



**EPICS**

# **CONGRESS COVERAGE: ASCO/EHA 2021 – FOCUS ON MULTIPLE MYELOMA**

Wednesday, June 23, 2021

**FULL REPORT**

# REPORT CONTENTS

Content	Slide
Meeting Snapshot	3 →
Faculty Panel	4 →
Meeting Agenda	5 →
Strategic Recommendations	6 →
Congress Highlights	8 →
Key Insights	44 →

EPICS

## VIRTUAL CLOSED-DOOR ROUNDTABLE



**DATE:**  
June 23, 2021



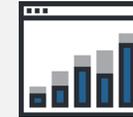
**PANEL:** Key experts in  
multiple myeloma  
> 3 from US  
> 4 from Europe



**SELECTED ASCO AND  
EHA 2021 ABSTRACT  
PRESENTATIONS** by  
key experts



**MULTIPLE MYELOMA-  
SPECIFIC DISCUSSIONS**  
on latest research updates,  
therapeutic advances, and  
their application in clinical  
decision-making



**INSIGHTS REPORT**  
including postmeeting  
analyses and actionable  
recommendations

# PANEL CONSISTING OF 3 US AND 4 EUROPEAN MULTIPLE MYELOMA EXPERTS

EPICS

**Gareth Morgan, MD, PhD**  
NYU Langone



**Irene Ghobrial, MD**  
Dana-Farber Cancer Institute



**Sagar Lonial, MD, FACP**  
Winship Cancer Institute of  
Emory University



**Mohamad Mohty, MD, PhD**  
Saint-Antoine Hospital and  
Sorbonne University



**Niels van de Donk, MD, PhD**  
Amsterdam University Medical Center



**Hermann Einsele, MD, FRCP**  
University Hospital Würzburg



**CHAIR:**  
**María-Victoria Mateos, MD, PhD**  
University of Salamanca



# MEETING AGENDA

EPICS

Time (CEST)	Topic	Speaker/Moderator
16.00 – 16.05	Welcome and Introductions	María-Victoria Mateos, MD, PhD
16.05 – 16.15	First Line (1): Smoldering and Transplant-Ineligible Multiple Myeloma	Irene Ghobrial, MD
16.15 – 16.30	Discussion and Key Takeaways	
16.30 – 16.40	First Line (2): Induction in Transplant-Eligible Multiple Myeloma	Mohamad Mohty, MD, PhD
16.40 – 16.55	Discussion and Key Takeaways	
16.55 – 17.05	First Line (3): Maintenance and MRD	Sagar Lonial, MD, FACP
17.05 – 17.20	Discussion and Key Takeaways	
17.20 – 17.30	R/R MM: First and Second Relapse	María-Victoria Mateos, MD, PhD
17.30 – 17.50	Discussion and Key Takeaways	
17.50 – 17.55	Break	
17.55 – 18.05	Triple-Refractory R/R MM: Novel Agents	Niels van de Donk, MD, PhD
18.05 – 18.25	Discussion and Key Takeaways	
18.25 – 18.35	Triple-Refractory R/R MM: Antibodies and Bispecifics	Hermann Einsele, MD, FRCP
18.35 – 18.55	Discussion and Key Takeaways	
18.55 – 19.05	Triple-Refractory R/R MM: CAR Ts	Gareth Morgan, MD, PhD
19.05 – 19.25	Discussion and Key Takeaways	
19.25 – 19.30	Summary and Closing Remarks	María-Victoria Mateos, MD, PhD





EPICS

CONGRESS HIGHLIGHTS

**EPICS****CONGRESS HIGHLIGHTS****First Line (1): Smoldering and  
Transplant-Ineligible Multiple Myeloma**

# OS AND PFS UPDATES FROM THE MAIA TRIAL: DARA-RD VS RD IN TRANSPLANT-INELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA

FACON T, ET AL. 2021, EHA LB1901

## STUDY POPULATION

> NDMM ineligible for high-dose chemotherapy and autologous

## OS (A) AND PFS (B) WITH D-Rd VS Rd

*[Faded text area containing study details]*





**EPICS**

**CONGRESS HIGHLIGHTS**  
**First Line (2): Induction in Transplant-Eligible Multiple Myeloma**

# CARDAMON TRIAL: ASCT VS Kcd CONSOLIDATION WITH K MAINTENANCE IN NDTE MULTIPLE MYELOMA

YONG K, ET AL. 2021, ASCO 8000

## STUDY POPULATION

> NDTE patients received 4 x Kcd induction before 1:1 randomization to ASCT or K maintenance

ASCT group: 100% received ASCT, 100% received K maintenance

K maintenance group: 100% received K maintenance, 100% received ASCT

ASCT group: 100% received ASCT, 100% received K maintenance

K maintenance group: 100% received K maintenance, 100% received ASCT

## PFS BY RANDOMIZATION ARM



# SUBGROUP ANALYSIS OF THE FORTE TRIAL: EFFICACY OF KRd ± ASCT AND K ± R MAINTENANCE IN HIGH-RISK PATIENTS

GAY F, ET AL. 2021, ASCO 8002 (EHA S182)

## STUDY POPULATION

> MM patients were randomized to KRd\_ASCT vs Kcd\_ASCT vs

## PFS OF KRd\_ASCT VS KRd12 VS Kcd\_ASCT

*[Faded text area containing study details]*



# RESULTS OF THE UK optimum/MUKnine TRIAL: ULTRA HIGH-RISK (UHiR) NDMM PATIENTS TREATED WITH DARA-CVRd

KAISER MF, ET AL. 2021, ASCO 8001 (EHA S181)

