

 EPICS

# EPICS: Multiple Myeloma in 2022 and Beyond

September 23–24, 2022

FULL REPORT

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## VIRTUAL CLOSED-DOOR ROUNDTABLE



**DATE:**  
September 23–24,  
2022



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



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

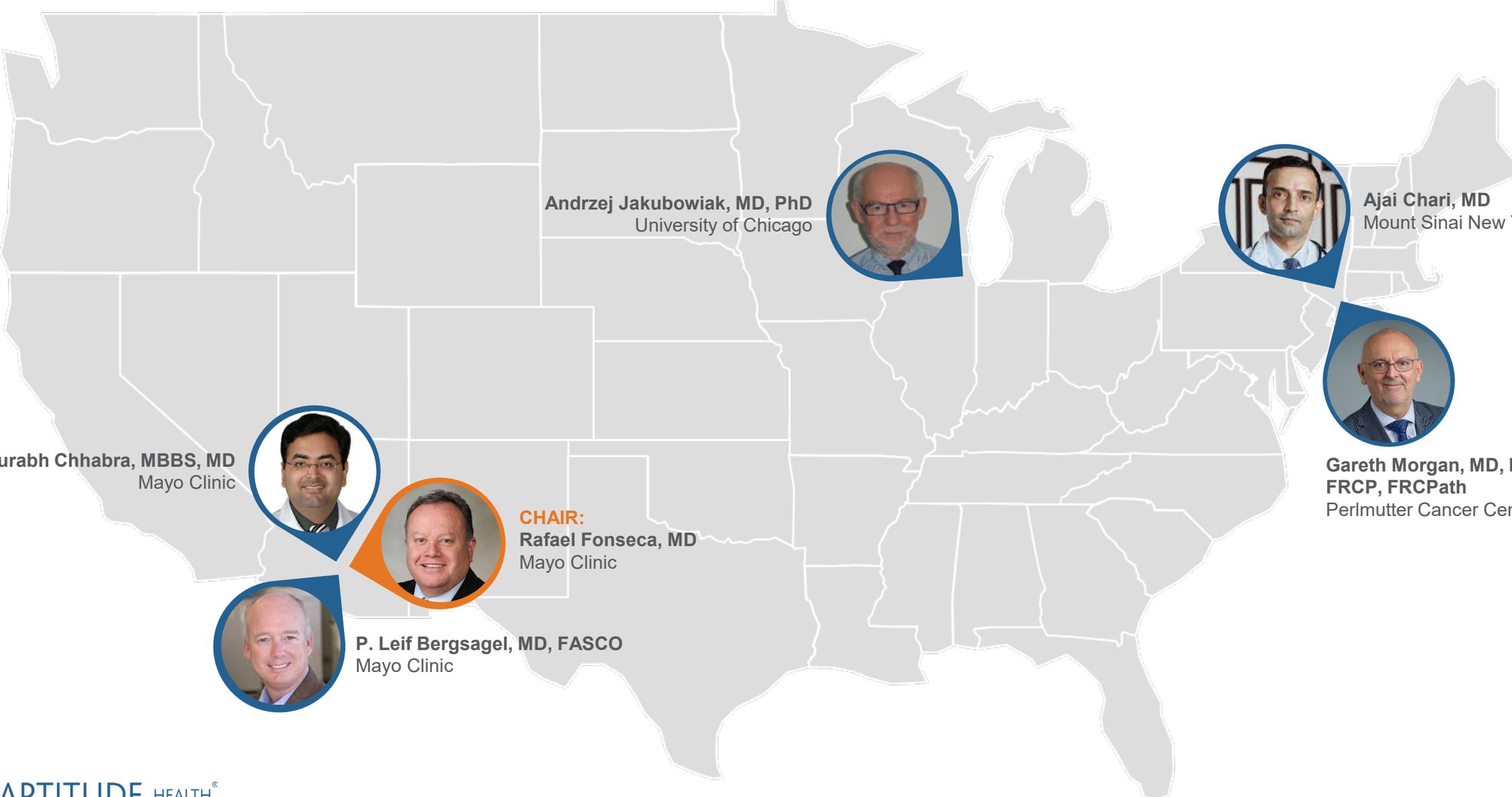


**PANEL:** Key experts in  
multiple myeloma  
> 6 from US



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

# Panel Consisting of 6 US Multiple Myeloma Experts



# Meeting Agenda (Day 1 – September 23, 2022)

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Time (MST)	Topic	Speaker/Moderator
2.00 PM – 2.10 PM (10 min)	<b>Welcome and Introductions</b>	Rafael Fonseca, MD
2.10 PM – 2.30 PM (20 min)	<b>Frontline Transplant-Eligible MM</b>	Leif Bergsagel, MD, FASCO
2.30 PM – 3.05 PM (35 min)	<b>Key Questions and Topics for Discussion</b>	
3.05 PM – 3.20 PM (15 min)	<b>Frontline Transplant-Ineligible MM</b>	Rafael Fonseca, MD
3.20 PM – 3.55 PM (35 min)	<b>Key Questions and Topics for Discussion</b>	
3.55 PM – 4.05 PM (10 min)	<i>BREAK</i>	
4.05 PM – 4.20 PM (15 min)	<b>MRD, Maintenance, and Consolidation Update</b>	Andrzej Jakubowiak, MD, PhD
4.20 PM – 5.00 PM (40 min)	<b>Key Questions and Topics for Discussion</b>	
5.00 PM – 5.20 PM (20 min)	<b>Summary Discussion: Key Takeaways on Multiple Myeloma</b>	Rafael Fonseca, MD
5.20 PM – 5.30 PM (10 min)	<b>Wrap-up and Overview</b>	Rafael Fonseca, MD



# Meeting Agenda (Day 2 – September 24, 2022)

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Time (MST)	Topic	Speaker/Moderator
8.00 AM – 8.05 AM (5 min)	<b>Agenda Review</b>	Rafael Fonseca, MD
8.05 AM – 8.20 AM (15 min)	<b>The Continued Role of Immunomodulatory Agents (IMiDs) and Proteasome Inhibitors (PIs)</b>	Gareth Morgan, MD, PhD, FRCP, FRCPATH
8.20 AM – 8.55 AM (35 min)	<b>Key Questions and Topics for Discussion</b>	
