



EPICS

EPICS: Multiple Myeloma in 2021 and Beyond

September 17–18, 2021

FULL REPORT

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VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
September 17–18,
2021



**DISEASE STATE AND
DATA PRESENTATIONS**
by key experts



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
multiple myeloma
> 10 from US
> 1 from Canada



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

Panel Consisting of 10 US and 1 Canadian Multiple Myeloma Experts



Keith Stewart, MB, ChB
University Health Network

Faith Davies, MD
NYU Langone

Irene Ghobrial, MD
Dana-Farber Cancer Institute

Peter Voorhees, MD
Levine Cancer Institute

Craig C. Hofmeister, MD, MPH
Emory University

Suzanne Lentzsch, MD, PhD
Columbia University

Sagar Lonial, MD, FACP
Emory University

CHAIR: Rafael Fonseca, MD
Mayo Clinic

P. Leif Bergsagel, MD, FASCO
Mayo Clinic

Thomas G. Martin, MD
University of California
San Francisco

Nina Shah, MD
University of California
San Francisco



Meeting Agenda (Day 1 – September 17, 2021)

Time	Topic	Speaker/Moderator
9.00 AM – 9.10 AM (10 min)	Welcome and Introductions	Rafael Fonseca, MD
9.10 AM – 9.30 AM (20 min)	Pursuing the Cure for Myeloma	Keith Stewart, MB, ChB
9.30 AM – 10.00 AM (30 min)	Discussion – Pursuing the Cure for Myeloma	Moderator: Rafael Fonseca, MD
10.00 AM – 10.15 AM (15 min)	Immunomodulatory Agents – With Us Since 1999	Sagar Lonial, MD
10.15 AM – 10.50 AM (35 min)	Discussion – Immunomodulatory Agents – With Us Since 1999	Moderator: Rafael Fonseca, MD
10.50 AM – 11.00 AM (10 min)	BREAK	
11.00 AM – 11.15 AM (15 min)	The Evolving Role of Proteasome Inhibitors (PIs)	Irene Ghobrial, MD
11.15 AM – 11.50 AM (35 min)	Discussion – The Evolving Role of Proteasome Inhibitors (PIs)	Moderator: Rafael Fonseca, MD
11.50 AM – 12.10 PM (20 min)	Summary Discussion: Key Takeaways on Multiple Myeloma	Rafael Fonseca, MD
12.10 PM – 12.20 PM (10 min)	Wrap-up and Overview	Rafael Fonseca, MD



Meeting Agenda (Day 2 – September 18, 2021)

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Time	Topic	Speaker/Moderator
9.00 AM – 9.05 AM (5 min)	Agenda Review	Rafael Fonseca, MD
9.05 AM – 9.20 AM (15 min)	Monoclonal Anti-CD38	Thomas Martin, MD
9.20 AM – 10.00 AM (40 min)	Discussion – Monoclonal Anti-CD38	Moderator: Rafael Fonseca, MD
10.00 AM – 10.15 AM (15 min)	CAR T Therapies for the Treatment of MM	Peter Voorhees, MD
10.15 AM – 10.45 AM (30 min)	Discussion – CAR T Therapies for the Treatment of MM	Moderator: Rafael Fonseca, MD
10.45 AM – 11.00 AM (15 min)	Bispecific Agents for the Treatment of MM	Craig Hofmeister, MD, MPH
11.00 AM – 11.20 AM (20 min)	Discussion – Bispecific Agents for the Treatment of MM	Moderator: Rafael Fonseca, MD
11.20 AM – 11.30 AM (10 min)	BREAK	
11.30 AM – 11.40 AM (10 min)	Other Agents on the Horizon in MM and Moving the Needle Forward	Leif Bergsagel, MD, FASCO
11.40 AM – 12.10 PM (30 min)	Discussion – Other Agents on the Horizon in MM and Moving the Needle Forward	Moderator: Rafael Fonseca, MD
12.10 PM – 12.30 PM (20 min)	Summary Discussion: Key Takeaways on Multiple Myeloma	Rafael Fonseca, MD
12.30 PM – 12.40 PM (10 min)	Wrap-up and Overview	Rafael Fonseca, MD