## STUDY POPULATION

> UHiR NDMM patients received Dara-CVRd, V-HD-MEL + ASCT,

## CENTRAL RESPONSE RESULTS

*[Blurred text area containing study details]*



# INTERIM ANALYSIS OF THE GMMG-CONCEPT TRIAL: FRONTLINE ISA-KRD IN HIGH-RISK MULTIPLE MYELOMA PATIENTS

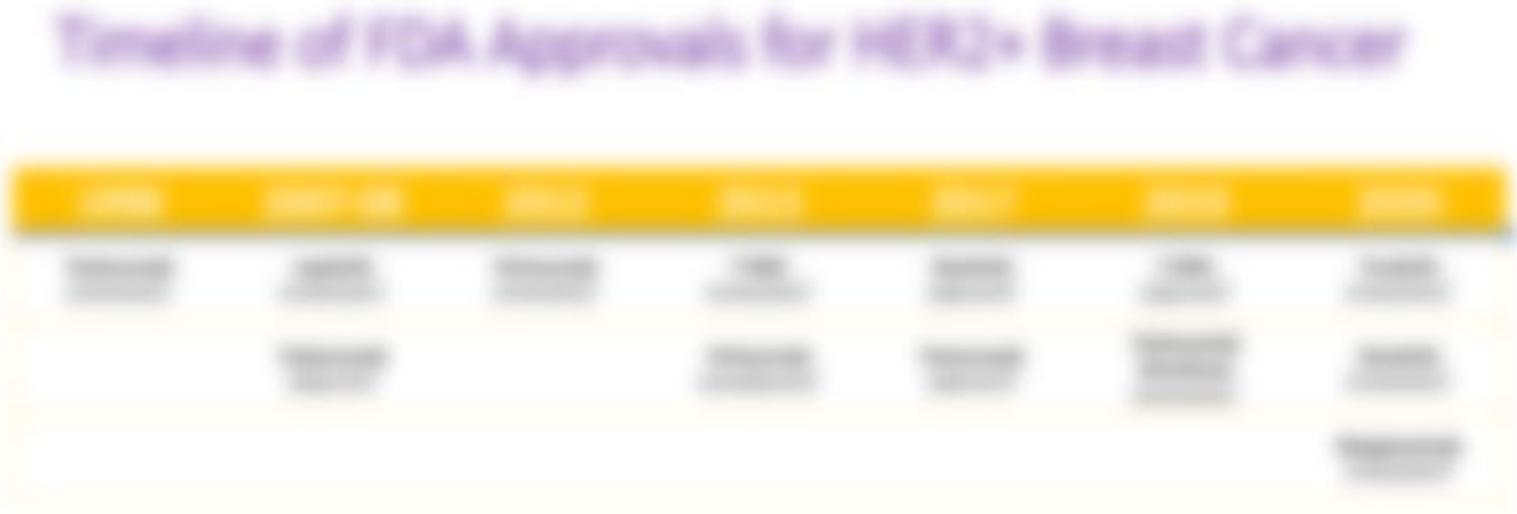
LEYPOLDT L, ET AL. 2021, EHA S183

## STUDY POPULATION

> HR NDMM patients received Isa-KRd, ASCT (TE patients; Arm A)

## PFS OF INTERIM ANALYSIS POPULATION (46 PATIENTS ARM A AND 4 PATIENTS ARM B)

*[Blurred text area containing study details]*





**EPICS**

**CONGRESS HIGHLIGHTS**  
**First Line (3): Maintenance and MRD**

# CASSIOPEIA PART 2: DARATUMUMAB MAINTENANCE AFTER VTd ± DARA AND ASCT IN NDMM PATIENTS

LEYPOLDT L, ET AL. 2021, ASCO 8004 (EHA S180)

## STUDY POPULATION

> TE NDMM patients were randomized to D-VTd or VTd (Part 1;

## PFS OF INDUCTION AND MAINTENANCE THERAPY RANDOMIZATION

*[Blurred text area containing study details]*



# FINAL ANALYSIS OF LYRA TRIAL: EFFICACY OF DARATUMUMAB IN COMBINATION WITH CyBORd AND AS MAINTENANCE THERAPY

RIFKIN R, ET AL. 2021, ASCO 8035 (EHA EP969)

## STUDY POPULATION

> Patients with MM and ≤1 prior line of therapy received induction

## EFFICACY OUTCOMES

*[Blurred text area containing study details]*



# RESULTS FROM BMT CTN 1302: MAINTENANCE IXAZOMIB AFTER alloHCT FOR HIGH-RISK MULTIPLE MYELOMA

NISHIHORI T, ET AL. 2021, ASCO 7003

## STUDY POPULATION

> Patients with HR MM received allogeneic HCT and were

## PFS AND OS POST-RANDOMIZATION

*[Blurred text area containing study details]*



# MRD EVALUATION DURING IXAZOMIB MAINTENANCE OF MM PATIENTS ENROLLED IN TOURMALINE-MM3 AND -MM4

PAIVE B, ET AL. 2021, EHA S184

## STUDY POPULATION

> MRD evaluation of patients from the TOURMALINE-MM3 AND

## PFS ACCORDING TO EVOLVING MRD KINETICS

*[Blurred text from a slide, likely containing study details and results.]*



# CIRCULATING TUMOR CELLS (CTC) AS A DIAGNOSTIC BIOMARKER IN TRANSPLANT-ELIGIBLE MULTIPLE MYELOMA

GARCÉS JJ, ET AL. 2021, EHA S185

## STUDY POPULATION

> CTCs in peripheral blood at diagnosis and MRD in BM were

## OPTIMAL CUTOFFS FOR RISK-STRATIFICATION USING CTCs

*[Blurred text from a slide, likely containing study details and results.]*



**EPICS**

**CONGRESS HIGHLIGHTS**  
**R/R MM: First and Second Relapse**

# FINAL ANALYSIS OF TOURMALINE-MM1: IRd VS PLACEBO-Rd IN RRMM PATIENTS

GARCÉS JJ, ET AL. 2021, EHA EP963

OS IN ITT POPULATION AND IN PATIENTS WITH HR

## STUDY POPULATION

1. 1000 patients with RRMM, 500 in each arm, were included in the ITT population. All patients were treated with Rd. The ITT population was defined as all patients who were included in the ITT population and who were treated with Rd. The ITT population was defined as all patients who were included in the ITT population and who were treated with Rd.

## RESULTS

1. OS in ITT population was significantly better in the IRd arm compared to the placebo-Rd arm. The median OS was 12.5 months in the IRd arm and 10.5 months in the placebo-Rd arm. The difference was statistically significant (p < 0.001).

## CONCLUSIONS

Continuing treatment with Rd for 24 months significantly improved OS in RRMM patients and decreased the proportion of patients with HR.

## OS IN ITT POPULATION AND IN PATIENTS WITH HR



## RESPONSE RATE AND OS IN PATIENTS WITH HR



# IXA-DEX VS POM-DEX IN LENALIDOMIDE-REFRACTORY, PI-EXPOSED MM PATIENTS

DIMOPOULOS M, ET AL. 2021, ASCO 8020

## STUDY POPULATION

1. 1000 patients with relapsed and/or refractory multiple myeloma (MM) who were refractory to lenalidomide (LEN) and/or proteasome inhibitors (PI) and had received at least one prior treatment with a proteasome inhibitor (PI) and/or LEN. The patients were randomized to receive either Ixazomib (IXA) or Pomalidomide (POM) in combination with dexamethasone (DEX). The primary endpoint was overall survival (OS) at 24 weeks. The secondary endpoint was progression-free survival (PFS) at 24 weeks. The study was conducted in a randomized, controlled, phase 3 setting.

## RESULTS

2. OS at 24 weeks was significantly higher in the IXA-DEX group compared to the POM-DEX group. PFS at 24 weeks was also significantly higher in the IXA-DEX group. The study was well-tolerated with no significant differences in adverse events between the two groups.

## KEY CONCLUSIONS

Combining ixazomib with dexamethasone (IXA-DEX) significantly improved overall survival (OS) and progression-free survival (PFS) compared to pomalidomide with dexamethasone (POM-DEX) in lenalidomide-refractory, proteasome inhibitor-exposed multiple myeloma patients.

## OS AT 24 WEEKS



## RESPONSE RATE AT 24 WEEKS



# DARIA TRIAL: SAFETY AND EFFICACY OF DARATUMUMAB + IXA-DEX IN RRMM PATIENTS AFTER FRONTLINE LENALIDOMIDE

TERPOS E, ET AL. 2021, EHA EP1014

## STUDY POPULATION

1. 1000 RRMM patients with a 1<sup>st</sup> relapse, who were treated with a 1<sup>st</sup> line of RRMM treatment, with a median time to relapse of 18 months. The patients were randomized to receive either daratumumab + ixazomib + dexamethasone (DAR+IXA+DEX) or lenalidomide + dexamethasone (LEN+DEX). The primary endpoint was overall survival (OS) at 24 weeks. The secondary endpoint was progression-free survival (PFS) at 24 weeks. The median OS was 18.5 months in the DAR+IXA+DEX group and 16.5 months in the LEN+DEX group. The median PFS was 10.5 months in the DAR+IXA+DEX group and 9.5 months in the LEN+DEX group.

## RESULTS

1. OS at 24 weeks was significantly higher in the DAR+IXA+DEX group compared to the LEN+DEX group (p < 0.001). The median OS was 18.5 months in the DAR+IXA+DEX group and 16.5 months in the LEN+DEX group.