8.55 AM – 9.10 AM (15 min)	<b>Next-Generation Small Molecules: BCL2, XPO1, BCMA Inhibitors, and Beyond</b>	Rafael Fonseca, MD
9.10 AM – 9.45 AM (35 min)	<b>Key Questions and Topics for Discussion</b>	
9.45 AM – 10.00 AM (15 min)	<b>CAR T Therapies for the Treatment of MM</b>	Saurabh Chhabra, MBBS, MD
10.00 AM – 10.35 AM (35 min)	<b>Key Questions and Topics for Discussion</b>	
10.35 AM – 10.50 AM (15 min)	<i>BREAK</i>	
10.50 AM – 11.05 AM (15 min)	<b>Bispecific Agents for the Treatment of MM</b>	Ajai Chari, MD
11.05 AM – 11.40 AM (35 min)	<b>Key Questions and Topics for Discussion</b>	
11.40 AM – 11.55 AM (15 min)	<b>Summary Discussion: Key Takeaways on Multiple Myeloma</b>	Rafael Fonseca, MD
11.55 AM – 12.00 PM (5 min)	<b>Wrap-up and Overview</b>	Rafael Fonseca, MD



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**Frontline Transplant-Eligible  
MM**



# Frontline Transplant-Eligible MM

Presented by Leif Bergsagel, MD

## Genetic testing in BC

> DETERMINATION trial (NCT01208662) data confirmed the

## Transplant is still an important treatment goal

> Transplantation remains an important treatment goal for transplant-



# Discussion: Frontline Transplant-Eligible MM (1/3)

## Frontline: Carfilzomib or bortezomib

There was no consensus on which should be used in frontline, carfilzomib or bortezomib. Some experts



### STUDY POPULATION

1. 1000 patients with MM, 500 on bortezomib, 500 on carfilzomib. All patients had relapsed or refractory MM. Median age 65 years. 70% male. 30% had prior autologous stem cell transplant. Median time to relapse 18 months. Median time to treatment 24 months. Median time to diagnosis 12 months. Median time to relapse 18 months. Median time to treatment 24 months. Median time to diagnosis 12 months. Median time to relapse 18 months. Median time to treatment 24 months. Median time to diagnosis 12 months.