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Updates in Multiple Myeloma

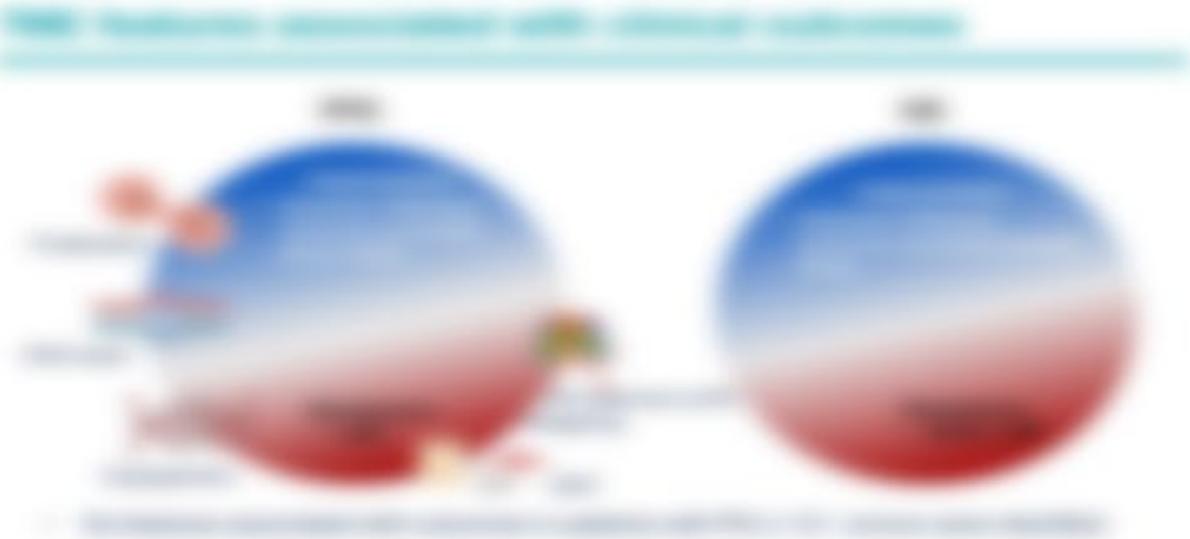
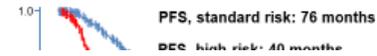


Pursuing the Cure for Myeloma

Presented by Keith Stewart, MB, ChB

Goals of therapy and the role of cytogenetic abnormalities

High-risk patients continue to do worse than



MRD-	164	155	135	97	10	0
MRD+	960	456	269	179	11	0



Key Insights: Pursuing the Cure for Myeloma

Goals of therapy

Experts are uncertain if multiple myeloma (MM) is a curable disease, as

Role of cytogenetic abnormalities

Risk stratification of patients remains important, but

Chromosomal abnormalities

The presence of the t(4;14) translocation (t(4;14)) in the MM genome is associated with a poor prognosis. It is a prognostic factor for the outcome of patients with t(4;14) in high-risk multiple myeloma (MM).

- Patients with t(4;14) have a poor prognosis with standard and non-standard treatment in the progression-free survival (PFS) and overall survival (OS) populations. Higher proliferation, more stem cell self-renewal, and higher relapse rates are observed in patients with t(4;14).
- The t(4;14) negative t(4;14) population did not benefit from the addition of daratumumab to standard of care (SOC) in any clinical setting.

Chromosomal abnormalities in relapsed and refractory MM

There are clinical trials with the aim to "test out" the best drug sequence to increase remission rates in relapsed and refractory MM.

- The addition of an antibody drug conjugate (ADC) may provide the necessary cytotoxicity to reach responses in the t(4;14) population, as shown in the t(4;14) pop. The addition of daratumumab to SOC in a randomized clinical trial showed a higher OS in t(4;14) and t(4;14) population.
- The use of proteasome inhibitors (PIs) may increase remission rates, improve progression-free survival, and increase OS in t(4;14) patients. Daratumumab in combination with t(4;14) and t(4;14) showed a higher response rate, suggesting that t(4;14) can be effectively treated as a group.



Immunomodulatory Agents – With Us Since 1999

Presented by Sagar Lonial, MD

IMiDs and potential impact of CELMoDs on SOC

IMiDs and dexamethasone are the central core for

Iberdomide in combination with dexamethasone and daratumumab, bortezomib, or carfilzomib





The Evolving Role of Proteasome Inhibitors (PIs)

Presented by Irene Ghobrial, MD

Frontline and maintenance therapy

Current data support the use of PIs in addition to Rd +

STUDY POPULATION

1. 1000 patients with relapsed and refractory multiple myeloma (RRMM) were enrolled in the study. The study population was divided into two groups: Group A (500 patients) and Group B (500 patients). Group A received Rd + PI, and Group B received Rd + PI + another agent. The study was a randomized, controlled trial. The primary endpoint was overall survival (OS). The secondary endpoints were progression-free survival (PFS), time to next treatment (TTNT), and quality of life (QoL). The study was conducted in a multicenter setting. The results of the study are presented in the following slides.