## KEY CONCLUSIONS

Combining daratumumab with ixazomib and dexamethasone significantly improved overall survival and progression-free survival in RRMM patients after frontline lenalidomide.

## OS AT 24 WEEKS IN THE DAR+IXA+DEX GROUP



## RESPONSE RATE AT 24 WEEKS IN THE DAR+IXA+DEX GROUP



# BOSTON TRIAL SUBGROUP ANALYSIS: SURVIVAL AMONG OLDER PATIENTS TREATED WITH XVd

FACON T, ET AL. 2021, ASCO 8019 (EHA EP976)

## STUDY POPULATION

1. 1000 patients with MM, age ≥ 65, no prior systemic therapy, ECOG 0-1, performance grade 1-2, hemoglobin > 10g/dL, platelets > 100,000/mm<sup>3</sup>, creatinine < 2.0 mg/dL, and no active infections. Randomized to receive either 1000 mg of IVd or 1000 mg of IVd + 20 mg of oral dexamethasone daily. The primary endpoint was overall survival (OS) at 12 weeks. The secondary endpoint was OS at 24 weeks. OS was significantly improved in the 1000 mg IVd + 20 mg dexamethasone group (P = 0.001).

## RESULTS

1. OS at 12 weeks: 1000 mg IVd + 20 mg dexamethasone (n=500) vs 1000 mg IVd (n=500). OS at 24 weeks: 1000 mg IVd + 20 mg dexamethasone (n=500) vs 1000 mg IVd (n=500).

## KEY CONCLUSIONS

Combining dexamethasone with IVd significantly improved OS at 12 weeks and 24 weeks in older patients with MM.

## OS AT 12 WEEKS



## RESPONSE RATE AT 12 WEEKS



# UPDATES FROM ICARIA-MM: ISATUXIMAB AND LOW-DOSE Pd vs Pd IN RRMM

RICHARDSON P, ET AL. 2021, ASCO 8017 (EHA S186)

## STUDY POPULATION

1. 1000 patients with RRMM, 500 patients with a 100% response to Pd and 500 patients with a 100% response to Pd and low-dose Isatuximab. The study population was stratified by response to Pd and low-dose Isatuximab. The study population was stratified by response to Pd and low-dose Isatuximab. The study population was stratified by response to Pd and low-dose Isatuximab.

## RESULTS

1. 1000 patients with RRMM, 500 patients with a 100% response to Pd and 500 patients with a 100% response to Pd and low-dose Isatuximab. The study population was stratified by response to Pd and low-dose Isatuximab. The study population was stratified by response to Pd and low-dose Isatuximab.

## KEY CONCLUSIONS

1. 1000 patients with RRMM, 500 patients with a 100% response to Pd and 500 patients with a 100% response to Pd and low-dose Isatuximab. The study population was stratified by response to Pd and low-dose Isatuximab. The study population was stratified by response to Pd and low-dose Isatuximab.

## RESPONSE RATE OVER TIME IN THE STUDY



## RESPONSE RATE OVER TIME IN THE STUDY





**EPICS**

**CONGRESS HIGHLIGHTS**  
**Triple-Refractory R/R MM: Novel Agents**

# EFFECTS OF XVd (BOSTON TRIAL) AND Xd (STORM TRIAL) ON RAS-MUTATED RRMM

WALKER CJ, ET AL. 2021, ASCO 8027

## STUDY POPULATION

### STUDY POPULATION

1. 1000 patients with RRMM, 500 patients with RASmut, 500 patients with RASwt. All patients received 1000 mg of lenalidomide daily for 21 days, followed by 1000 mg of lenalidomide daily for 14 days. Patients were randomized to receive either 100 mg of Xd or 100 mg of XVd. The primary endpoint was overall survival (OS) at 24 weeks. Secondary endpoints included progression-free survival (PFS), time to next treatment (TTNT), and quality of life (QoL). The study was conducted in a multicenter, randomized, controlled, phase 3 setting.

### RESULTS

2. OS was significantly higher in the XVd group compared to the Xd group (p < 0.001). PFS was also significantly higher in the XVd group (p < 0.001). TTNT was significantly higher in the XVd group (p < 0.001). QoL was significantly higher in the XVd group (p < 0.001).

### KEY CONCLUSIONS

3. Combining lenalidomide with XVd significantly improved OS, PFS, TTNT, and QoL in RAS-mutated RRMM patients compared to Xd.

## PFS AND OS of RAS<sup>mut</sup> PATIENTS

PROGRESSION-FREE SURVIVAL (PFS) IN RAS<sup>MUT</sup> PATIENTS



OS IN RAS<sup>MUT</sup> PATIENTS











**EPICS**

**CONGRESS HIGHLIGHTS**  
**Triple-Refractory R/R MM: Antibodies**  
**and Bispecifics**

# LocoMMotion: NON-INTERVENTIONAL STUDY OF CURRENT STANDARDS OF CARE IN HEAVILY PRETREATED RRMM PATIENTS

MATEOS MV, ET AL. 2021, ASCO 8041

## STUDY POPULATION

**Study Population**

Patients with RRMM who had received ≥ 2 prior lines of systemic therapy for RRMM, including ≥ 1 prior line of treatment with a proteasome inhibitor, an immunomodulatory drug, and a thalidomide derivative.

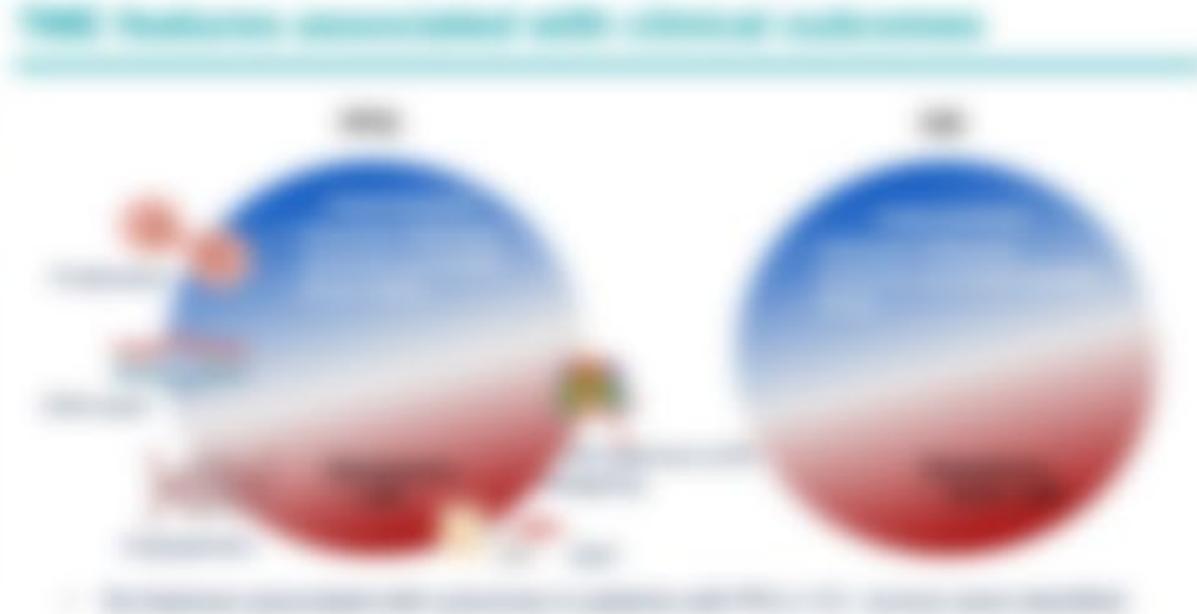
**Study Design**

Non-interventional study of current standards of care in heavily pretreated RRMM patients.