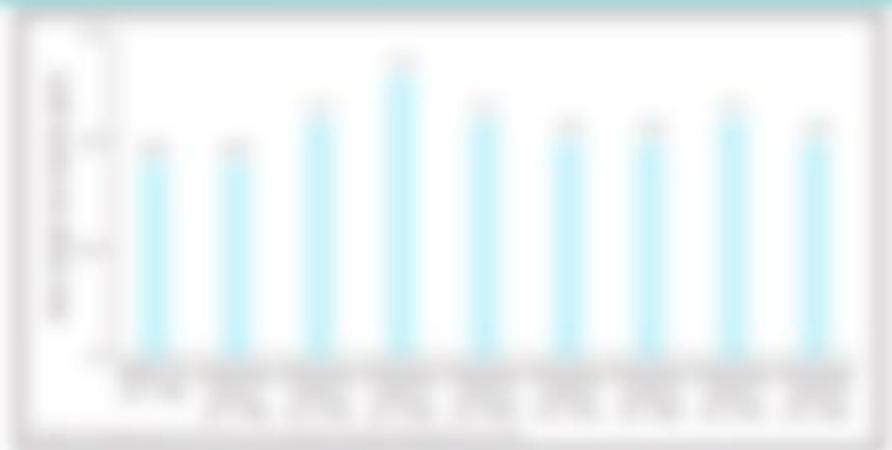
### RESULTS

1. 1000 patients with MM, 500 on bortezomib, 500 on carfilzomib. All patients had relapsed or refractory MM. Median age 65 years. 70% male. 30% had prior autologous stem cell transplant. Median time to relapse 18 months. Median time to treatment 24 months. Median time to diagnosis 12 months. Median time to relapse 18 months. Median time to treatment 24 months. Median time to diagnosis 12 months.

### EXPERT CONCLUSIONS

Continuing to evaluate treatment options. Some experts favor bortezomib and others favor carfilzomib. There is no consensus on which should be used in frontline, carfilzomib or bortezomib.

### RESPONSE RATES



### RESPONSE RATES BY TREATMENT PERIOD



# Discussion: Frontline Transplant-Eligible MM (2/3)

## High-risk population and quad regimens

**Quads are better than triplet regimens, regardless of choosing carfilzomib- or bortezomib-based therapy**

### STUDY POPULATION

1. 1000 patients with MM, 500 patients with high-risk, 500 patients with low-risk. All patients received 4 cycles of treatment. The high-risk group received a quad regimen (carfilzomib, bortezomib, lenalidomide, and dexamethasone) and the low-risk group received a triplet regimen (bortezomib, lenalidomide, and dexamethasone). The high-risk group had a significantly higher response rate (ORR) and progression-free survival (PFS) compared to the low-risk group. The high-risk group also had a significantly higher overall survival (OS) compared to the low-risk group.

