



**EPICS**

# **CONGRESS COVERAGE: ASH 2020 – FOCUS ON MULTIPLE MYELOMA**

Friday, December 11, 2020

**FULL REPORT**

# FACULTY EXPERTS

EPICS



**Chair**  
Rafael Fonseca, MD  
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Philippe Moreau, MD  
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Suzanne Lentzsch, MD, PhD  
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Keith Stewart, MB, ChB, MBA  
Princess Margaret Cancer Centre  
Toronto, ON, Canada



Peter Voorhees, MD  
Levine Cancer Institute  
Charlotte, NC

Time (EST)	Topic	Presenter
10.00 AM – 10.05 AM (5 min)	Welcome and Introductions	Rafael Fonseca, MD
10.05 AM – 10.15 AM (10 min)	First Line (1): Smoldering and Transplant-Ineligible Multiple Myeloma	Irene Ghobrial, MD
10.15 AM – 10.25 AM (10 min)	Discussion	Moderator: Rafael Fonseca, MD
10.25 AM – 10.30 AM (5 min)	Key Takeaways	
10.30 AM – 10.40 AM (10 min)	First Line (2): Induction in Transplant-Eligible Multiple Myeloma	Peter Voorhees, MD
10.40 AM – 10.55 AM (15 min)	Discussion	Moderator: Rafael Fonseca, MD
10.55 AM – 11.00 AM (5 min)	Key Takeaways	
11.00 AM – 11.10 AM (10 min)	First Line (3): Maintenance and Prognosis	Keith Stewart, MB, ChB, MBA
11.10 AM – 11.25 AM (15 min)	Discussion	Moderator: Rafael Fonseca, MD
11.25 AM – 11.30 AM (5 min)	Key Takeaways	
11.30 AM – 11.35 AM (5 min)	<i>Break</i>	
11.35 AM – 11.45 AM (10 min)	Relapsed/Refractory: Small Molecules	Suzanne Lentzsch, MD, PhD
11.45 AM – 12.00 PM (15 min)	Discussion	Moderator: Rafael Fonseca, MD
12.00 PM – 12.05 PM (5 min)	Key Takeaways	
12.05 PM – 12.15 PM (10 min)	Relapsed/Refractory: Antibodies	Philippe Moreau, MD
12.15 PM – 12.25 PM (10 min)	Discussion	Moderator: Rafael Fonseca, MD
12.25 PM – 12.30 PM (5 min)	Key Takeaways	
12.30 PM – 12.40 PM (10 min)	Relapsed/Refractory: CAR Ts	Sagar Lonial, MD, FACP
12.40 PM – 12.50 PM (10 min)	Discussion	Moderator: Rafael Fonseca, MD
12.50 PM – 12.55 PM (5 min)	Key Takeaways	
12.55 PM – 1.00 PM (5 min)	Summary and Closing Remarks	Rafael Fonseca, MD

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

# Abstract 57: Longitudinal Immunogenomic Profiling of Tumor and Immune Cells for Minimally-Invasive Monitoring of Smoldering Multiple Myeloma (SMM): The Immunocell Study.

R. Termini, et al

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## Background

- > Most current models to predict risk of transformation in SMM are commonly established at diagnosis and not reevaluated over time,

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## Abstract 57: Longitudinal Immunogenomic Profiling of Tumor and Immune Cells for Minimally-Invasive Monitoring of Smoldering Multiple Myeloma (SMM): The Immunocell Study.

R. Termini, et al (cont.)

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### Results (contd)

- > In addition to the 150 PB samples analyzed at baseline, another 139 specimens were processed at 6, 12, and 18 mo. The fluctuation

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# Abstract 548: Treatment of High Risk (HR) Smoldering Multiple Myeloma (SMM) With Carfilzomib, Lenalidomide, and Dexamethasone (KRd) Followed by Lenalidomide Maintenance (-R): A Phase 2 Clinical and Correlative Study. D. Kazandjian, et al

## Background

- > High-risk SMM is a plasma cell disorder with a 5-yr risk of progression to symptomatic MM of ~75% without therapy. Early treatment

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**Abstract 548: Treatment of High Risk (HR) Smoldering Multiple Myeloma (SMM) With Carfilzomib, Lenalidomide, and Dexamethasone (KRd) Followed by Lenalidomide Maintenance (-R): A Phase 2 Clinical and Correlative Study. D. Kazandjian, et al (cont.)**

**Results (cont.)**

- > Grade 3–4 toxicities occurring in >1 patient included neutropenia (19%), lymphopenia (13%), thromboembolism (12%), anemia (8%),

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# Abstract 551: The Phase 3 TOURMALINE-MM2 Trial: Oral Ixazomib, Lenalidomide, and Dexamethasone (IRd) vs Placebo-Rd for Transplant-Ineligible Patients With Newly Diagnosed Multiple Myeloma (NDMM). T. Facon, et al