RESULTS

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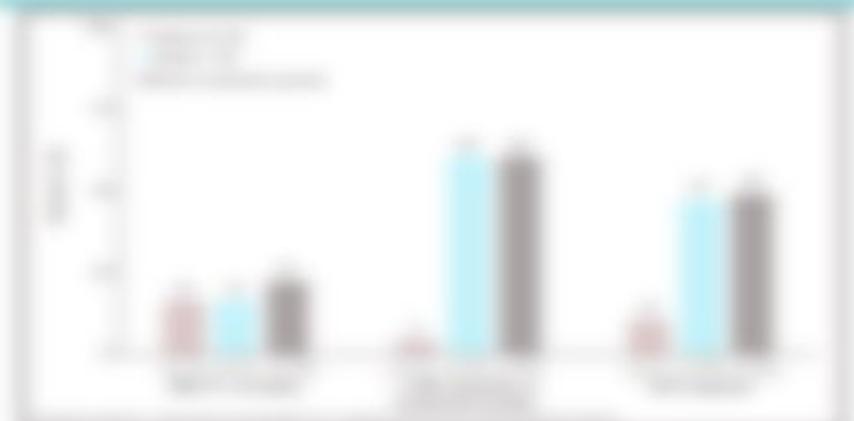
KEY CONCLUSIONS

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OS: TIME TO NEXT TREATMENT (TTNT) IN THE STUDY POPULATION



RESPONSE: PROGRESSION-FREE SURVIVAL (PFS) IN THE STUDY POPULATION



Key Insights: The Evolving Role of Proteasome Inhibitors (PIs)



Frontline therapy

Experts are divided on the role of frontline

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Maintenance therapy

Due to recently released data on mortality rates from the TOURMALINE trials,

[Blurred content area for Maintenance therapy insights]



Key Insights: Monoclonal Anti-CD38

Frontline setting

Most experts have adopted regimens that include a monoclonal anti-

monoclonal anti-CD38

The addition of the monoclonal antibody (mAb) to the standard of care (SOC) for multiple myeloma (MM) is a key component for the positive effect of various treatment regimens (TRs) in high-risk and newly diagnosed (ND) MM.

- Patients who received SOC with mAb and SOC without mAb in the progression-free survival (PFS) and overall survival (OS) endpoints showed significantly higher PFS and OS compared to patients who received SOC without mAb.
- The addition of mAb to SOC is well-tolerated in any clinical setting.

Relapsed/refractory setting

Anti-CD38 antibody regimens are the preferred

regimen for relapsed/refractory MM

There are clinical trials with the aim to "test up" the SOC using mAb to increase mAb concentration to address progression-free survival (PFS) and OS.

- The addition of an antibody drug conjugate (ADC) may provide the necessary immunogenicity and death support by the activity of CD38 in the MM cell population, as shown in the clinical trial. The addition of monoclonal antibody (mAb) to standard SOC showed response rate in PFS, OS and OS.
- The use of mAb in combination with SOC may increase immunogenicity, immunogenicity, immunogenicity, and increase OS and PFS. Knowledge is consistent with mAb and mAb-based SOC. Clinical response, supporting the mAb use in effective in testing up a SOC.