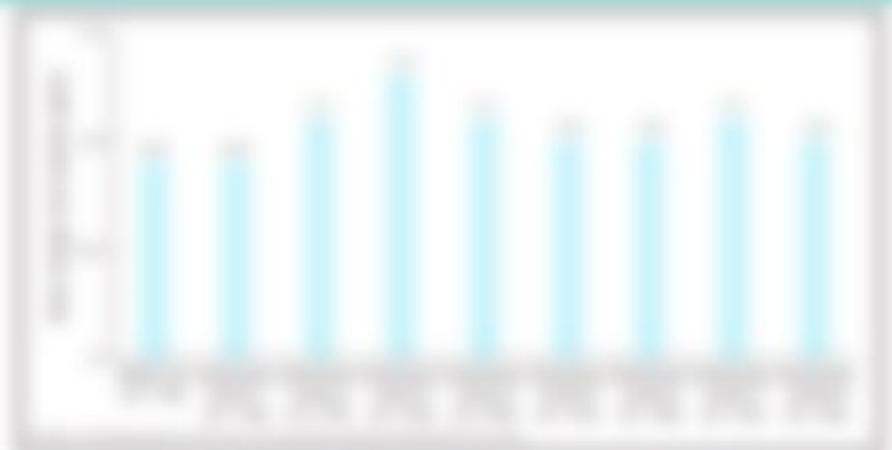
### RESULTS

1. ORR: 85% (high-risk) vs 75% (low-risk)  
2. PFS: 24 months (high-risk) vs 18 months (low-risk)  
3. OS: 36 months (high-risk) vs 30 months (low-risk)

### KEY TAKEAWAYS

1. Quad regimens are superior to triplet regimens in high-risk MM patients.  
2. The high-risk group had a significantly higher response rate, PFS, and OS compared to the low-risk group.

### RESPONSE RATE (ORR) BY RISK GROUP



### RESPONSE RATE (ORR) BY RISK GROUP AND THERAPY





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# **Frontline Transplant-Ineligible MM**



# Frontline Transplant-Ineligible MM

Presented by Rafael Fonseca, MD

## Genetic testing in BC

> In the US, the only relevant options are MAIA vs VRd in

## Frail patients have better outcomes with a triplet than doublet

> MAIA remains the standard; improving on these results will be difficult







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# MRD, Maintenance, and Consolidation Update



# MRD, Maintenance, and Consolidation Update (1/2)

Presented by Andrzej Jakubowiak, MD, PhD

## Maintenance

> There is a paucity of evidence for using the proteasome

## Long-term lenalidomide maintenance

> Both the STAMINA and DETERMINATION trials reported longer



Supporting conclusions...  
...and decreases the maintenance rate in patients.





# MRD, Maintenance, and Consolidation Update (2/2)

Presented by Andrzej Jakubowiak, MD, PhD

## Consolidation and MRD

> The STAMINA trial reported positive outcomes after re-

## MRD-guided treatment

> In the future, MRD may help determine when to stop treatment



# Discussion: MRD, Maintenance, and Consolidation Update (1/3)

## MRD-directed maintenance and consolidation

Maintenance may not need to be given until progression in all patients; MRD may be useful to help determine when to stop maintenance treatment

### STUDY POPULATION

1. 1000 patients with MRD at baseline, 500 patients with MRD at baseline and 500 patients with MRD at baseline and 500 patients with MRD at baseline. The study population was divided into two groups: 500 patients with MRD at baseline and 500 patients with MRD at baseline. The study population was divided into two groups: 500 patients with MRD at baseline and 500 patients with MRD at baseline.

### RESULTS

1. 500 patients with MRD at baseline achieved MRD. 500 patients with MRD at baseline achieved MRD. 500 patients with MRD at baseline achieved MRD.

### KEY CONCLUSIONS

1. Maintenance treatment should be given until progression in all patients. MRD may be useful to help determine when to stop maintenance treatment.

### MRD-DIRECTED MAINTENANCE AND CONSOLIDATION



### RESPONSE, MAINTENANCE, AND CONSOLIDATION



## MRD negativity and de-escalation

Improvements in MRD testing to increase sensitivity will play an important role in prognosis, treatment plans, and de-escalation/escalation of therapy

### STUDY POPULATION

1. 1000 patients with MRD negativity at week 28, 500 patients with MRD positivity at week 28, 500 patients with MRD negativity at week 48, 500 patients with MRD positivity at week 48, 500 patients with MRD negativity at week 72, 500 patients with MRD positivity at week 72. The patients were randomized to receive either 1000 mg or 2000 mg of [drug name] through week 72.

### RESULTS

1. 1000 patients with MRD negativity at week 28, 500 patients with MRD positivity at week 28, 500 patients with MRD negativity at week 48, 500 patients with MRD positivity at week 48, 500 patients with MRD negativity at week 72, 500 patients with MRD positivity at week 72.