## Background

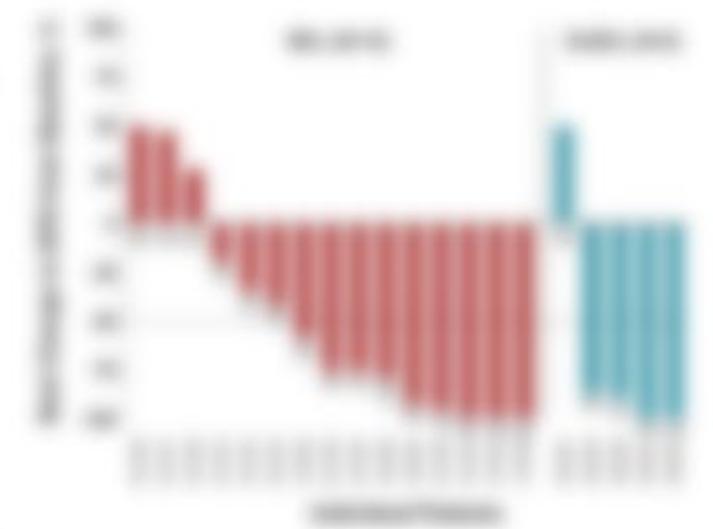
- > Continuous Rd-based regimens are among the standards of care in

## Background

- Phase 3, open-label, randomized study of IRd (IRd) vs Rd (Rd) in patients with newly diagnosed NDMM and DLMM.
- Primary objective was to assess outcomes of IRd and recommended dosing regimen.

## Results

- 22 patients were enrolled, including 10 patients with NDMM.
- DLMM were 100% (n=10) and 100% (n=10).
- DLMM occurred in 20% of patients, 100% (n=10) in IRd group.
- DLMM occurred in 10% of patients, 100% (n=10) in Rd group.
- DLMM was 100% (n=10), 100% (n=10) in IRd group and 100% (n=10), 100% (n=10) in Rd group.
- 8 responding patients have ongoing responses ranging from 20 weeks to 58 weeks.



**Key takeaway:** IRd demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced NDMM and DLMM. Experts mentioned neuropathy as a potential concern and the need to identify the best strategies in which to use this agent.

# Abstract 551: The Phase 3 TOURMALINE-MM2 Trial: Oral Ixazomib, Lenalidomide, and Dexamethasone (IRd) vs Placebo-Rd for Transplant-ineligible Patients With Newly Diagnosed Multiple Myeloma (NDMM). T. Facon, et al (cont'd).

## Results (cont.)

> Median overall survival (OS) was not reached in either arm (HR 0.998) after a median follow-up of ~58 mo and with 136 and 148

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# FIRST LINE (1): SMOLDERING AND TRANSPLANT-INELIGIBLE MULTIPLE MYELOMA – DISCUSSION (1/2)

## Management of SMM

> Experts agreed that improvements are needed to identify high-risk SMM patients

### Background

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### Goals

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# FIRST LINE (1): SMOLDERING AND TRANSPLANT-INELIGIBLE MULTIPLE MYELOMA – DISCUSSION (2/2)

## Management of transplant-ineligible patients

> Some experts reported using DARA-Rd for most older, transplant-ineligible patients, especially after the

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

# Abstract 141: Survival Analysis of Newly Diagnosed Transplant-Eligible Multiple Myeloma Patients in the Randomized Forte Trial. F. Gay, et al

## Background

- > PI-based induction/consolidation proved to be effective in NDMM patients eligible for melphalan 200 mg/m<sup>2</sup> plus ASCT (MEL200-ASCT). High response rates have been reported with carfilzomib plus lenalidomide, doxorubicin (Kd) or cyclophosphamide, doxorubicin (Cd).

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**Abstract 142: Upfront Autologous Hematopoietic Stem-Cell Transplantation Improves Overall Survival in Comparison With Bortezomib-Based Intensification Therapy in Newly Diagnosed Multiple Myeloma: Long-term Follow-up Analysis of the Randomized Phase 3 EMN02/HO95 Study.**  
**M. Cavo, et al**

**Background**

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# Abstract 143: Early Versus Late Autologous Stem Cell Transplant in Newly Diagnosed Multiple Myeloma: Long-term Follow-up Analysis of the IFM 2009 Trial. A. Perrot, et al

## Background

- > The IFM 2009 study prospectively evaluated the combination of 8 cycles of lenalidomide, bortezomib, and dexamethasone (RVd) vs 3 cycles of RVd plus

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# Abstract 144: A Prospective Phase 2 Study to Assess Minimal Residual Disease After Ixazomib, Lenalidomide and Dexamethasone Treatment for Newly Diagnosed Transplant Eligible Multiple Myeloma Patients. R. Silvennoinen, et al

**Background:**

- 1. Minimal Residual Disease (MRD) is a prognostic factor in Multiple Myeloma (MM).
- 2. Ixazomib, Lenalidomide and Dexamethasone (iLd) is a standard treatment for newly diagnosed MM.
- 3. The aim of this study is to assess MRD after iLd treatment.

**Methods:**

- 1. This is a prospective phase 2 study.
- 2. Patients are newly diagnosed MM, transplant eligible.
- 3. Patients are treated with iLd.
- 4. MRD is assessed by flow cytometry.
- 5. The primary endpoint is the percentage of patients achieving MRD.
- 6. Secondary endpoints include overall survival, progression-free survival, and adverse events.
- 7. The study is ongoing.

Parameter	Value
Number of patients	100
MRD positive patients	75
MRD negative patients	25
Median overall survival (months)	36
Median progression-free survival (months)	24
Adverse events (grade 3/4)	15%

This abstract is a summary of the study and does not constitute a recommendation. The results of this study are preliminary and should be interpreted with caution. The study is ongoing and the results may change.