CAR T Therapies for the Treatment of MM

Presented by Peter Voorhees, MD

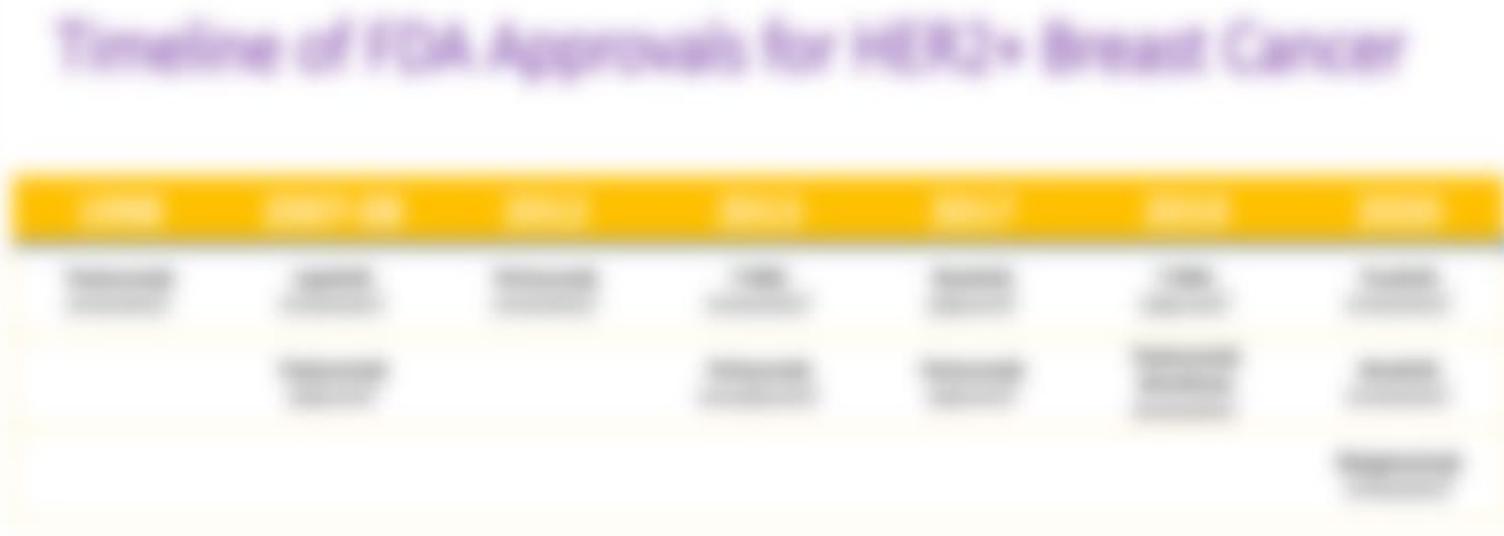
CAR Ts

BCMA-targeted CAR T-cell therapy in R/RMM is active

Idecabtagene Vicleucel: The KarMMa-2 Trial

BCMA-targeted CAR T-cell therapy is active in R/RMM. The KarMMa-2 trial (NCT02689779) is a phase 1/2 study evaluating the safety and efficacy of Idecabtagene Vicleucel (idecabtagene vicleucel) in R/RMM. The study is active and ongoing, with results showing promising efficacy and manageable toxicity.

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- The study is active and ongoing, with results showing promising efficacy and manageable toxicity.



Key Insights: CAR T Therapies for the Treatment of MM

CAR Ts

CAR Ts are exciting options in MM, but more investigation is needed to improve on them and move them to earlier lines of therapy

KEY TAKEAWAYS

The current landscape of CAR T cell therapy in MM is promising, with several studies showing high response rates. However, more research is needed to optimize CAR T cell design and manufacturing, and to evaluate their use in earlier lines of therapy.

- CAR T cell therapy has shown high response rates in MM, particularly in relapsed and refractory disease.
- Current CAR T cell therapies are primarily used in later lines of therapy, but there is a need to move them to earlier lines.
- More research is needed to optimize CAR T cell design and manufacturing, and to evaluate their use in earlier lines of therapy.

CHALLENGES

Despite the promising results, several challenges remain in the development and use of CAR T cell therapy for MM. These include the need for more research to optimize CAR T cell design and manufacturing, and to evaluate their use in earlier lines of therapy.

- CAR T cell therapy is currently limited to relapsed and refractory disease, and there is a need to move it to earlier lines of therapy.
- Current CAR T cell therapies are primarily used in later lines of therapy, but there is a need to move them to earlier lines.
- More research is needed to optimize CAR T cell design and manufacturing, and to evaluate their use in earlier lines of therapy.