### KEY CONCLUSIONS

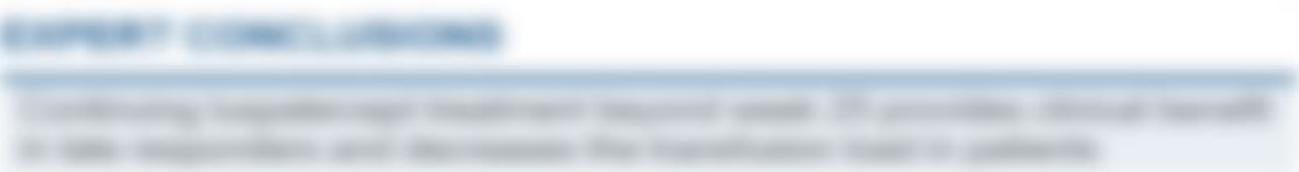
1. Improvements in MRD testing to increase sensitivity will play an important role in prognosis, treatment plans, and de-escalation/escalation of therapy.



## MRD negativity and trials

**MRD has now become a surrogate endpoint but needs to be considered as an actual endpoint**

- > One expert noted that while MRD is useful in the clinic, the evidence is limited for regulators, as many trials do not include MRD data for all patients
- > Future trials should aim to collect MRD data from the majority of patients where possible, as more complete data sets from trials will allow more



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# The Continued Role of Immunomodulatory Agents (IMiDs) and Proteasome Inhibitors (PIs)



# The Continued Role of Immunomodulatory Agents (IMiDs) and Proteasome Inhibitors (PIs)

Presented by Gareth Morgan, MD, PhD

## IMiD resistance

> Resistance can occur by mutation of the cereblon pathway,

## IMiDs

> A comparison below shows minor groups added to IMiDs;

**STUDY POPULATION**

**RESULTS**

**CONCLUSIONS**

**RESPONSE RATES**

**RESPONSE RATES**

# Discussion: The Continued Role of Immunomodulatory Agents (IMiDs) and Proteasome Inhibitors (PIs) (1/4)

## Mechanisms of resistance

The experts agreed that more research is needed on resistance to IMiDs

### STUDY POPULATION

1. 1000 patients with relapsed and/or refractory multiple myeloma (RRMM) were included in the study. The study population was divided into two groups: 500 patients who had received at least one IMiD and 500 patients who had not received any IMiD. The study population was further divided into two subgroups: 250 patients who had received at least one PI and 250 patients who had not received any PI. The study population was further divided into two subgroups: 125 patients who had received at least one IMiD and at least one PI, and 125 patients who had not received any IMiD and any PI.

### RESULTS

1. The study population was divided into two groups: 500 patients who had received at least one IMiD and 500 patients who had not received any IMiD. The study population was further divided into two subgroups: 250 patients who had received at least one PI and 250 patients who had not received any PI. The study population was further divided into two subgroups: 125 patients who had received at least one IMiD and at least one PI, and 125 patients who had not received any IMiD and any PI.

### CONCLUSIONS

1. The study population was divided into two groups: 500 patients who had received at least one IMiD and 500 patients who had not received any IMiD. The study population was further divided into two subgroups: 250 patients who had received at least one PI and 250 patients who had not received any PI. The study population was further divided into two subgroups: 125 patients who had received at least one IMiD and at least one PI, and 125 patients who had not received any IMiD and any PI.



# Discussion: The Continued Role of Immunomodulatory Agents (IMiDs) and Proteasome Inhibitors (PIs) (2/4)

## Lenalidomide-refractory patients

Experts discussed the selection of agents in triplets and quadruplets in relapsed/refractory MM patients

*[Blurred text area containing a list of bullet points, likely detailing clinical trial results or treatment strategies for lenalidomide-refractory patients.]*