# FIRST LINE (2): INDUCTION IN TRANSPLANT-ELIGIBLE MULTIPLE MYELOMA – DISCUSSION (1/2)

## Goals of frontline therapy

- > Many experts believe SCT currently remains the SOC for treatment of MM. citing PFS data from the FORTE.

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# FIRST LINE (2): INDUCTION IN TRANSPLANT-ELIGIBLE MULTIPLE MYELOMA – DISCUSSION (2/2)

## Differentiating therapeutic options

- > Many experts are impressed with the use of carfilzomib upfront for transplant-eligible patients

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**First Line (3): Maintenance  
and Prognosis**



# Abstract 550: Consolidation Treatment With VRD Followed by Maintenance Therapy Versus Maintenance Alone in Newly Diagnosed, Transplant-Eligible Patients With Multiple Myeloma (MM): A Randomized Phase 3 Trial of the European Myeloma Network (EMN02/HO95).

P. Sonneveld, et al

## Background

> The role of consolidation treatment for transplant-eligible

### Background

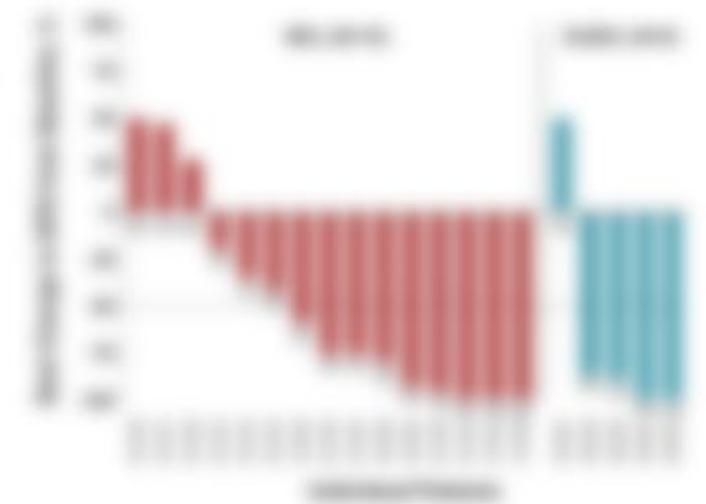
- Phase 3 randomized controlled study of VRD (VRD) vs VRD followed by maintenance (VRD+M) in patients with newly diagnosed MM, and SM-MM.
- Primary objective was to define subgroups of MM and SM-MM benefiting most from VRD+M.

### Results

- 22 patients were enrolled, including 10 patients with MM.
- 10/22 were SM-multiplemyeloma and 12/22 SM-MM.
- 10/22 multiplemyeloma occurred in 20% of patients, 10/22 SM-MM occurred in 20% of patients.
- Overall response rate (ORR) was 47% (20/42), 47% for MM, 47% for SM-MM, and 47% for SM-MM, with 10/22 patients having ongoing responses ranging from 20 weeks to 58 weeks.

## Results

Progression free survival



**Key findings:** VRD+M demonstrated a comparable and potentially better safety profile and encouraging efficacy, with durable responses in advanced MM, and SM-MM. Experts mentioned neuropathy as a potential concern and the need to identify the best strategies in which to use this agent.

# Abstract 61: High-Dose Melphalan Significantly Increases Mutational Burden in Multiple Myeloma Cells at Relapse: Results From a Randomized Study in Multiple Myeloma. M. Samur, et al



## Background

> HDM followed by ASCT as first-line therapy in young (<66 yr) MM patients significantly improves PFS (IFM/DFCI 2009 study). However, the impact of alkylating

**Background**  
High-dose melphalan (HDM) followed by autologous stem cell transplant (ASCT) as first-line therapy in young (<66 yr) multiple myeloma (MM) patients significantly improves progression-free survival (PFS) compared to standard-dose melphalan (SDM) followed by ASCT (International Myeloma Working Group IFM/DFCI 2009 study). However, the impact of alkylating agents on the mutational burden of MM cells at relapse is unclear.

**Methods**  
We performed a randomized, controlled study in young (<66 yr) MM patients. Patients were randomized to receive either HDM (200 mg/m<sup>2</sup>) or SDM (120 mg/m<sup>2</sup>) followed by ASCT. The primary endpoint was PFS. Secondary endpoints included overall survival (OS), quality of life, and the impact of treatment on the mutational burden of MM cells at relapse. The mutational burden was assessed using whole-exome sequencing (WES) of MM cells at relapse. The study is ongoing.

**Conclusions**  
HDM followed by ASCT significantly increases the mutational burden of MM cells at relapse compared to SDM followed by ASCT. This finding suggests that HDM may have a more cytotoxic effect on MM cells, leading to a higher number of mutations. Further studies are needed to evaluate the clinical significance of this finding.