**Study Objectives**

To evaluate the efficacy and safety of current standards of care in heavily pretreated RRMM patients.

## EFFICACY BY SUBGROUPS



# EFFICACY AND SAFETY OF SUBCUTANEOUS ELRANATAMAB (PF-06863135), A BCMA × CD3 BISPECIFIC ANTIBODY, IN RRMM PATIENTS

BAHLIS NJ, ET AL. 2021, ASCO 8006 (EHA S192)

## STUDY POPULATION

**Study Population**

Patients with relapsed and refractory multiple myeloma (RRMM) who had received at least one prior systemic therapy for multiple myeloma and were ineligible for or had relapsed after autologous stem cell transplantation (ASCT).

**Study Design**

A phase 1b/2a study evaluating the efficacy and safety of subcutaneous (SC) elranatamab in RRMM patients. The study was conducted in a multicenter, open-label, phase 1b/2a design.

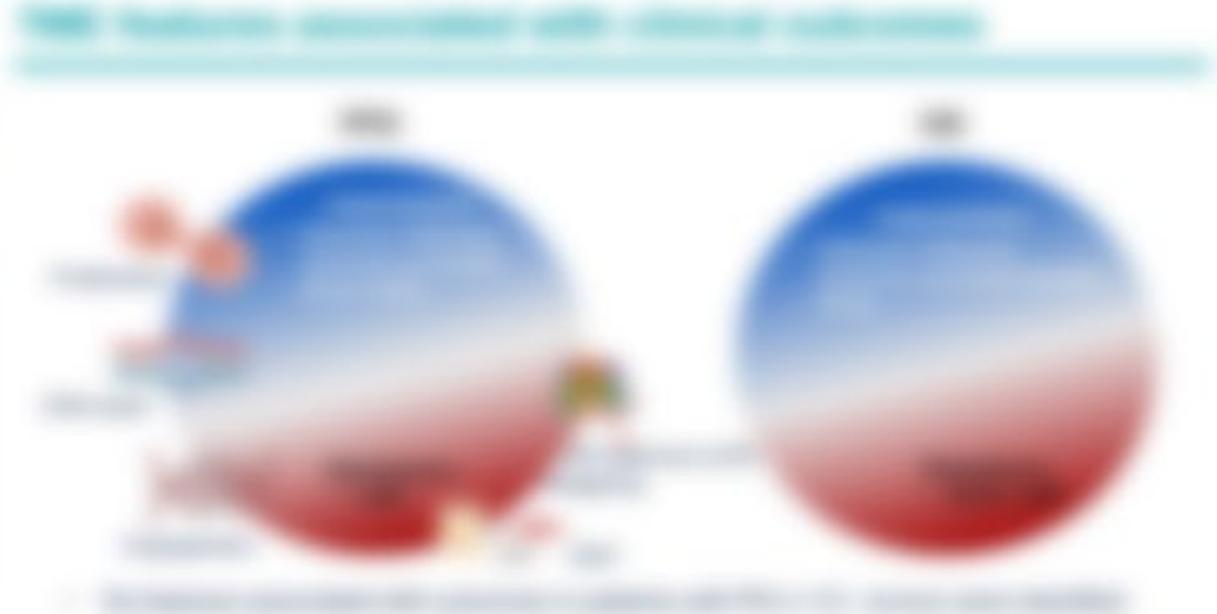
**Study Arms**

The study included two main arms: the SC elranatamab arm and the SC elranatamab plus SC daratumumab arm. The SC elranatamab arm included two sub-arms: the 100 mg SC elranatamab arm and the 200 mg SC elranatamab arm. The SC elranatamab plus SC daratumumab arm included two sub-arms: the 100 mg SC elranatamab plus 100 mg SC daratumumab arm and the 200 mg SC elranatamab plus 100 mg SC daratumumab arm.

**Study Endpoints**

The primary endpoint was the overall response rate (ORR) in the SC elranatamab plus SC daratumumab arm compared to the SC elranatamab arm. Secondary endpoints included progression-free survival (PFS), overall survival (OS), and safety.

## RESPONSE BY DOSING



# UPDATED RESULTS FOR TECLISTAMAB, BCMA × CD3 BISPECIFIC ANTIBODY IN RRMM

KRISHNAN AY, ET AL. 2021, ASCO 8007 (EHA S193)

## STUDY POPULATION

**Study Population**

Patients with relapsed and refractory multiple myeloma (RRMM) who had received at least one prior systemic therapy for multiple myeloma and were eligible for the study.

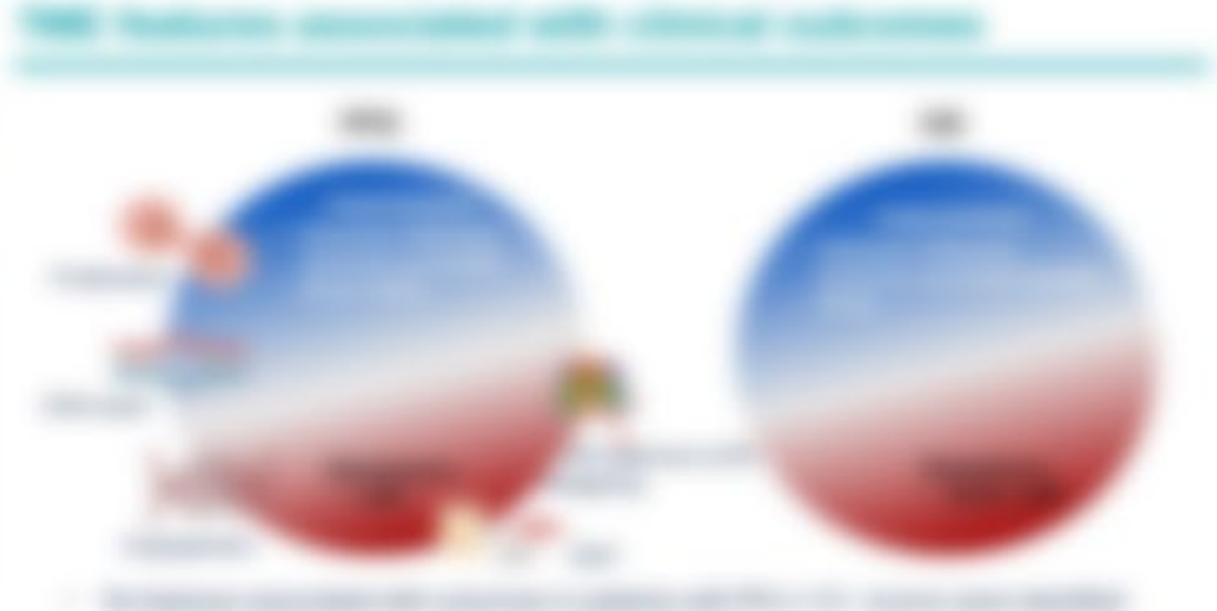
**Study Design**

A phase 1b/2 study evaluating the efficacy and safety of teclistamab in RRMM. The study was conducted in a multicenter, open-label, phase 1b/2 design.

**Study Population Characteristics**

The study population consisted of patients with RRMM who had received at least one prior systemic therapy for multiple myeloma. The median age was 70 years, and the majority of patients were male.

## ORR



**Key Findings**

The study demonstrated that teclistamab significantly improved the ORR in RRMM patients compared to the control group. The most common adverse events were related to the infusion of teclistamab, including fatigue, fever, and chills.