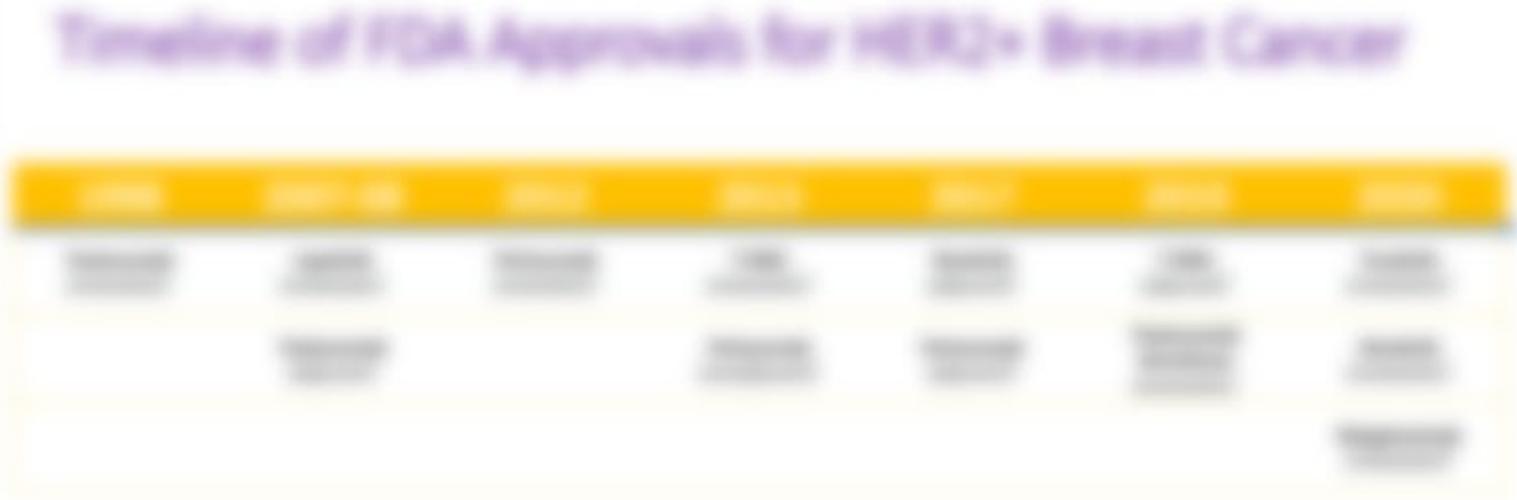
# Discussion: The Continued Role of Immunomodulatory Agents (IMiDs) and Proteasome Inhibitors (PIs) (3/4)

## IMiDs

All experts agreed that single-agent elotuzumab has low activity,

## PIs

The experts mostly agreed that the clinical data for ixazomib



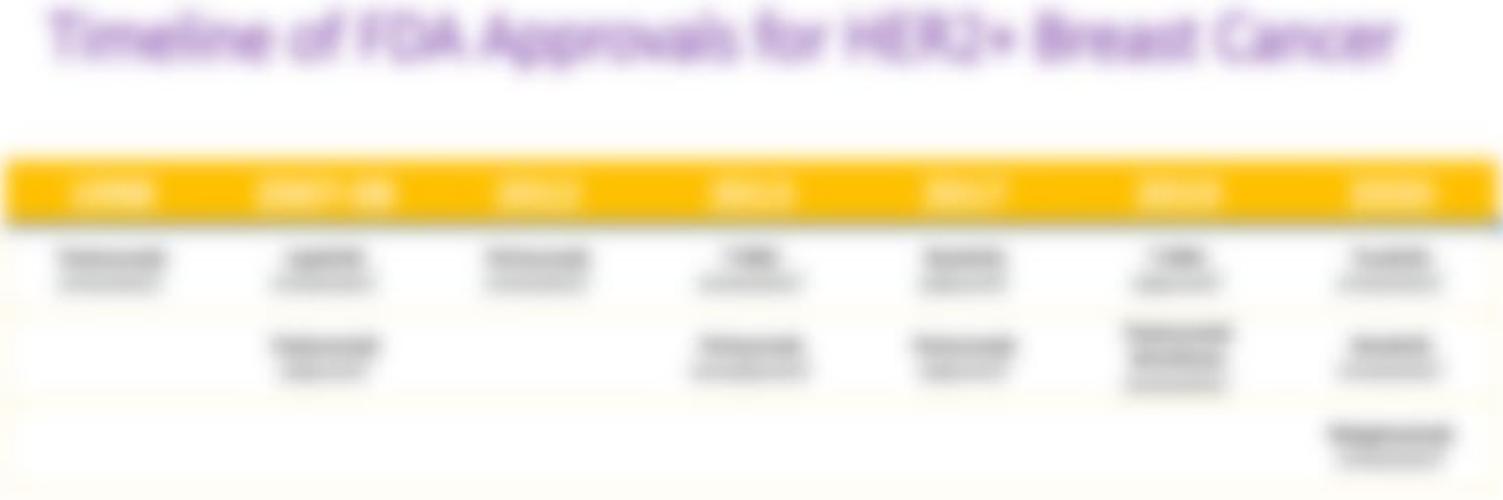
# Discussion: The Continued Role of Immunomodulatory Agents (IMiDs) and Proteasome Inhibitors (PIs) (4/4)