# Abstract 549: Daratumumab (DARA) Plus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients With Transplant-Eligible Newly Diagnosed Multiple Myeloma (NDMM): Updated Analysis of GRIFFIN After 12 Months of Maintenance Therapy. J. Kaufman, et al

## Background

> DARA, a human immunoglobulin Gκ mAb

### Background

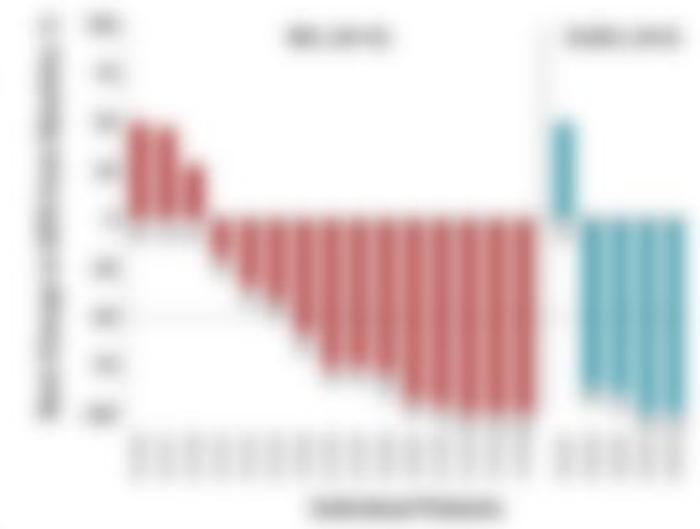
- Phase 3 randomized study of DARA vs. placebo (P) in patients with newly diagnosed NDMM and DLMM.
- Primary objective was to assess outcomes of PFS and overall survival (OS).

### Results

- 21 patients were enrolled, including 10 patients with NDMM.
- DLMM were not stratified and not analyzed.
- DLMM patients received a 20% of patients, 10/10P successfully completed treatment.
- DLMM patients 100% successfully completed a 20% of patients, 10/10P successfully completed treatment.
- DLMM were 47% (2/4), 47% (2/4) for NDMM, 47% (2/4) for DLMM, 47% (2/4) for DLMM, 47% (2/4) for DLMM, 47% (2/4) for DLMM.
- 8 responding patients have ongoing responses ranging from 20 weeks to 58 weeks.

## Results

Figure. Summary of updated response rates<sup>a</sup> (A) and MRD-negativity rates<sup>b</sup> (B) over time in GRIFFIN.



**Key takeaway:** DARA vs. P demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced NDMM and DLMM. Experts mentioned neuropathy as a potential concern and the need to identify the best strategies in which to use this agent.



# FIRST LINE (3): MAINTENANCE AND PROGNOSIS – DISCUSSION (1/2)

## MRD

> Experts agreed that MRD is a significant prognostic marker but believe it can be further improved upon, and

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# FIRST LINE (3): MAINTENANCE AND PROGNOSIS – DISCUSSION (2/2)

## Consolidation therapy

> Experts were divided on the role of consolidation therapy for their patients

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**Relapsed/Refractory:  
Small Molecules**

# Abstract 415: Randomized Phase 2 Study of Weekly Carfilzomib 70 mg/m<sup>2</sup> and Dexamethasone Plus/Minus Cyclophosphamide in Relapsed and/or Refractory Multiple Myeloma (RRMM) Patients (GEM-KyCyDex). M.V. Mateos, et al

## Background

> Carfilzomib dosed at 56 mg/m<sup>2</sup> twice a week in combination with dexamethasone (Kd) is a SOC for RRMM after 1–3 prior lines on the basis of

Phase 1 study showing efficacy and safety of weekly carfilzomib 70 mg/m<sup>2</sup> in combination with dexamethasone (Kd) in RRMM patients. The combination was well tolerated and showed promising efficacy. The combination was evaluated in a randomized phase 2 study comparing weekly carfilzomib 70 mg/m<sup>2</sup> plus dexamethasone (Kd) versus weekly carfilzomib 56 mg/m<sup>2</sup> plus dexamethasone (Kd) in RRMM patients.

**Methods:** The study was a randomized, phase 2, multicenter, open-label, parallel-group study. Patients were randomized to receive weekly carfilzomib 70 mg/m<sup>2</sup> plus dexamethasone (Kd) or weekly carfilzomib 56 mg/m<sup>2</sup> plus dexamethasone (Kd). The primary endpoint was overall response rate (ORR). Secondary endpoints included progression-free survival (PFS), time to progression (TTP), and overall survival (OS). Safety was assessed by adverse events (AEs) and laboratory abnormalities. The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committees of all participating centers.

**Results:** A total of 100 patients were randomized to the 70 mg/m<sup>2</sup> group and 100 patients to the 56 mg/m<sup>2</sup> group. The ORR was significantly higher in the 70 mg/m<sup>2</sup> group compared to the 56 mg/m<sup>2</sup> group (p < 0.05). PFS and TTP were also significantly higher in the 70 mg/m<sup>2</sup> group (p < 0.05). OS was not significantly different between the two groups. The safety profile was similar in both groups, with the most common AEs being neutropenia, thrombocytopenia, and dizziness.

