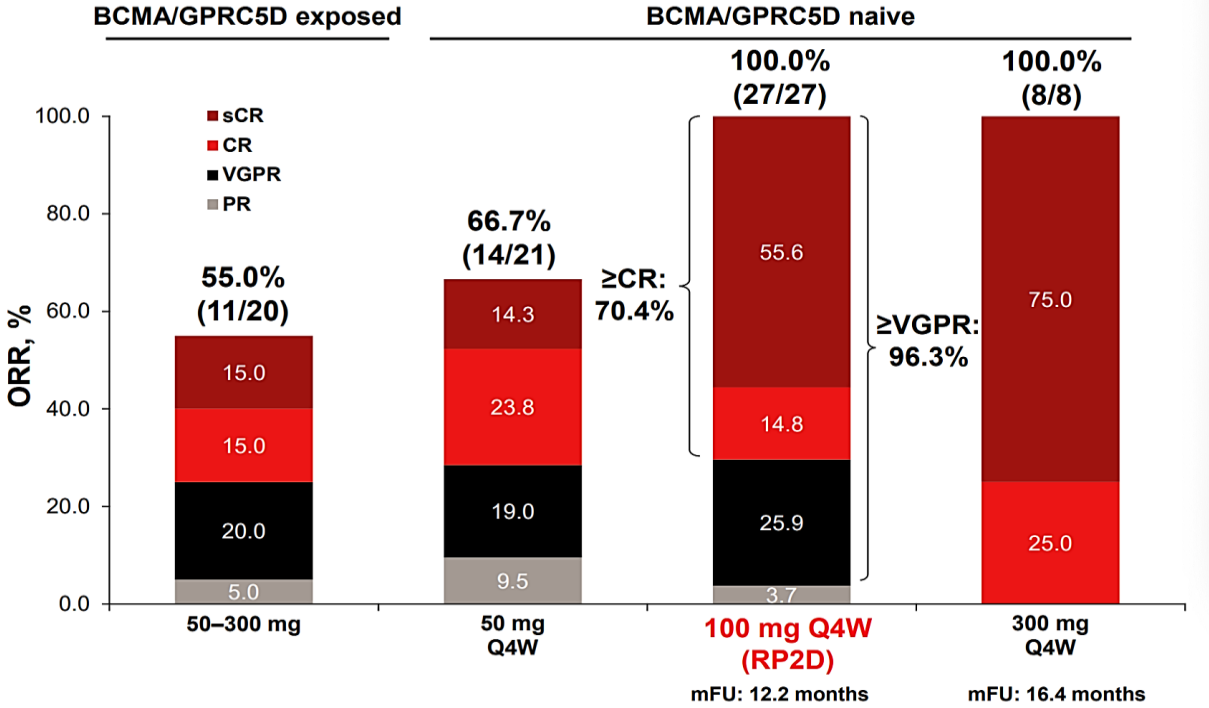
EPICS

Study Design and Patients

- Initial results from a first-in-human phase I trial of the novel trispecific antibody JNJ-5322
- Molecule includes CD3, BCMA, and GPRC5D binding domains

Outcomes

- 100 mg Q4W with one 5-mg step-up dose identified as the recommended phase II dose (RP2D)
- At RP2D
  - 1 dose-limiting toxicity (neutropenia) and 1 G5 TEAE (pneumonia)
  - No pts experienced ICANS
  - Infections in 80.6%, with G3/4 in 33.3%
- Use of prophylactic tocilizumab decreased CRS incidence and severity (any-G CRS: 69.2% vs 20.0%)
- ORR 100% at RP2D in BCMA/GPRC5D-naive pts



Author Conclusions

- JNJ-5322 demonstrated manageable safety and an ORR comparable with CAR T, with convenient, off-the-shelf Q4W dosing

APTITUDE HEALTH®

Linvoseltamab + Carfilzomib in Patients With RRMM: Initial Results From the LINKER-MM2 Trial