## IMiDs and PIs

Experts discussed the various factors that affect choice of triplet vs



*[Blurred text area containing a list of bullet points, likely detailing clinical trial results or treatment comparisons.]*



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# Next-Generation Small Molecules: BCL2, XPO1, BCMA Inhibitors, and Beyond

Rafael Fonseca, MD



# Next-Generation Small Molecules: BCL2, XPO1, BCMA Inhibitors, and Beyond

Presented by Rafael Fonseca, MD

## Belantamab mafodotin

## Selinexor

## Venetoclax

> Like many other agents in multiple myeloma,

> In R/R MM, selinexor has been

> Venetoclax is a generally well-tolerated drug

*(This section contains a blurred list of bullet points, likely detailing clinical trial results or drug characteristics for Belantamab mafodotin.)*



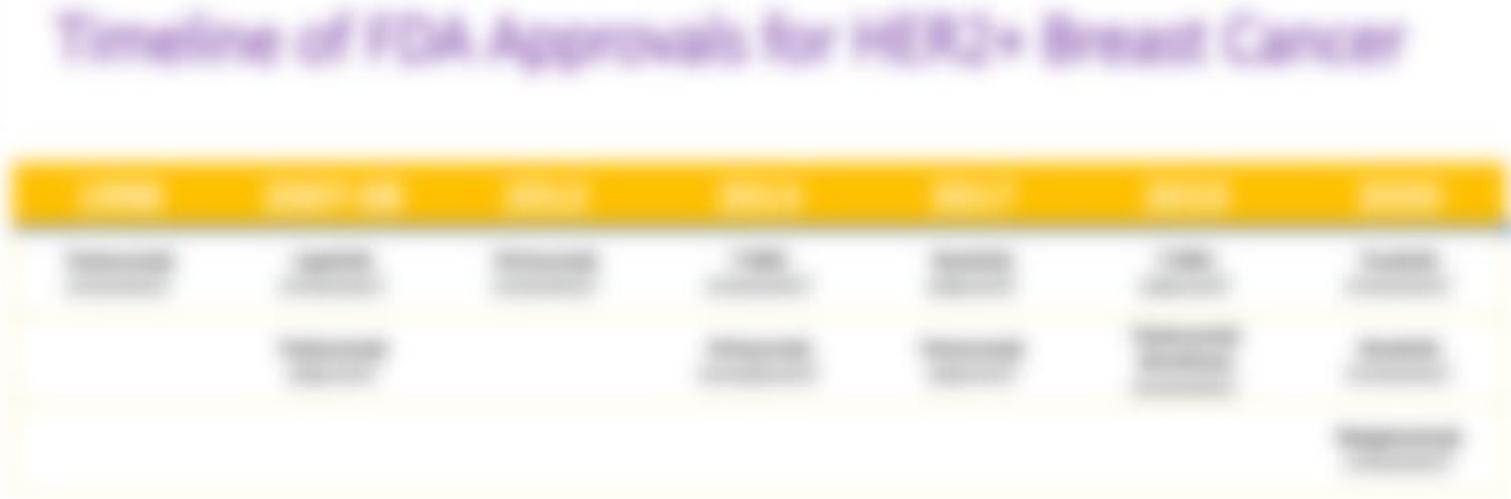
# Discussion: Next-Generation Small Molecules – BCL2, XPO1, BCMA Inhibitors, and Beyond (1/3)