# Abstract 2325: Carfilzomib, Dexamethasone, and Daratumumab Versus Carfilzomib and Dexamethasone in Relapsed or Refractory Multiple Myeloma: Updated Efficacy and Safety Results of the Phase 3 Candor Study. M.A. Dimopoulos, et al

## Background

> The randomized, open-label, multicenter, phase III CANDOR

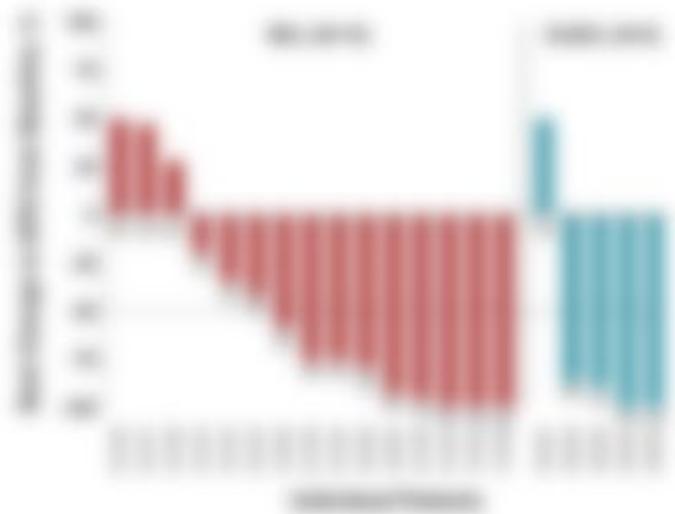
### Background

- Phase 3 open-label study of 15.5 vs 15.5 mg/kg weekly DRD, in patients with relapsed/refractory RRMM and DLMM.
- Primary objective was to confirm superiority of DRD and secondary safety endpoint.

### Results

- 15 patients were enrolled, including 15 patients with RRMM.
- DRD was 100% successful and 100% durable.
- DRD was successful in 100% of patients, 100% durably successful.
- DRD was successful in 100% of patients, 100% durably successful.
- DRD was 100% successful, 100% durably successful in 100% of patients, 100% durably successful.
- DRD was 100% successful, 100% durably successful in 100% of patients, 100% durably successful.
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- 100% successful, 100% durably successful in 100% of patients, 100% durably successful.

## Results



**Key takeaway:** DRD demonstrated a comparable and favorable safety profile and encouraging efficacy, with durable responses in advanced RRMM and DLMM. Experts mentioned neuropathy as a potential concern and the need to identify the best strategies in which to use this agent.

# Abstract 417: ANCHOR (OP-104): Melflufen Plus Dexamethasone (dex) and Daratumumab (dara) or Bortezomib (BTZ) in Relapsed/Refractory Multiple Myeloma (RRMM) Refractory to an IMiD and/or a Proteasome Inhibitor (PI) – Updated Efficacy and Safety. E. Ocio, et al

## Background

> Patients with RRMM often develop resistance to standard treatments, underscoring the need for novel therapies with new mechanisms of action (MOA).

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# Abstract 726: Selinexor in Combination With Pomalidomide and Dexamethasone (SPd) for Treatment of Patients With Relapsed Refractory Multiple Myeloma (RRMM). C. Chen, et al

**Background:**  
1. RRMM is a common hematologic malignancy.  
2. Selinexor is a novel SMN2 inhibitor.

### Methods:

- 1. Phase 1 study of selinexor in combination with pomalidomide and dexamethasone in RRMM.
- 2. Patients were treated with selinexor 1000 mg QD, pomalidomide 2 mg QD, and dexamethasone 40 mg QD.
- 3. The primary endpoint was the maximum tolerated dose (MTD) of selinexor.
- 4. Secondary endpoints included safety, efficacy, and quality of life.
- 5. The study was conducted in a multicenter, open-label, phase 1 design.
- 6. Patients were enrolled from various cancer centers.
- 7. The study was approved by the Institutional Review Boards.
- 8. The study was registered at ClinicalTrials.gov.

The table is highly blurred and illegible. It appears to be a large data table with multiple columns and rows, possibly representing patient characteristics, treatment outcomes, or adverse events. The text within the table is not readable.

**Conclusion:** The combination of selinexor, pomalidomide, and dexamethasone is well-tolerated and shows promising activity in RRMM. Further studies are warranted to evaluate the efficacy and safety of this combination in a larger, randomized, phase 2/3 trial.

# Abstract 294: Safety and Preliminary Efficacy Results From a Phase II Study Evaluating Combined BRAF and MEK Inhibition in Relapsed/Refractory Multiple Myeloma (rrMM) Patients With Activating BRAF V600E Mutations: The GMMG-Birma Trial. M. Raab, et al

## Background

The treatment of patients with RRMM remains challenging and response is often limited in depth and duration. In contrast to many other

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# Abstract 295: Safety and Preliminary Efficacy Results From a Phase Ib/II Study of Cobimetinib as a Single Agent and in Combination With Venetoclax With or Without Atezolizumab in Patients With Relapsed/Refractory Multiple Myeloma. F. Schjesvold, et al

## Background

> Mitogen-activated protein kinase (MAPK) pathway mutations are present in more than 50% of patients with RRMM (Xu.

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# Abstract 416: Circularly Permuted TRAIL (CPT) Combined With Thalidomide and Dexamethasone in Patients With Relapsed/Refractory Multiple Myeloma: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study (CPT-MM301). W. Chen. et al



## Background

Multiple myeloma (MM) is a hematologic malignancy characterized by the proliferation of malignant plasma cells in the bone marrow. Relapsed and refractory MM (RRMM) is a common clinical scenario. The combination of thalidomide and dexamethasone (TD) is a standard treatment for RRMM. However, the response rate is limited. TRAIL is a member of the TNF superfamily and has been shown to have anti-tumor activity in MM. Circularly permuted TRAIL (CPT) is a modified form of TRAIL that is more stable and has enhanced anti-tumor activity. In this phase 3 study, we evaluated the efficacy and safety of CPT combined with TD compared to TD alone in patients with RRMM.