Manier S, et al. EHA 2025. Abstract S202

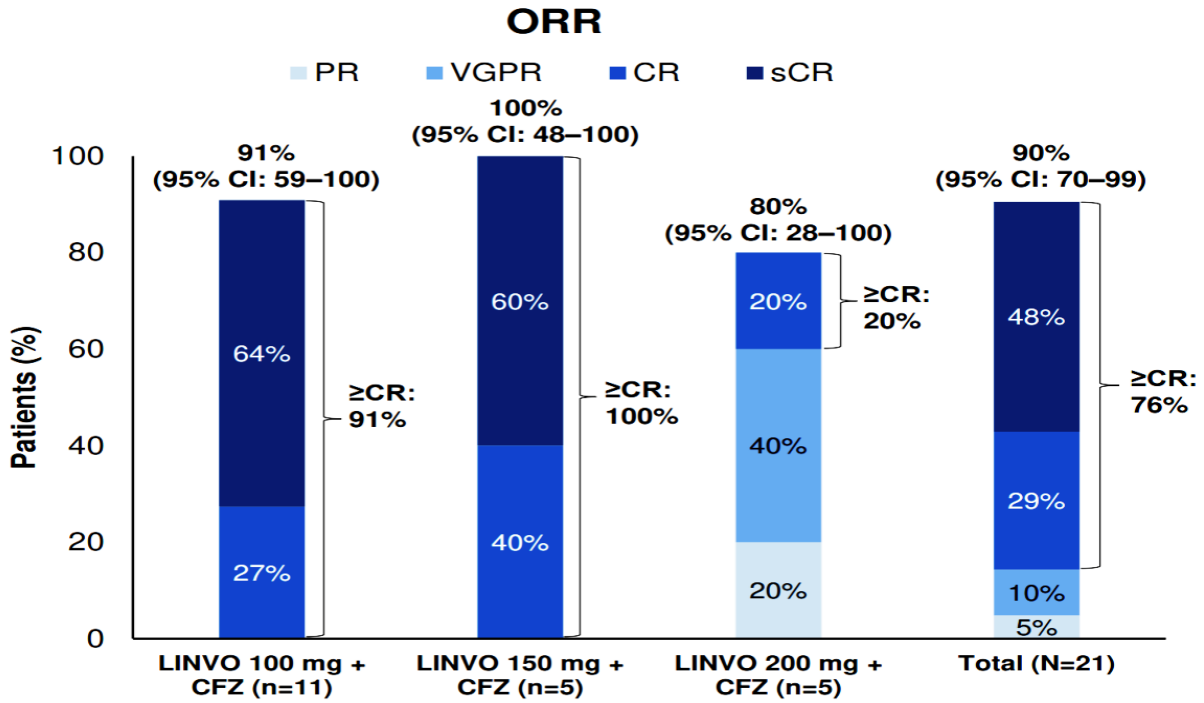
EPICS

Study Design and Patients

- Phase Ib multicohort study testing the combination of linvoseltamab, a BCMA × CD3 bispecific antibody, with several established and investigational antimyeloma therapies
- This report detailed the cohort evaluating linvoseltamab and carfilzomib in 23 pts with RRMM

Outcomes

- Only 1 pt experienced a dose-limiting toxicity, which was G4 thrombocytopenia at the dose of 100 mg linvo
- TEAEs occurred in 100%, including G≥3 in 82.6%
  - 43.5% experienced G≥3 infection, including 1 fatal infection
- ORR 90%, with 76% CR
- 12-mo DOR rate: 87%
- 12-mo PFS rate: 83%



Author Conclusions

- The combination of linvoseltamab and carfilzomib resulted in a high rate of durable responses with a manageable safety profile
- Similar outcomes with an ORR of 85% were seen with the combination of linvoseltamab and bortezomib (abstract PS1716)

Talquetamab + Cetrelimab in Patients With RRMM: Initial Safety and Efficacy Results From the Phase Ib TRIMM-3 Study

Perrot A, et al. EHA 2025. Abstract S200

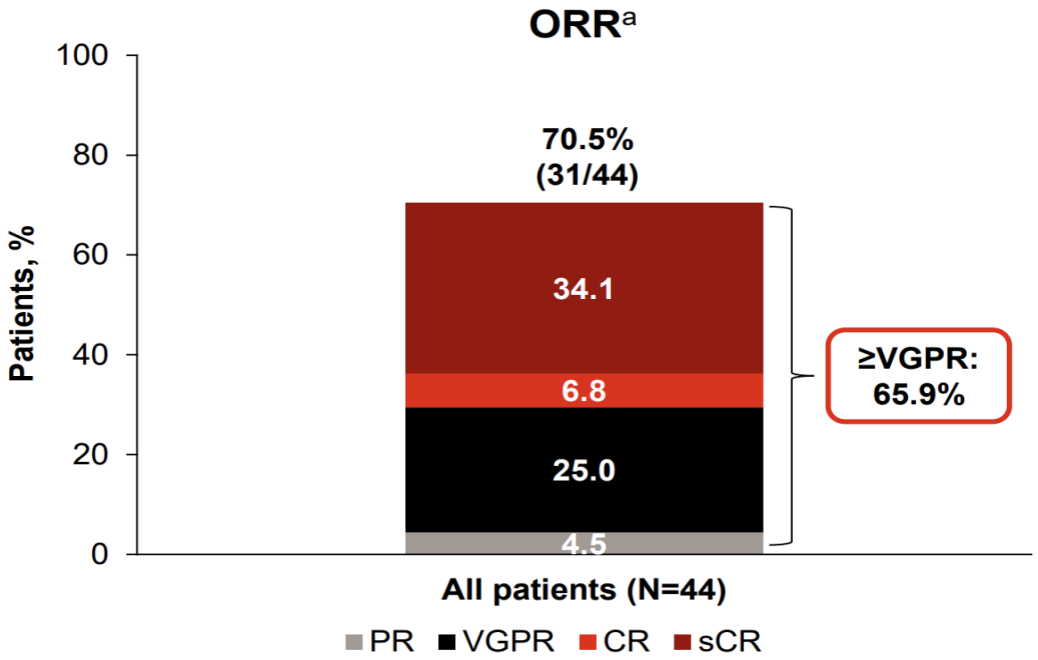
EPICS

Study Design and Patients

- Phase Ib trial evaluating the combination of talquetamab and the PD-1 inhibitor cetrelimab in RRMM
- Initial safety and efficacy results in 44 pts

Outcomes

- TEAEs were consistent with the known safety profiles of talquetamab and cetrelimab
- CRS mostly confined to initial step-up dose with no G≥3 CRS
- ICANS G1 in 2 pts
- Infections of G3/4 in 29.5% of pts
  - 1 pt died due to pneumonia
- ORR: 70.5% with CR/sCR in 40.9%
- mDOR: 16.8 mo
- 6-mo PFS rate: 69.9%
- In pts previously treated with bsAbs
  - ORR: 68.4% with 31.6% CR
  - mDOR: 12 mo