**Conclusion**

Teclistamab is a promising treatment option for RRMM, demonstrating a high ORR and manageable safety profile.

# UPDATED RESULTS OF TALQUETAMAB, A GPRC5D × CD3 BISPECIFIC ANTIBODY IN RRMM

BERDEJA JG, ET AL. 2021, ASCO 8008 (EHA S191)

## STUDY POPULATION

## ORR

**Study Population**

Patients with relapsed and refractory multiple myeloma (RRMM) who had received at least one prior systemic therapy for multiple myeloma and were ineligible for autologous stem cell transplant (ASCT) or had relapsed within 6 months of ASCT.

**Study Design**

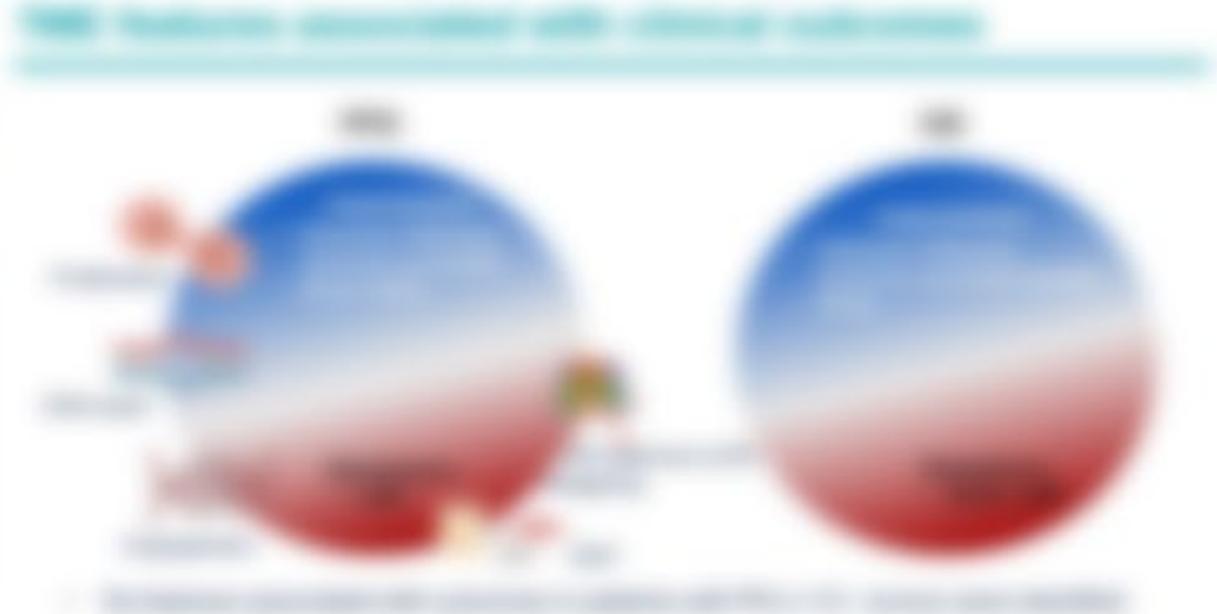
A phase 1b/2 study evaluating the efficacy and safety of talquetamab in RRMM. The study was conducted in a multicenter, open-label, phase 1b/2 design. Patients were randomized to receive talquetamab or a placebo.

**Primary Endpoints**

The primary endpoint was overall response rate (ORR), defined as the percentage of patients achieving a partial response (PR) or better.

**Secondary Endpoints**

Secondary endpoints included progression-free survival (PFS), overall survival (OS), and safety.



**Key Findings**

The study demonstrated that talquetamab significantly improved ORR compared to placebo in RRMM patients. The ORR was significantly higher in the talquetamab group, indicating a higher percentage of patients achieving a partial response or better.

**Conclusion**

Talquetamab is a promising treatment for RRMM, showing significant efficacy in improving ORR compared to placebo.

**EPICS**

**CONGRESS HIGHLIGHTS**  
**Triple-Refractory R/R MM: CAR Ts**

# UPDATED RESULTS FROM KarMMa: IDECABTAGENE VICLEUCEL (IDEC-CEL, BB2121), A BCMA-DIRECTED CAR T CELL THERAPY IN RRMM

ANDERSON LD, ET AL. 2021, ASCO 8016 (EHA EP1009)

## STUDY POPULATION

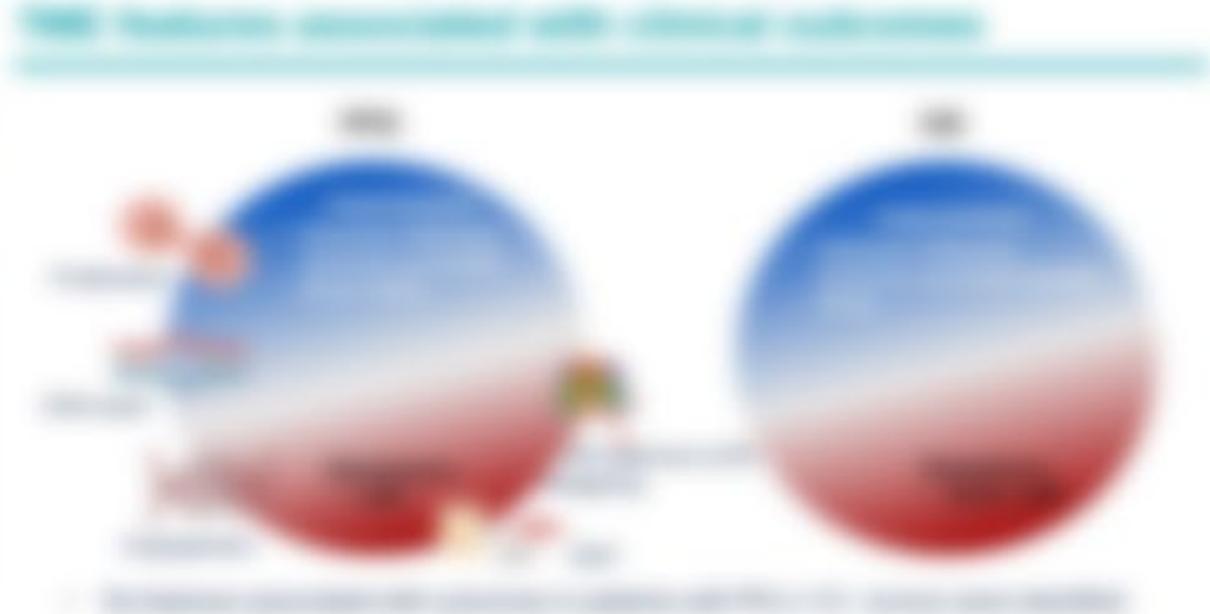
**Study Population**

Patients with relapsed and/or refractory multiple myeloma (RRMM) who had received at least one prior systemic therapy and were eligible for the study.