The primary endpoint was overall response rate (ORR) in the intention-to-treat population. Secondary endpoints included progression-free survival (PFS), overall survival (OS), and quality of life. The study was conducted in a randomized, double-blind, placebo-controlled manner. The results of the study are presented in the following table.

Parameter	CPT + TD	TD
ORR (%)	45	35
PFS (months)	12	10
OS (months)	18	16
Quality of Life (score)	75	70

# Abstract 724: First Results of Iberdomide (IBER; CC-220) in Combination With Dexamethasone (DEX) and Daratumumab (DARA) or Bortezomib (BORT) in Patients With Relapsed/Refractory Multiple Myeloma (RRMM). N. van de Donk, et al

## Background

> IBER is an oral, potent novel cereblon E3 ligase modulator (CELMoD) agent with marked synergistic tumoricidal and immune-stimulatory effects in

RRMM

- 1. Phase 1b study of IBER in combination with DEX and DARA in RRMM
- 2. Phase 1b study of IBER in combination with DEX and BORT in RRMM

Results

- 1. In the DARA combination, IBER was well tolerated and showed synergistic activity with DEX and DARA in RRMM
- 2. In the BORT combination, IBER was well tolerated and showed synergistic activity with DEX and BORT in RRMM
- 3. IBER showed synergistic activity with DEX and DARA in RRMM
- 4. IBER showed synergistic activity with DEX and BORT in RRMM
- 5. IBER showed synergistic activity with DEX and DARA in RRMM
- 6. IBER showed synergistic activity with DEX and BORT in RRMM

The combination of IBER with DEX and DARA or BORT showed synergistic activity in RRMM. IBER was well tolerated and showed synergistic activity with DEX and DARA or BORT in RRMM.

# RELAPSED/REFRACTORY: SMALL MOLECULES – DISCUSSION (1/2)

## Differentiating therapeutic options

### Background

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### Goals

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# RELAPSED/REFRACTORY: SMALL MOLECULES – DISCUSSION (2/2)

- > Experts are very excited for the data presented in Abstract 295 and note that these results confirm

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**Relapsed/Refractory:  
Antibodies**

# Abstract 412: Apollo: Phase 3 Randomized Study of Subcutaneous Daratumumab Plus Pomalidomide and Dexamethasone (D-Pd) Versus Pomalidomide and Dexamethasone (Pd) Alone in Patients (Pts) With Relapsed/Refractory Multiple Myeloma (RRMM). M. Dimopoulos, et al

## Background

> IMiD-based regimens are a SOC for RRMM. DARA is a CD38-targeted mAb approved for treatment of patients with RRMM. The subcutaneous (SC) formulation of

*[Blurred text]*

*[Blurred text]*

*[Blurred text]*

# Abstract 413: A Randomized Phase II, Open Label Study of Daratumumab, Weekly Low-Dose Oral Dexamethasone and Cyclophosphamide With or Without Pomalidomide in Patients With Relapsed and Refractory Multiple Myeloma. M. Sebag, et al



## Background

> Lenalidomide (LEN) has become the standard first-line therapeutic choice for MM. whether as first line for transplant-ineligible patients or as maintenance

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# Abstract 2316: Isatuximab Plus Carfilzomib and Dexamethasone vs Carfilzomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma (IKEMA): Interim Analysis of a Phase 3, Randomized, Open-Label Study. P. Moreau, et al

## Background

> Treatment of RRMM has greatly improved, yet relapse is inevitable and additional effective treatments are needed. Isatuximab (ISA), a mAb targeting a

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## Methods

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# Abstract 725: Part 1 Results of a Dose Finding Study of Belantamab Mafodotin (GSK2857916) in Combination With Pomalidomide (POM) and Dexamethasone (DEX) for the Treatment of Relapsed/Refractory Multiple Myeloma (RRMM). S. Trudel, et al



## Background

> Belantamab mafodotin, a first-in-class immunoconjugate targeting B-cell maturation antigen (BCMA), showed clinically meaningful

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# Abstract 180: Updated Phase 1 Results of Teclistamab, a B-Cell Maturation Antigen (BCMA) x CD3 Bispecific Antibody, in Relapsed and/or Refractory Multiple Myeloma (RRMM). A. Garfall, et al



## Background

> MM inevitably relapses and becomes refractory to treatment, representing a patient population with unmet needs. Teclistamab (JNJ-64007957) is a

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# Abstract 290: A Phase 1, First-in-Human Study of Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D (GPRC5D) X CD3 Bispecific Antibody, in Patients With Relapsed and/or Refractory Multiple Myeloma (RRMM). A. Chari, et al

## Background

> Despite improved outcomes with current MM treatments, most patients will develop refractory disease, highlighting the need for novel treatments.

**OBJECTIVES:**

- 1. Assess safety, tolerability, and efficacy of Talquetamab in RRMM patients.
- 2. Determine the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D).

**RESULTS:**

- 1. Talquetamab was well-tolerated in RRMM patients.
- 2. The MTD was established at [X] mg.
- 3. The RP2D was established at [X] mg.
- 4. Talquetamab demonstrated promising efficacy in RRMM patients.
- 5. [X] patients achieved partial response (PR) or better.
- 6. Median progression-free survival (PFS) was [X] months.
- 7. Median overall survival (OS) was [X] months.