Author Conclusions

- Talquetamab + cetrelimab elicited deep and durable responses in pts with RRMM and prior exposure to bsAbs

APTITUDE HEALTH®

Updated Results From Phase III DREAMM-8 Study of Belantamab Mafodotin + Pomalidomide and Dexamethasone vs Pomalidomide + Bortezomib and Dexamethasone in RRMM

EPICS

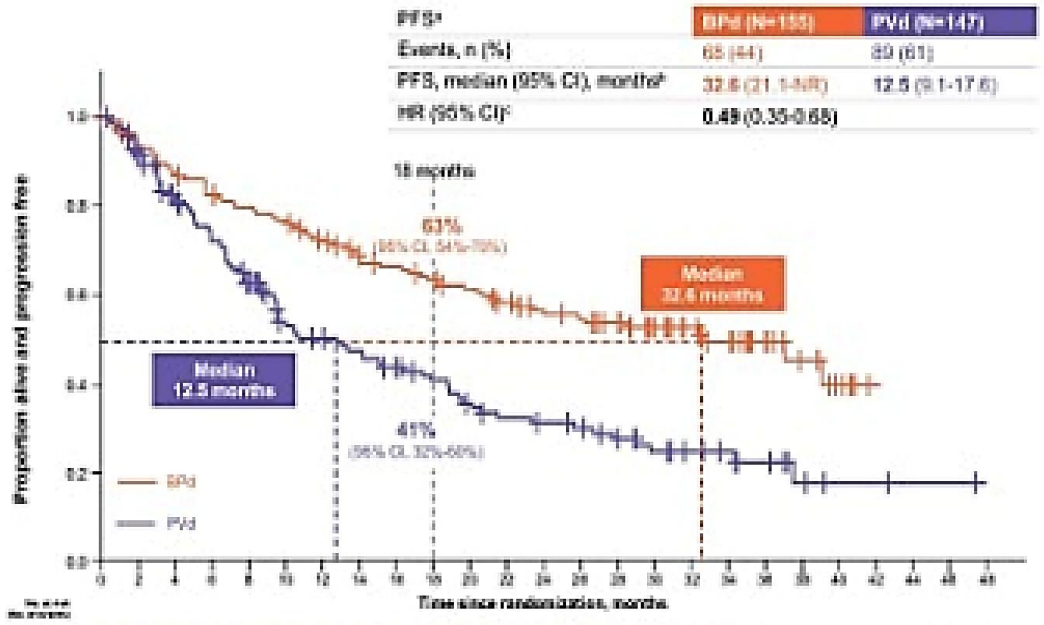
Dimopoulus M, et al. EHA 2025. Abstract PF728

Study Design and Patients

- Phase III trial evaluating belantamab mafodotin + pomalidomide and dexamethasone (BPd) vs pomalidomide + bortezomib and dexamethasone (PVd) in pts with RRMM
- Post hoc analysis reporting efficacy and safety with 8 additional mo of study follow-up

Outcomes

- Median follow-up: 28 mo
- PFS benefit of BPd maintained with additional follow-up (32.5 mo vs 12.5 mo; HR 0.49)
  - Benefit was maintained across all evaluated subgroups
- Updated safety results were consistent with the primary analysis
  - Exposure-adjusted rates of thrombocytopenia, neutropenia, and infections similar between the 2 arms
  - Ocular AEs (any G: 89%, G≥3: 44%) were managed by dose holds and dose reductions



Author Conclusions

- BPd continued to demonstrate clinically meaningful PFS benefit in pts with RRMM with ≥1 prior line of therapy

DREAMM-7: Study of Belantamab Mafodotin + Bortezomib + Dexamethasone vs Daratumumab + Bortezomib + Dexamethasone in RRMM: Efficacy in Patients by Subsequent Therapy

EPICS

Hungria V, et al. EHA 2025. Abstract PS1734

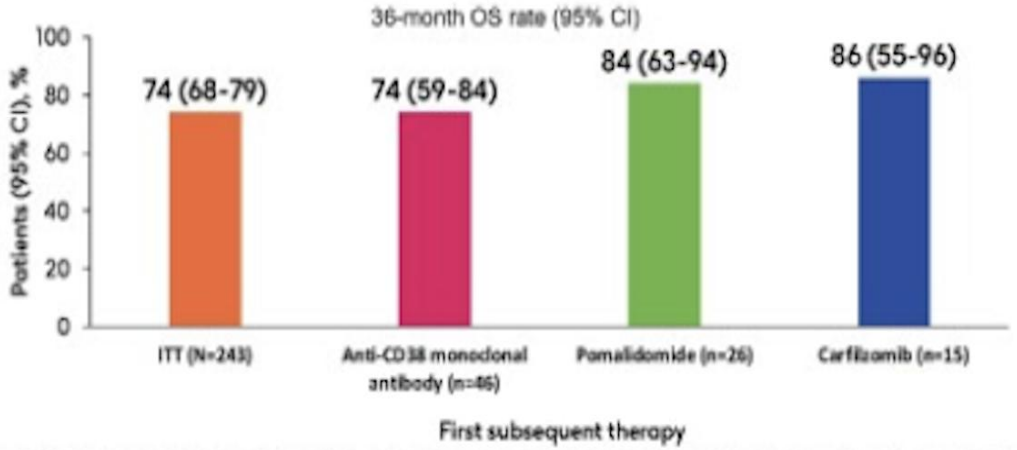
Study Design and Patients

- Phase III study comparing belantamab mafodotin, bortezomib, and dex (BVd) to daratumumab, bortezomib, and dex (DVd) in pts with RRMM
- Analysis of outcomes by subsequent therapy in 87 pts from the BVd arm and 130 from the DVd arm