**Key Characteristics:**

- Median age: 70 years
- Median time from diagnosis to first relapse: 1.5 years
- Median time from first relapse to study entry: 1.5 years
- Median number of prior systemic therapies: 2
- Median number of prior autologous stem cell transplant (ASCT): 1
- Median number of prior bortezomib treatments: 1
- Median number of prior lenalidomide treatments: 1
- Median number of prior daratumumab treatments: 1

## RESPONSE RATES



# UPDATED RESULTS FROM CARTITUDE-1: CILTACABTAGENE AUTOLEUCEL, A BCMA-DIRECTED CAR T-CELL THERAPY IN RRMM

USMANI SZ, ET AL. 2021, ASCO 8005 (EHA EP964)

## STUDY POPULATION

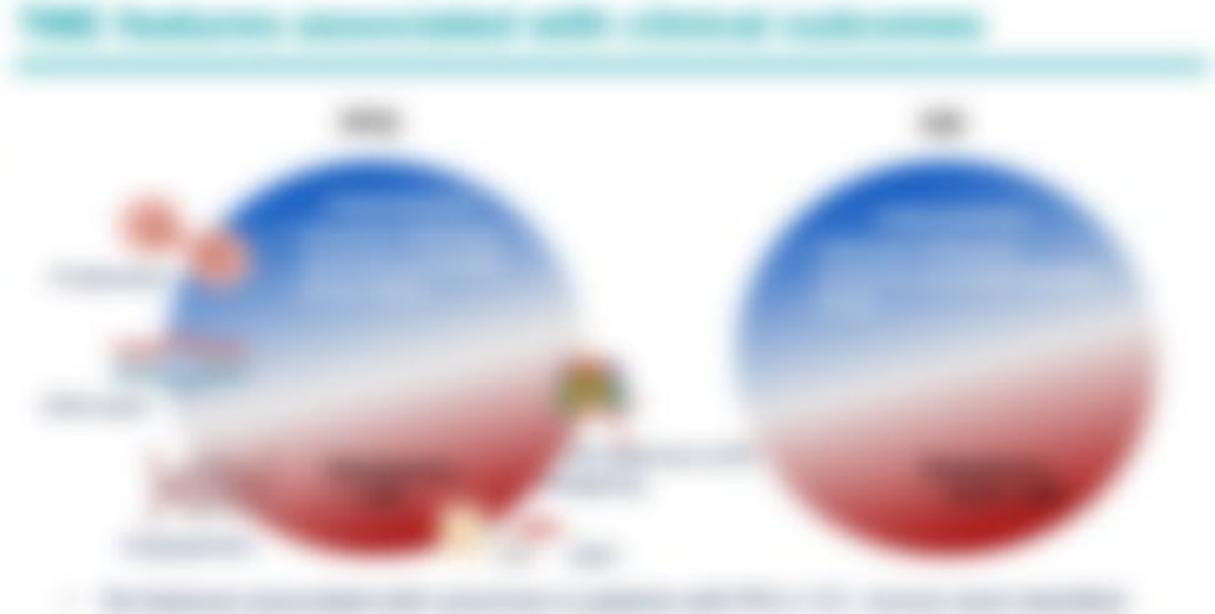
**Study Population**

Patients with relapsed and/or refractory multiple myeloma (RRMM) who had received at least one prior systemic therapy and were eligible for CARTITUDE-1.

**Key Characteristics:**

- Median age: 67 years
- Median duration of disease: 4.5 years
- Median number of prior systemic therapies: 3
- Median time to progression: 12.5 months

## PFS



# CILTA-CEL VERSUS CONVENTIONAL TREATMENT IN PATIENTS WITH RELAPSE/REFRACTORY MULTIPLE MYELOMA

COSTA LJ, ET AL. 2021, ASCO 8030

## STUDY POPULATION

**Study Population**

Patients with relapsed/refractory multiple myeloma (RRMM) who had received at least one prior systemic therapy for RRMM and were eligible for the study.

**Study Design**

A phase III, randomized, controlled trial comparing cilta-cel to a conventional treatment (dexamethasone, lenalidomide, and bortezomib [DLB2]).

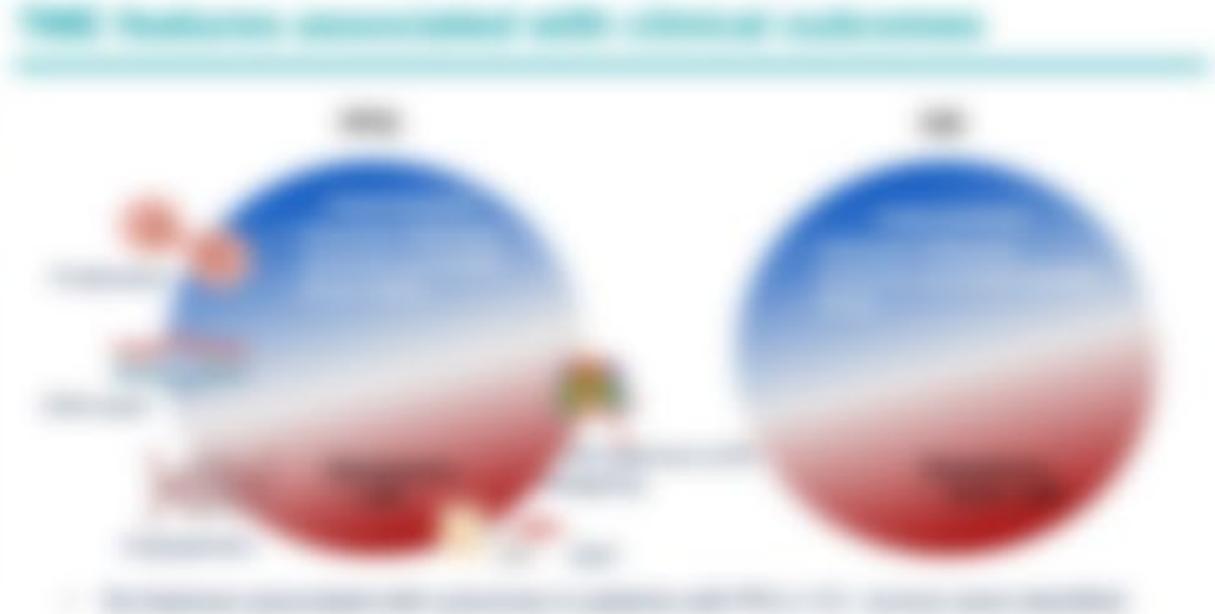
**Primary Endpoints**

The primary endpoint was overall survival (OS), defined as the time from random assignment to death due to any cause.

**Secondary Endpoints**

Secondary endpoints included progression-free survival (PFS), time to next treatment (TTNT), and quality of life (QoL).

## EFFICACY RATES



# CARTITUDE-2: EFFICACY AND SAFETY OF CILTACABTAGENE AUTOLEUCEL IN PATIENTS WITH 1-3 PRIOR LINES OF THERAPY

USMANI SZ, ET AL. 2021, ASCO 8005 (EHA EP964)