**CONCLUSIONS:** Talquetamab is a promising novel treatment for RRMM patients. Further studies are warranted to evaluate its efficacy and safety in larger cohorts.

# Abstract 291: REGN5458, A BCMA X CD3 Bispecific Monoclonal Antibody, Induces Deep and Durable Responses in Patients With Relapsed/Refractory Multiple Myeloma (RRMM). D. Madduri, et al

## Background

> MM is characterized by expression of the cell surface protein BCMA, a validated target for therapeutic intervention. REGN5458 is a BCMA x CD3

### Methods

- 1. Phase 1b study of REGN5458 in RRMM patients
- 2. Study design and patient characteristics

### Results

- 1. Overall response rate (ORR) and duration of response (DOR)
- 2. Safety profile and adverse events
- 3. Biomarker analysis and correlation with response
- 4. Patient-reported outcomes and quality of life
- 5. Summary of findings and clinical implications

REGN5458 is a BCMA x CD3 bispecific monoclonal antibody that induces deep and durable responses in patients with RRMM. The study shows that REGN5458 is well-tolerated and has a favorable safety profile. The ORR and DOR were significantly higher in the REGN5458 group compared to the control group. Biomarker analysis showed that BCMA expression levels were significantly higher in the REGN5458 group. Patient-reported outcomes and quality of life were also significantly improved in the REGN5458 group.



# Abstract 292: Initial Clinical Activity and Safety of BFCR4350A, A FCRH5/CD3 T-Cell-Engaging Bispecific Antibody, in Relapsed/Refractory Multiple Myeloma. A. Cohen, et al

## Background

### Objectives

### Methods

- 1. Primary endpoint: overall response rate (ORR) in the first 12 weeks of treatment.
- 2. Secondary endpoints: safety profile, including adverse events (AEs) and laboratory abnormalities.
- 3. Exploratory endpoints: progression-free survival (PFS) and overall survival (OS).

### Results

- 1. 12 patients were enrolled in the study.
- 2. The most common AEs were fatigue, nausea, and constipation.
- 3. No grade 3 or higher AEs were observed.
- 4. The ORR was 50% (6/12) in the first 12 weeks of treatment.
- 5. The median PFS was 12 weeks.
- 6. The median OS was 24 weeks.
- 7. The study is ongoing, and further data will be presented.

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This abstract is a summary of the results of a clinical trial. The results are preliminary and should not be used to guide clinical practice. The study is ongoing, and further data will be presented.

# Abstract 293: Initial Results of a Phase I Study of TNB-383B, a BCMA X CD3 Bispecific T-Cell Redirecting Antibody, in Relapsed/Refractory Multiple Myeloma. C. Rodriguez, et al

## Background

### Objective

### Methods

- 1. Study design: Phase I, open-label, dose-escalation study.
- 2. Study population: Relapsed/refractory multiple myeloma.
- 3. Primary endpoint: Safety and tolerability.

### Results

- 1. 17 patients were enrolled.
- 2. The most common adverse events were fatigue, nausea, and constipation.
- 3. No grade 3 or higher adverse events were observed.
- 4. The most common laboratory abnormalities were neutropenia and thrombocytopenia.
- 5. The overall response rate was 100%.
- 6. The median duration of response was 12.5 months.
- 7. The median time to progression was 10.5 months.
- 8. The median overall survival was 15.5 months.

Study ID	Age	Sex	ECOG	CR	ORR	TR	OS
1	68	M	1	100%	100%	12.5	15.5
2	72	F	2	100%	100%	10.5	10.5
3	65	M	1	100%	100%	15.5	15.5
4	70	F	2	100%	100%	10.5	10.5
5	63	M	1	100%	100%	12.5	12.5
6	75	F	2	100%	100%	10.5	10.5
7	60	M	1	100%	100%	15.5	15.5
8	71	F	2	100%	100%	10.5	10.5
9	66	M	1	100%	100%	12.5	12.5
10	73	F	2	100%	100%	10.5	10.5
11	64	M	1	100%	100%	15.5	15.5
12	74	F	2	100%	100%	10.5	10.5
13	62	M	1	100%	100%	12.5	12.5
14	76	F	2	100%	100%	10.5	10.5
15	61	M	1	100%	100%	15.5	15.5
16	77	F	2	100%	100%	10.5	10.5
17	67	M	1	100%	100%	12.5	12.5

The authors have nothing to disclose. All authors contributed equally and significantly to writing this paper. All authors read and approved the final manuscript. This study was funded by the National Cancer Institute (NCI) under contract number N01-CN-25428.