Outcomes

- Most common first subsequent therapy for pts treated with BVd was an anti-CD38 antibody (53%), with isa-pom-dex as the most frequently given therapy
  - Pomalidomide was the second most common (30%)
- Time from first subsequent therapy to progression or death was similar regardless of subsequent therapy received
- 36-mo OS rate: 74%; rates by first subsequent therapy can be seen in figure

Figure 6: **OS Rates at 36 Months in the ITT Population and in Each First Subsequent Therapy Group[a]**



Author Conclusions

- Subsequent therapies with common classes of agents were effective and had consistent benefits after BVd treatment

APTITUDE HEALTH®

EPICS

Relapsed/Refractory Multiple Myeloma: ADCs and Multispecifics

Discussion

Update on RRMM: ADCs and Multispecifics (1/3)

EPICS

General

- PI-bispecific combinations
  - On the basis of the impressive outcomes seen with linvoseltamab in LINKER-MM2 as well as data from ASH evaluating elranatamab in combination with carfilzomib, many experts wonder whether PIs are an ideal combination partner for BCMA-targeting bispecific antibodies, in terms of efficacy
  - However, the toxicity of PIs combined with the toxicity of bispecifics might limit utility, as there are high rates of PI discontinuation due to AEs
    - More thought is needed on when and how long to treat with a PI in this scenario

- Role for ADCs
  - While the treatment landscape is becoming crowded with new modalities, the experts are excited about the potential of ADCs
  - Previous concerns about toxicity associated with belantamab mafodotin have been mostly addressed by the new dosing schema
  - One expert speculated that ADCs might be an interesting addition to frontline treatment in transplant-eligible patients and would like to see more trials evaluating that approach
    - Use of ADCs in patients with highly proliferative disease would be logical, and efforts should focus on identifying these subgroups of patients
    - This would be a strategy to balance efficacy with toxicity as well, as this represents a high-need population that would be willing to tolerate more side effects

Update on RRMM: ADCs and Multispecifics (2/3)

EPICS

General (cont.)

- Trispecific antibodies
  - The experts are interested in these agents but not convinced that this is the best path forward
  - Combining the 2 main therapeutic targets in MM may be a method to achieve deep and durable remission, but it also limits options for later lines of therapy
    - Further insight on when and for how long to treat with a PI in this setting is required
    - It is unclear where CAR T-cell therapy will fit into a treatment paradigm with trispecific antibodies

- Community adoption of bispecific antibodies
  - Bispecific antibodies present a logistic challenge for many community practices that has prevented them from adopting these treatments thus far
  - However, the experts believe this is just an issue of time and training
    - To keep up with current standards of care and remain relevant, community practices will have to develop the infrastructure to manage these kinds of therapies
    - Because bispecifics are also moving into the solid-tumor space, it is more likely that community practices will adapt

Update on RRMM: ADCs and Multispecifics (3/3)

EPICS

Abstract S202: Linvoseltamab + Carfilzomib in Patients With Relapsed/Refractory Multiple Myeloma: Initial Results From the LINKER-MM2 Trial (Manier S, et al)

- Experts were pleasantly surprised by the results of this trial, citing the high response rate and CR rate along with the long duration of responses

Abstract PF728: Updated Results From Phase 3 DREAMM-8 Study of Belantamab Mafodotin Plus Pomalidomide and Dexamethasone vs Pomalidomide Plus Bortezomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma (Dimopoulos M, et al)

- While the experts believe DREAMM-8 is a good trial and that belantamab mafodotin is a promising drug, they were displeased with the inconsistent dosing throughout the trial
  - Frequent dose interruptions and holds modified the actual dosing schedule so that the trial design is not indicative of how patients were actually treated
  - They indicated these issues with dosing need to be addressed in phase I trials and that by a phase III trial, the dose and schedule should be set in such a way that frequent interruptions and holds are not needed