## STUDY POPULATION

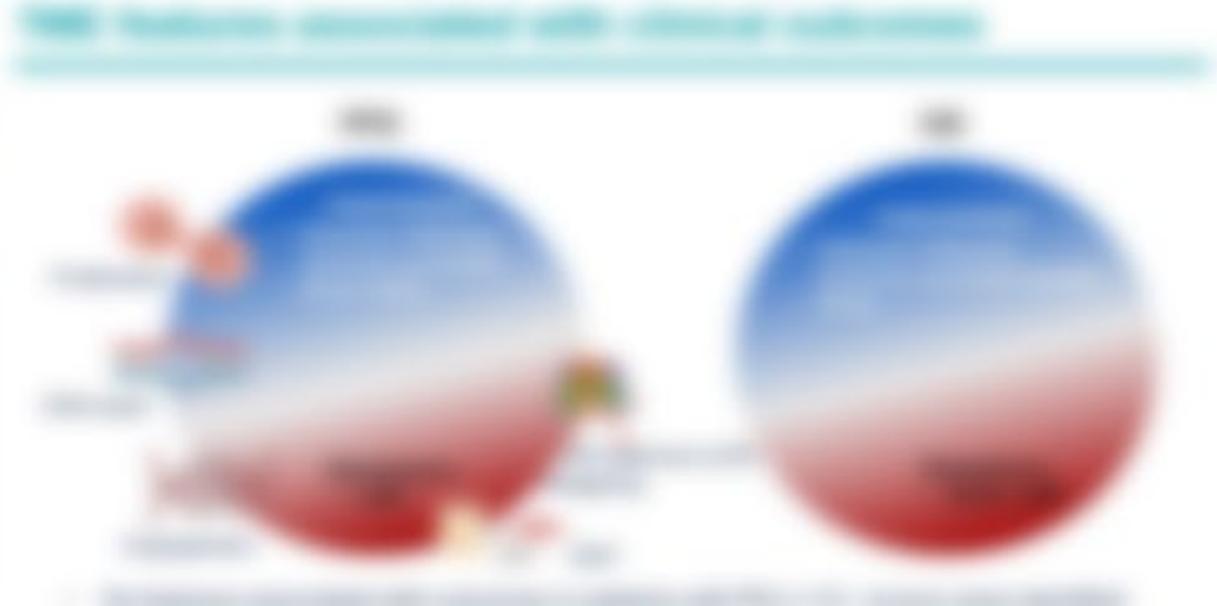
**Study Population**

Patients with relapsed and/or refractory multiple myeloma (RRMM) who had received 1-3 prior lines of therapy (including bortezomib, lenalidomide, and thalidomide) and were eligible for autologous stem cell transplant (ASCT) were enrolled in the study. The study population was divided into two groups: the Ciltacabtagene group and the Control group.

**Key Characteristics:**

- Median age: 67 years
- Median time from last prior therapy to study entry: 12.5 months
- Median number of prior lines of therapy: 2
- Median time from diagnosis to study entry: 48.5 months

## DURATION OF RESPONSE



**Conclusion**

The results of the CARTITUDE-2 study demonstrate that Ciltacabtagene autoleucel significantly improves the duration of response compared to the control group in patients with relapsed and/or refractory multiple myeloma who have received 1-3 prior lines of therapy. This finding supports the use of Ciltacabtagene as a treatment option for this patient population.



**EPICS**

**KEY INSIGHTS**

## SMOLDERING MULTIPLE MYELOMA

**KEY TAKEAWAYS**

The majority of patients with smoldering multiple myeloma (SMM) will never progress to multiple myeloma (MM) and will not require systemic therapy. However, a subset of patients will progress to MM, and the timing of progression is highly variable. The majority of patients with SMM will die of causes unrelated to their myeloma, such as cardiovascular disease or infection. Therefore, the primary goal of management for SMM is to optimize overall health and quality of life, rather than to delay or prevent progression to MM.

**CLINICAL RECOMMENDATIONS**

Although the majority of patients with SMM will never progress to MM, the risk of progression is higher in certain subgroups. These include patients with high levels of monoclonal protein, abnormal free light chain ratios, or other markers of disease activity. For these patients, closer monitoring and consideration of early treatment may be warranted. However, for the majority of patients, the focus should be on maintaining good overall health, managing comorbidities, and ensuring access to supportive care services such as pain management and physical therapy.



**CONCLUSION**

Smoldering multiple myeloma is a complex condition with a wide range of outcomes. While many patients will never progress to multiple myeloma, others will. The key to successful management is individualized care that focuses on overall health and quality of life, rather than solely on delaying progression to multiple myeloma.

# KEY INSIGHTS: TRANSPLANT-INELIGIBLE MULTIPLE MYELOMA

## TRANSPLANT-INELIGIBLE MULTIPLE MYELOMA

**KEY INSIGHTS**

The majority of patients with multiple myeloma are not eligible for transplant due to age, comorbidities, or performance. This group represents a significant unmet need for effective treatment options.

Key findings include:

- High rates of relapse and progression.
- Limited options for second-line and subsequent therapy.
- Significant impact on quality of life and healthcare costs.

**CLINICAL IMPLICATIONS**

Understanding the unique challenges of this patient population is essential for developing targeted therapies and supportive care strategies. Key areas for focus include:

- Improving patient selection for transplant.
- Developing novel agents for relapsed and refractory disease.
- Enhancing supportive care to manage symptoms and improve quality of life.



# KEY INSIGHTS: INDUCTION IN TRANSPLANT-ELIGIBLE MULTIPLE MYELOMA

## EARLY VS DELAYED TRANSPLANT

**KEY TAKEAWAYS**

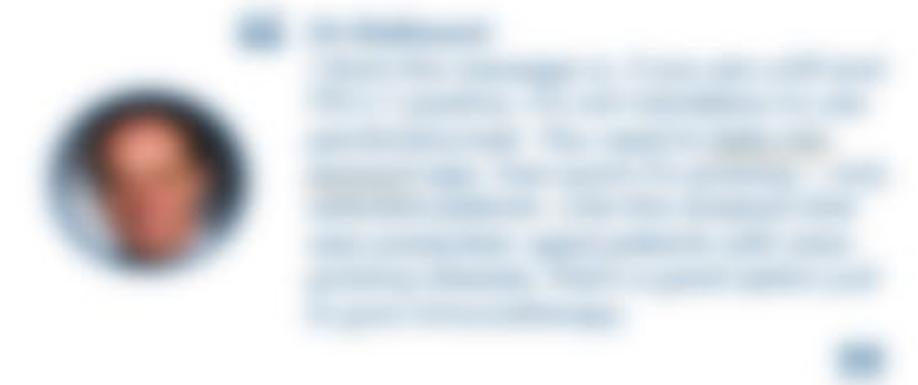
The majority of patients with multiple myeloma are not eligible for transplant at diagnosis. For those who are, the timing of transplant is a critical decision. Early transplant (within 6-12 months of diagnosis) is associated with improved overall survival compared to delayed transplant (more than 12 months after diagnosis).

Key factors influencing the decision include patient performance, organ function, and the availability of transplant services. Early transplant may also allow for the use of newer, more effective induction regimens.

**CLINICAL EVIDENCE**

Several clinical trials have compared early versus delayed transplant in transplant-eligible multiple myeloma patients. The most significant findings include:

- Overall Survival:** Patients who received transplant within 6-12 months of diagnosis had significantly better overall survival compared to those who received transplant more than 12 months after diagnosis.
- Quality of Life:** Early transplant was associated with improved quality of life, including less fatigue and better performance.
- Response Rates:** Early transplant was associated with higher response rates to induction therapy.



## MAINTENANCE THERAPY

**KEY INSIGHTS: MAINTENANCE THERAPY**

The majority of patients on maintenance therapy are on long-term treatment, with a significant portion of patients on maintenance therapy for more than 10 years. This indicates a high level of patient adherence and a strong commitment to their treatment plan.

Patients on maintenance therapy are more likely to be on multiple medications, suggesting a complex medical history and a need for comprehensive management. This highlights the importance of coordinated care and regular monitoring for these patients.

**KEY INSIGHTS: MAINTENANCE THERAPY**

Patients on maintenance therapy are more likely to be on long-term treatment, with a significant portion of patients on maintenance therapy for more than 10 years. This indicates a high level of patient adherence and a strong commitment to their treatment plan.

Patients on maintenance therapy are more likely to be on multiple medications, suggesting a complex medical history and a need for comprehensive management. This highlights the importance of coordinated care and regular monitoring for these patients.



**KEY INSIGHTS: MAINTENANCE THERAPY**

The majority of patients on maintenance therapy are on long-term treatment, with a significant portion of patients on maintenance therapy for more than 10 years. This indicates a high level of patient adherence and a strong commitment to their treatment plan.