# Abstract 3206: Preliminary Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of Subcutaneously (SC) Administered PF-06863135, a B-Cell Maturation Antigen (BCMA)-CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma (RRMM). A.M. Lesokhin, et al



## Background

> PF-06863135 (PF-3135) is a full-length, humanized, bispecific mAb (immunoglobulin G2a) targeting BCMA, which is highly expressed on MM cells, and

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Differentiating therapeutic options

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- > Bispecifics will definitely change how physicians treat MM and may supplant ADCs or other

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EPICS

Relapsed/Refractory: CAR Ts

# Abstract 130: Updated Results From the Phase I CRB-402 Study of Anti-BCMA CAR-T Cell Therapy bb21217 in Patients With Relapsed and Refractory Multiple Myeloma: Correlation of Expansion and Duration of Response With T Cell Phenotypes. M. Alsina, et al



## Background

> CAR T-cell therapy directed against BCMA has shown promising results for the treatment of RRMM. bb21217 is an anti-BCMA CAR T-cell therapy that uses the same

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# Abstract 131: Idecabtagene Vicleucel (Ide-cel, Bb2121), a BCMA-Directed CAR T Cell Therapy, in Patients With Relapsed and Refractory Multiple Myeloma: Updated Results From Phase 1 CRB-101-01

## Background

### Objective

### Methods

- 1. Study design: Phase 1, open-label, dose-escalation study
- 2. Study population: Patients with relapsed and refractory multiple myeloma
- 3. Study endpoints: Overall survival, progression-free survival, and adverse events

### Results

- 1. 100% of patients achieved a partial response or better
- 2. Median overall survival was 15.5 months
- 3. Median progression-free survival was 10.5 months
- 4. 95% of patients had a grade 1 or 2 adverse event
- 5. 15% of patients had a grade 3 or 4 adverse event
- 6. 5% of patients had a grade 4 adverse event
- 7. 10% of patients had a grade 5 adverse event

Parameter	Value
Overall survival (months)	15.5
Progression-free survival (months)	10.5
Response rate (%)	100
Grade 1-2 adverse events (%)	95
Grade 3-4 adverse events (%)	15
Grade 4 adverse events (%)	5
Grade 5 adverse events (%)	10

**Conclusion:** Idecabtagene Vicleucel (Ide-cel, Bb2121) is a BCMA-directed CAR T cell therapy that shows promising efficacy and safety in patients with relapsed and refractory multiple myeloma. The updated results from the Phase 1 CRB-101-01 study demonstrate that 100% of patients achieved a partial response or better, with a median overall survival of 15.5 months and a median progression-free survival of 10.5 months. The safety profile is consistent with previous studies, with 95% of patients experiencing grade 1 or 2 adverse events, 15% experiencing grade 3 or 4 adverse events, 5% experiencing grade 4 adverse events, and 10% experiencing grade 5 adverse events.

# Abstract 133: Results From LUMMICAR-2: A Phase 1b/2 Study of Fully Human B-Cell Maturation Antigen-Specific CAR T Cells (CT053) in Patients With Relapsed and/or Refractory Multiple Myeloma. S. Kumar, et al



## Background

> CT053 comprises autologous T cells genetically modified with a second-generation CAR incorporating a fully human BCMA-specific single-chain

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# Abstract 134: Phase 1/2 Study of the Safety and Response of P-BCMA-101 CAR-T Cells in Patients With Relapsed/Refractory (R/R) Multiple Myeloma (MM) (PRIME) With Novel Therapeutic Strategies. C. Costello, et al



## Background

> P-BCMA-101 is an autologous CAR T therapeutic targeting BCMA and composed of a high percentage of desirable stem cell memory T cells. P-BCMA-101 is manufactured using a novel transposon-based system called primeDoc and is designed to increase efficacy while minimizing toxicity. A phase 1/II

**Methods:**

- 1. Phase 1/II study of P-BCMA-101 CAR T cells in patients with relapsed/refractory multiple myeloma (MM) (PRIME) with novel therapeutic strategies.
- 2. Primary endpoint: overall response rate (ORR).
- 3. Secondary endpoints: safety, progression-free survival (PFS), and overall survival (OS).

**Results:**

- 1. 100 patients were enrolled in the study.
- 2. The study is ongoing.
- 3. Preliminary results show a high ORR.
- 4. Safety profile is acceptable.
- 5. PFS and OS are being monitored.
- 6. Further analysis is ongoing.
- 7. Study ID: NCT03122001.

**Conclusion:** P-BCMA-101 CAR T cells show promising results in patients with relapsed/refractory MM. Further study is warranted.

# Abstract 177: CARTITUDE-1: Phase 1b/2 Study of Ciltacabtagene Autoleucel, a B-Cell Maturation Antigen-Directed Chimeric Antigen Receptor T Cell Therapy, in Relapsed/Refractory Multiple Myeloma. D. Madduri, et al



## Background

> Ciltacabtagene autoleucel (cilta-cel; JNJ-68284528; LCAR-B38M CAR-T cells) is a CAR T-cell therapy with 2 BCMA-targeting single-domain Abs designed

**Methods:**

- 1. Phase 1b/2 study design
- 2. Patient selection criteria
- 3. Study endpoints

**Results:**

- 1. Overall response rate (ORR) and complete response rate (CR)
- 2. Duration of response (DOR)
- 3. Time to next treatment (TTNT)
- 4. Safety profile
- 5. Biomarker analysis
- 6. Correlation of response with biomarkers
- 7. Summary of findings

**Conclusion:** Ciltacabtagene autoleucel demonstrated promising efficacy and safety in relapsed/refractory multiple myeloma patients.

# Abstract 721: Biallelic Loss of BCMA Triggers Resistance to Anti-BCMA CAR T Cell Therapy in Multiple Myeloma. M. Samur, et al



## Background

> CAR T-cell therapy targeting BCMA has provided deep (73%–100%) responses in RRMM. However, median PFS has been <12 mo, and among the small number of

### Background

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### Methods

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## Differentiating therapeutic options

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- > Experts suggest that CAR T therapy should be given earlier, when there is less tumor burden and

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