APTITUDE HEALTH®

EPICS

Relapsed/Refractory Multiple Myeloma: CAR Ts

Abstract Selection

EPICS

Abstract	Phase
Abstract S201: Phase 2 Registrational Study of Anitocabtagene Autoleucel for Relapsed and/or Refractory Multiple Myeloma (RRMM): Updated Results From iMMagine-1. (Kaur G, et al)	Phase II
Abstract S192: Long-Term (≥5 Year) Remission and Survival After Treatment With Ciltacabtagene Autoleucel in CARTITUDE-1 in Patients With Relapsed/Refractory Multiple Myeloma. (Jagannath S, et al)	Phase I Phase II
Abstract PS1723: Ciltacabtagene Autoleucel Versus Standard of Care in Patients With Relapsed/Refractory Multiple Myeloma: CARTITUDE-4 Survival Subgroup Analyses. (Cohen Y, et al)	Phase III
Abstract PF765: Survival Benefit of Ciltacabtagene Autoleucel in Second-Line Compared With Later-Line Treatment of Lenalidomide-Refractory Multiple Myeloma: Updated Treatment Positioning Model Analysis. (Mina R, et al)	Model Analysis
Abstract PS2119: Innovative sdAb-Based CAR-T Cells Targeting BCMA Outperform Current CAR-T Therapies for Multiple Myeloma. (Rodriguez-Madoz J, et al)	Preclinical
Abstract PS1740: OM336, a B-Cell Maturation Antigen (BCMA) Targeting T Cell Engager Antibody, Demonstrates Initial Safety and Efficacy in the Treatment of R/R Multiple Myeloma (MM). (Zhou C, et al)	Phase I Phase II

Phase 2 Registrational Study of Anitocabtagene Autoleucel for RRMM: Updated Results From iMMagine-1

Kaur G, et al. EHA 2025. Abstract S201

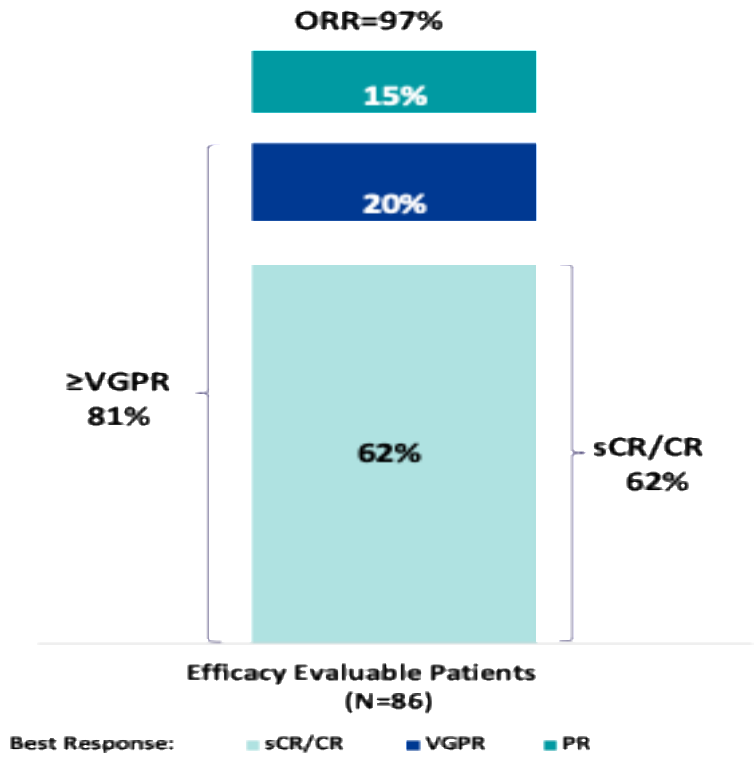
EPICS

Study Design and Patients

- Phase II study evaluating the novel BCMA CAR T cell anitocabtagene autoleucel (anito-cel) in RRMM
- N=86 evaluable pts

Outcomes

- Median follow-up: 9.5 mo
- ORR: 97% with 62% CR
- 93.1% of evaluable pts were MRD negative
- Survival outcomes
  - 6-mo PFS: 93.3%; OS: 96.5%
  - 12-mo PFS: 78.5%; OS: 96.5%
- Safety profile is predictable and manageable
  - 86% had no G>1 CRS
  - 9% had ICANS



Author Conclusions

- Anito-cel demonstrates deep and durable efficacy and manageable safety in pts with high-risk RRMM who have received >4 lines of therapy

Long-Term (≥5 year) Remission and Survival After Treatment With Ciltacabtagene Autoleucel in CARTITUDE-1 in Patients With RRMM