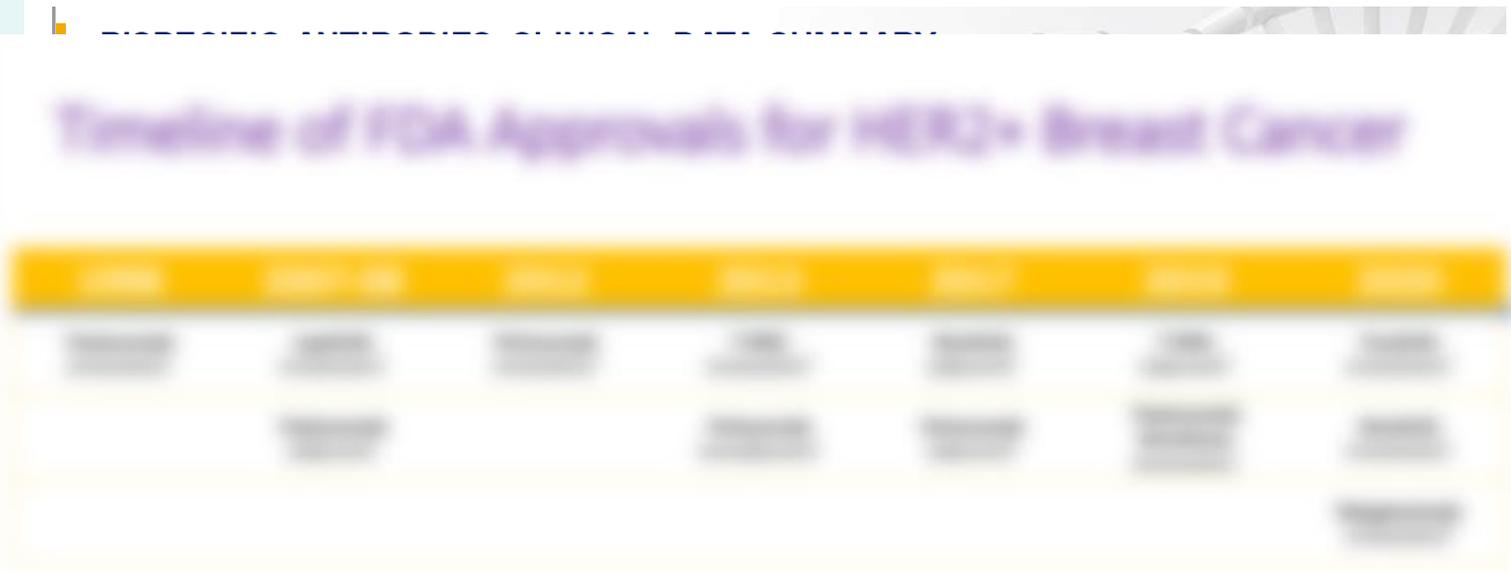
Bispecific Agents for the Treatment of MM

Presented by Craig Hofmeister, MD, MPH

Bispecific agents

Bispecifics are only just coming of age for MM

The first bispecific antibody was approved in 2015 for the treatment of multiple myeloma (MM). Since then, several other bispecific antibodies have been approved for MM, and many more are in development. These agents are designed to bind to both the tumor cell and the immune system, leading to tumor cell death and immune system activation. The first bispecific antibody approved for MM was belantamab umedin, which targets CD38 on the tumor cell and CD3 on the T cell. Other bispecific antibodies in development include epcorh2m, gatasfermin, and others. The approval of these agents represents a significant milestone in the treatment of MM, and they are expected to improve outcomes for patients with this disease.



Key Insights: Bispecific Agents for the Treatment of MM

Bispecific agents

While bispecific agents have shown promising results, experts called for further data to inform sequencing of the agents in relation to

SEQUENCING OF AGENTS

The sequencing of bispecific agents in relation to other treatments is a key area of interest. Experts are calling for further data to inform the optimal sequencing of these agents in relation to other treatments. This includes understanding the impact of sequencing on efficacy and toxicity. Key considerations include the timing of bispecific agent administration relative to other therapies, such as chemotherapy or immunomodulatory drugs. Clinical trials are ongoing to evaluate different sequencing strategies, and the results will help guide clinical practice.

TOXICITY MANAGEMENT

Managing the toxicity of bispecific agents is a critical component of their use. Common side effects include fatigue, nausea, and infections. Experts emphasize the importance of close monitoring and proactive management of these side effects to ensure patients can tolerate the full course of treatment. Strategies for toxicity management include dose adjustments, supportive care, and the use of prophylactic antibiotics. Clinical guidelines are being developed to standardize these approaches across different treatment settings.



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Key Insights: Other Agents on the Horizon in MM and Moving the Needle Forward

Other novel agents

Venetoclax is a promising treatment option for patients with t(11;14), and some experts called it a “game changer”

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