Recommendations for high-risk patients

# KEY INSIGHTS: MRD AND PROGNOSTIC FACTORS

## MRD AND PROGNOSTIC FACTORS

**KEY INSIGHTS: MRD AND PROGNOSTIC FACTORS**

The presence of MRD is a strong predictor of relapse and overall survival in patients with acute leukemia. MRD levels are measured using highly sensitive techniques such as flow cytometry and next-generation sequencing (NGS). High levels of MRD at the end of induction therapy are associated with a higher risk of relapse and shorter overall survival. Conversely, achieving MRD negativity is associated with a lower risk of relapse and longer overall survival.

**KEY INSIGHTS: MRD AND PROGNOSTIC FACTORS**

MRD levels are also used to guide treatment decisions. Patients with high levels of MRD may benefit from more intensive therapy, such as allogeneic stem cell transplantation. Patients with low levels of MRD may benefit from less intensive therapy, such as consolidation chemotherapy. MRD levels are also used to monitor response to therapy and to detect relapse early.



**KEY INSIGHTS: MRD AND PROGNOSTIC FACTORS**

MRD levels are also used to guide treatment decisions. Patients with high levels of MRD may benefit from more intensive therapy, such as allogeneic stem cell transplantation. Patients with low levels of MRD may benefit from less intensive therapy, such as consolidation chemotherapy. MRD levels are also used to monitor response to therapy and to detect relapse early.

# KEY INSIGHTS: R/R MM – FIRST AND SECOND RELAPSE

## FIRST AND SECOND RELAPSE

**KEY INSIGHTS: R/R MM – FIRST AND SECOND RELAPSE**

The majority of patients with relapsed multiple myeloma (R/R MM) are diagnosed with relapsed disease within 18 months of their first diagnosis. The median time to relapse is approximately 18 months, with a range from 6 to 36 months. The majority of patients with relapsed disease are diagnosed with relapsed disease within 18 months of their first diagnosis. The median time to relapse is approximately 18 months, with a range from 6 to 36 months.

**KEY INSIGHTS: R/R MM – FIRST AND SECOND RELAPSE**

Approximately 20% of patients with relapsed multiple myeloma (R/R MM) are diagnosed with relapsed disease within 6 months of their first diagnosis. The median time to relapse is approximately 18 months, with a range from 6 to 36 months. The majority of patients with relapsed disease are diagnosed with relapsed disease within 18 months of their first diagnosis. The median time to relapse is approximately 18 months, with a range from 6 to 36 months.



**KEY INSIGHTS: R/R MM – FIRST AND SECOND RELAPSE**

The majority of patients with relapsed multiple myeloma (R/R MM) are diagnosed with relapsed disease within 18 months of their first diagnosis. The median time to relapse is approximately 18 months, with a range from 6 to 36 months. The majority of patients with relapsed disease are diagnosed with relapsed disease within 18 months of their first diagnosis. The median time to relapse is approximately 18 months, with a range from 6 to 36 months.

# KEY INSIGHTS: TRIPLE-REFRACTORY R/R MM – NOVEL AGENTS

## NOVEL THERAPIES

**PROTEASOMES** (e.g., IMiD, Pomalidomide, Carfilzomib)  
The proteasome is a large protein complex that is involved in the degradation of proteins. In multiple myeloma, the proteasome is overactive, leading to the production of abnormal antibodies. Proteasome inhibitors block the proteasome, preventing the production of these antibodies and allowing the body's immune system to fight the cancer cells.

**CD38** (e.g., Monoclonal antibodies like Daratumumab)  
CD38 is a cell surface protein that is overexpressed on multiple myeloma cells. Monoclonal antibodies like daratumumab target CD38, leading to the destruction of the cancer cells and the inhibition of their growth.



**CD38**  
CD38 is a cell surface protein that is overexpressed on multiple myeloma cells. Monoclonal antibodies like daratumumab target CD38, leading to the destruction of the cancer cells and the inhibition of their growth.

# KEY INSIGHTS: TRIPLE-REFRACTORY R/R MM – ANTIBODIES AND BISPECIFICS

## ANTIBODIES AND BISPECIFIC AGENTS

**KEY INSIGHTS: TRIPLE-REFRACTORY R/R MM – ANTIBODIES AND BISPECIFICS**

The landscape of multiple myeloma (MM) treatment is rapidly evolving, with a focus on addressing triple-refractory relapsed and refractory (R/R) MM. This section highlights the role of antibodies and bispecific agents in this challenging patient population.

Key insights include:

- The emergence of novel antibody-based therapies, such as monoclonal antibodies and antibody-drug conjugates (ADCs), offering improved efficacy and safety profiles.
- The development of bispecific antibodies (BsAbs) that target multiple myeloma antigens, potentially overcoming drug resistance and enhancing anti-tumor activity.
- The importance of clinical trial design and patient selection in evaluating these novel agents, particularly in the R/R MM setting.

**KEY INSIGHTS: TRIPLE-REFRACTORY R/R MM – ANTIBODIES AND BISPECIFICS**

Despite the challenges of R/R MM, significant progress has been made in the development of novel antibody-based therapies. These include:

- **Monoclonal Antibodies (mAbs):** These agents target specific cell surface receptors and signaling pathways, leading to tumor cell death or inhibition of growth.
- **Antibody-Drug Conjugates (ADCs):** These agents combine the specificity of antibodies with the cytotoxicity of drugs, allowing for targeted delivery of chemotherapy to tumor cells.
- **Bispecific Antibodies (BsAbs):** These agents target two different antigens, potentially overcoming drug resistance and enhancing anti-tumor activity.

Key insights include:

- The importance of clinical trial design and patient selection in evaluating these novel agents, particularly in the R/R MM setting.
- The need for continued research and development to optimize the efficacy and safety of these therapies.



**KEY INSIGHTS: TRIPLE-REFRACTORY R/R MM – ANTIBODIES AND BISPECIFICS**

This section provides a detailed overview of the clinical trial results and patient outcomes for the novel antibody-based therapies and bispecific agents discussed in the previous sections. Key findings include:

- Improved overall survival (OS) and progression-free survival (PFS) compared to standard of care (SOC) in the R/R MM setting.
- Favorable safety profiles, with manageable adverse events.
- The potential for combination therapy with existing treatments to further improve outcomes.



# KEY INSIGHTS: TRIPLE-REFRACTORY R/R MM – CAR TS

## CAR Ts

**KEY TAKEAWAYS**

The majority of CAR T cells are CD19 targeted, with CD19 CAR T cells showing the highest response rates. CD19 CAR T cells are the most commonly used CAR T cell product, with a response rate of approximately 40% in patients with relapsed and refractory multiple myeloma. CD19 CAR T cells are also being evaluated in combination with other therapies, such as proteasome inhibitors and immunomodulatory drugs, to improve outcomes.

**CLINICAL TRIALS**

Several clinical trials are currently evaluating CAR T cell therapy in patients with relapsed and refractory multiple myeloma. The most advanced trial is the phase 1/2 study of CD19 CAR T cells (NCT02703895), which has shown promising results. Other trials are evaluating CD19 CAR T cells in combination with other therapies, such as proteasome inhibitors and immunomodulatory drugs, to improve outcomes.



**CONCLUSION**

CAR T cell therapy represents a significant advancement in the treatment of relapsed and refractory multiple myeloma. CD19 CAR T cells are the most commonly used CAR T cell product, with a response rate of approximately 40% in patients with relapsed and refractory multiple myeloma. Further research is needed to optimize CAR T cell therapy and improve outcomes for patients with relapsed and refractory multiple myeloma.