Jagannath S, et al. EHA 2025. Abstract S192

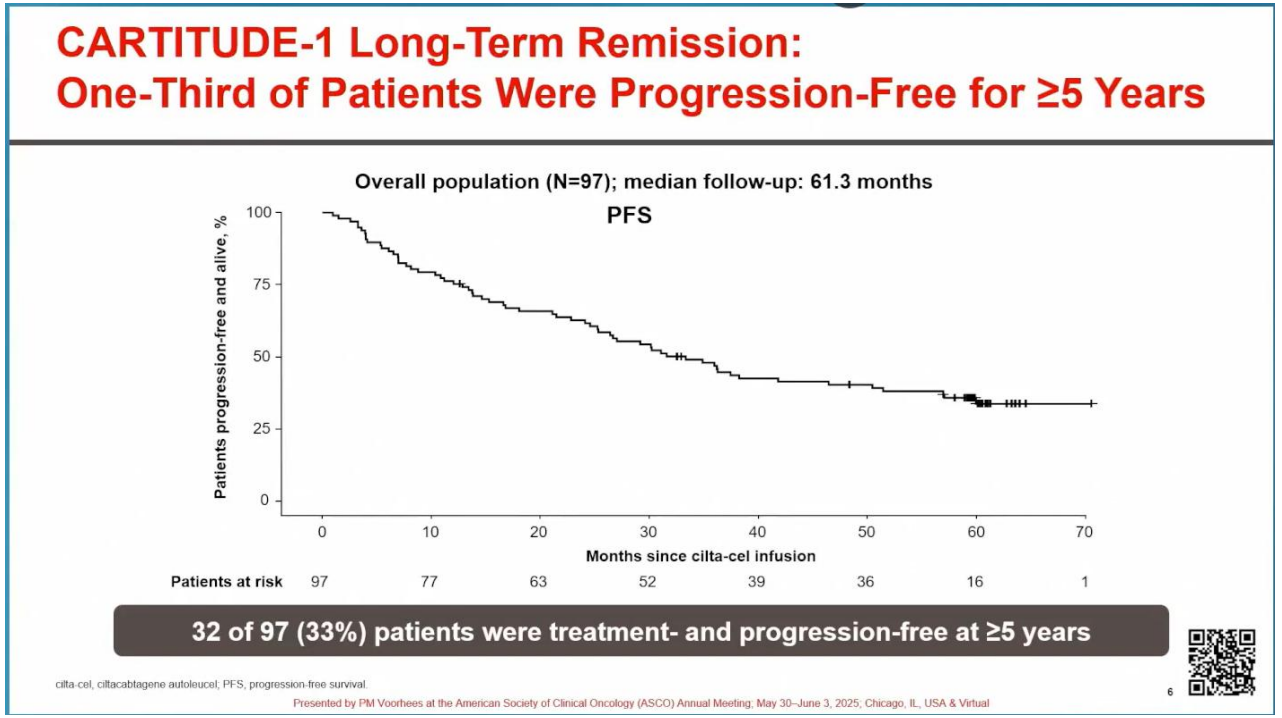
EPICS

Study Design and Patients

- Long-term follow up of phase I/II CARTITUDE-1 trial of ciltacabtagene autoleucel (cilta-cel) in RRMM (N=97)

Outcomes

- Median follow-up: 61.3 mo
- 33% of pts were treatment and progression free at 5+ yr
- Among progression-free pts in sCR, 100% (12/12) were MRD negative and imaging negative at 5+ yr following cilta-cel infusion
- No difference in baseline characteristics, including high-risk cytogenetics and extramedullary plasmacytomas, between pts with or without PD at 5 yr



Author Conclusions

- These data provide the first evidence that cilta-cel is potentially curative in RRMM

APTITUDE HEALTH®

Ciltacabtagene Autoleucel vs SOC in Patients With RRMM: CARTITUDE-4 Survival Subgroup Analyses

Cohen Y, et al. EHA 2025. Abstract PS1723

EPICS

Study Design and Patients

- Phase III study comparing cilta-cel to SOC in pts with RRMM
- Subgroup analyses evaluating outcomes in pts with extramedullary disease, by prior lines of therapy, and by cytogenetic risk status

Subgroup Outcomes (cilta-cel vs SOC)

- Extramedullary disease
  - mPFS: 13 mo vs 4 mo (HR 0.71)
  - mOS: NR vs 16 mo (HR 0.61)
- Line of therapy, mPFS
  - 1 line: NR vs 17 mo (HR 0.41)
  - 2 lines: NR vs 12 mo (HR 0.30)
  - 3 lines: NR vs 8 mo (HR 0.20)
- High-risk cytogenetics
  - mPFS: 37 mo vs 10 mo (HR 0.38)
  - mOS: HR 0.54

Cytogenetic risk: Median PFS*

Author Conclusions

- Cilta-cel offers a positive benefit-risk ratio vs SOC for pts with lenalidomide-refractory MM as early as after the first relapse
- It may overcome the poor prognosis associated with high-risk cytogenetics

APTITUDE HEALTH®

Survival Benefit of Ciltacabtagene Autoleucel in 2L Compared With Later-Line Treatment of Lenalidomide-Refractory MM: Updated Treatment Positioning Model Analysis

Mina R, et al. EHA 2025. Abstract PF765

Study Design and Patients

- Markov model analysis evaluating the survival benefit of cilta-cel as 2L therapy as compared with later lines in lenalidomide-refractory MM

Outcomes

- Best outcomes were seen when cilta-cel is given as 2L therapy vs in a 3L+ setting
  - 3.5-yr improvement in mOS
  - 14.0% improvement in 5-yr OS rate
  - 8.6% improvement in 10-yr OS

	2L cilta-cel to 3L+ SOC	2L SOC to 3L+ cilta-cel	Difference
Median OS, years	12.8	9.3	3.5
5 years	75.5%	61.6%	14.0%
10 years	57.2%	48.6%	8.6%

Author Conclusions

- Simulation shows that using a single cilta-cel infusion earlier results in better survival outcomes for pts with len-refractory RRMM

Innovative sdAb-Based CAR T Cells Targeting BCMA Outperform Current CAR T Therapies for MM

Rodriguez-Madoz J, et al. EHA 2025. Abstract PS2119

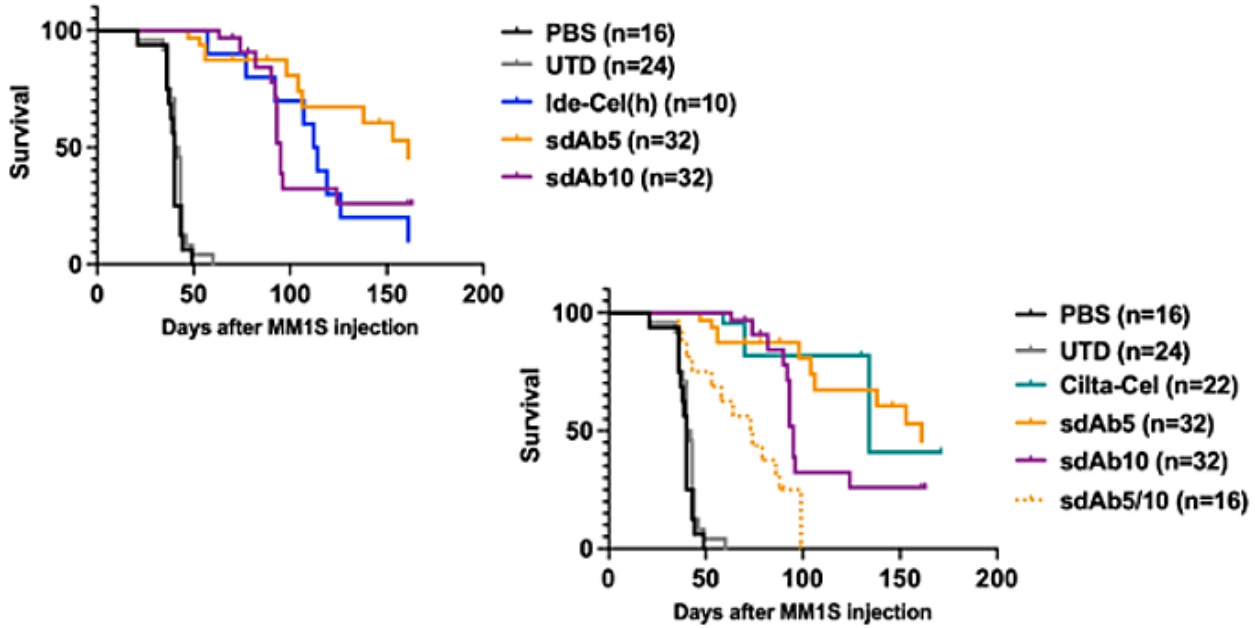
EPICS

Study Design and Patients

- Preclinical study comparing single-domain antibody (sdAb)-based CAR T cells with current CAR T-cell therapies (ide-cel and cilta-cel) in animal models

Outcomes

- 2 of the selected sdAb-based CAR T cells (sdAb5 and sdAb10) showed enhanced antitumoral efficacy with improved survival rate compared with ide-cel
- sdAb5 showed similar antitumor efficacy as cilta-cel
- sdAb-based CAR T cells were enriched in stem cell-like memory and central memory T cells with low expression levels of T-cell exhaustion markers



Author Conclusions

- These findings highlight the promise of sdAb-based CAR T cells as a novel and effective treatment for MM

OM336, a BCMA-Targeting T-Cell Engager Antibody, Demonstrates Initial Safety and Efficacy in the Treatment of RRMM

EPICS

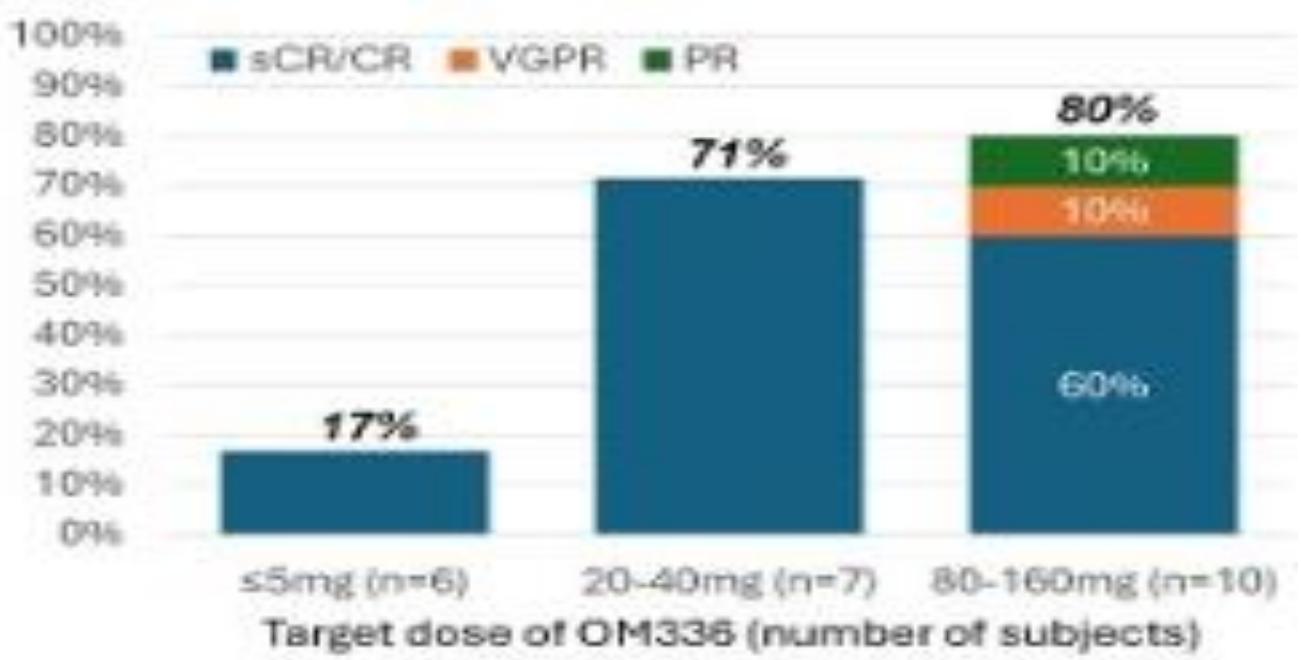
Zhou C, et al. EHA 2025. Abstract PS1740

Study Design and Patients

- Phase I/II first-in-human study evaluating the novel BCMA-targeted T-cell engager antibody OM336 in RRMM
- Evaluated 3 dose levels of OM336: ≤5, 20–40, and 80–160 mg
- 21 pts evaluable for response with median follow-up 12.1 mo

Outcomes

- ORR by dose level
  - ≤5 mg: 17%
  - 20–40 mg: 71%
  - 80–160 mg: 80%
- No G≥3 CRS observed in the expansion dose and no ICANS in any pt treated with OM336



Author Conclusions

- OM336 is a highly potent bispecific with promising initial efficacy and safety in the treatment of RRMM, warranting further investigation

APTITUDE HEALTH®

EPICS

Relapsed/Refractory Multiple Myeloma: CAR Ts

Discussion

Update on RRMM: CAR Ts (1/3)

EPICS

Inching closer to cure with CAR T-cell therapies

As understanding of how to give CAR T-cell therapies has improved, these agents have become instrumental components of the MM treatment algorithm

- After the learning curve of the early years of CAR T cells, physicians are very comfortable giving these therapies in a manner that is safe and effective
  - Bridging therapy and administering steroids to patients with more proliferative disease were highlighted as key strategies to ensure CAR T cells are safe and tolerable
- The experts indicated there are very few patients whom they would exclude from CAR T-cell therapy, such as those who are too frail to tolerate high-grade CRS; in general, they view CAR T-cell therapy as much more tolerable than transplant
- The major challenge with CAR T cells in myeloma is persistence of disease, which is something that is not seen in other disease settings like ALL and DLBCL

Bispecific antibodies and CAR T cells are complementary therapies that work in an almost synergistic manner, and more focus should be given to pairing these treatment modalities

- Bispecific antibodies can be given as a bridge to CAR T cells, or CAR T cells can be used after a full course of bispecific antibody therapy as a type of consolidation therapy
- Giving bispecific antibodies after CAR T-cell therapy is seen as a method to ensure that any residual disease is cleared up

The experts were highly impressed with the early data of the new CAR T-cell product anito-cel and believe this is a more effective and safer CAR T cell than currently available options

Update on RRMM: CAR Ts (2/3)

EPICS

General

- Improving CAR T-cell therapy
  - In general, the experts feel CAR T-cell therapies have become easier to manage as more has been learned about how to administer them and prevent toxicities
  - Using some form of debulking therapy prior to CAR T-cell therapy to minimize the risk of CRS and avoiding use of these agents in patients with highly active disease were key lessons that will improve the way current CAR T cells are used and how future agents will be developed
  - One expert indicated they are still concerned about the risk of long-term neurotoxicities and that they are hopeful new CAR T cells in development will address this
- Who should receive CAR T-cell therapy?
  - Overall, the experts think CAR T cells are appropriate for any patient who is able to tolerate potential high-grade CRS
  - Patients with extremely aggressive, highly proliferative disease may not be appropriate CAR T candidates. However, pretreatment with bridging or debulking therapy might allow for efficacious and safe treatment with CAR Ts
- CAR Ts vs bispecifics
  - The experts were clear that there is a role for both bispecific antibodies and CAR T cells in MM and there is no need to exclude one
    - These agents are very complementary in their impact on disease
    - Bispecific antibodies are an excellent bridge to CAR T-cell therapy, and CAR T cells may serve as an effective “end-of-therapy” treatment for bispecific antibodies

Update on RRMM: CAR Ts (3/3)

EPICS

Abstract S201: Phase 2 Registrational Study of Anitocabtagene Autoleucel for Relapsed and/or Refractory Multiple Myeloma (RRMM): Updated Results From iMMagine-1 (Kaur G, et al)

- The experts are very impressed with the outcomes seen with anito-cel, in particular the improved toxicity profile of this agent compared with previous CAR T-cell products
  - While some of the improvement in toxicity may derive from a better understanding of how to manage CAR T cells, the experts believe the differences in the anito-cel construct compared with prior CAR T cells, such as its faster “off-rate” and use of a fully synthetic D-domain rather than a Fab to bind to BCMA, may be the key to its diminished neurotoxicity

Abstract S192: Long-Term (≥5 Year) Remission and Survival After Treatment With Ciltacabtagene Autoleucel in CARTITUDE-1 in Patients With Relapsed/Refractory Multiple Myeloma (Jagannath S, et al)

- These results were intriguing, and the experts were surprised by the impressive durability of response in patients with extramedullary disease and those with high-risk cytogenetics
  - With 5-year follow-up data, the experts indicated it may be time to start using the word “cure” for some patients treated with CAR T cells

APTITUDE HEALTH®

US 5901-B Peachtree Dunwoody Road
Suite 415, Atlanta, GA 30328, US

EU Laan van Nieuw Oost-Indië 133 F
2593 BM The Hague, the Netherlands

UK 6th Floor, 2 Kingdom Street
London, W2 6BD, United Kingdom

aptitudehealth.com