## Selinexor



The experts stated that the current starting dose for selinexor may be too high, but they

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# Discussion: Next-Generation Small Molecules – BCL2, XPO1, BCMA Inhibitors, and Beyond (2/3)

## Venetoclax

Venetoclax is considered extremely useful for treatment of t(11:14) MM and has potential as a frontline therapy in this patient population

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# Discussion: Next-Generation Small Molecules – BCL2, XPO1, BCMA Inhibitors, and Beyond (3/3)

## Belantamab

Belantamab is preferred as a bridging therapy to CAR T: most experts are concerned about toxicities even



### Timeline of FDA Approvals for HER2+ Breast Cancer

Year	2012	2013	2014	2015	2016	2017	2018
Trastuzumab							
Perjeta							
Enhanced Perjeta							
Enhanced Trastuzumab							
Enhanced Trastuzumab Derivat							
Enhanced Trastuzumab Derivat							
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# CAR T Therapies for the Treatment of MM

Saurabh Chhabra, MBBS, MD



# CAR T Therapies for the Treatment of MM (1/2)

Presented by Saurabh Chhabra, MBBS, MD

## CAR T therapies in multiple myeloma

> There is an unmet need in triple-, quad-, and penta-refractory MM patients, and CAR T serves this population very well

*[Blurred content]*

*[Blurred content]*

*[Blurred content]*





# CAR T Therapies for the Treatment of MM (2/2)

Presented by Saurabh Chhabra, MBBS, MD

## CAR T-Cell Toxicities

**KarMMa:**  
Idecabtagene  
Vicleucel (N = 128)

**CARTITUDE-1:**  
Ciltacabtagene  
Autoleucel (N = 97)

*(The content of this table is blurred in the image)*



# Discussion: CAR T Therapies for the Treatment of MM (1/3)

## CAR T

**CAR T is a powerful tool in the treatment of MM; it could be moved to earlier lines of therapy, in combination with other treatments, or even transplant to potentially cure MM**

*[Blurred text block]*

*[Blurred text block]*

*[Blurred text block]*

# Discussion: CAR T Therapies for the Treatment of MM (2/3)

## Access to CAR T

**Access to CAR T will hinder its widespread use. Research should be focused on shortening production times, but the experts recognize there will be regulatory hurdles to overcome with new production methods**

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[Blurred text block]



*[CAR T] always going to be transplant centers.*



# Discussion: CAR T Therapies for the Treatment of MM (3/3)

## CAR T

Cilta-cel may have potential in high-risk patients, but the experts noted that any of these patients included in trials are not reflective of the larger population, as many do not reach >6 lines of therapy

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[Blurred text block]

[Blurred text block]



experiences with [B-cell palsy] after cilta-cel. Two patients. One patient had recovered, but the other patient did not recover after 3 months.



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# Bispecific Agents for the Treatment of MM

Ajai Chari, MD



# Bispecific Agents for the Treatment of MM (1/3)

Presented by Ajai Chari, MD

## Other than BCMA and GPRC5D, what targets have promise?

> While BCMA and GPRC5D are the most common targets, others

## In addition to efficacy, what other factors will impact the widespread use of bispecifics?

> Safety is another major factor to consider in addition to efficacy





# Bispecific Agents for the Treatment of MM (2/3)

Presented by Ajai Chari, MD

## Should patients be treated with bispecifics until progression?

*[Blurred text block]*

*[Blurred text block]*

*[Blurred text block]*





# Bispecific Agents for the Treatment of MM (3/3)

Presented by Ajai Chari, MD

## CAR T vs bispecifics – who wins? Does transplant eligibility make a difference?

> A hypothetical randomized study with intention-to-treat analysis without bridging chemo

*[Blurred text area]*

*[Blurred text area]*

*[Blurred text area]*



## Bispecific agents

**The experts questioned why the bispecifics are administered until progression, especially with the increased risk of infection and other AEs**

- > For patients with cumulative AEs, a fixed-duration treatment may be more appropriate, and they could potentially receive the same or

*[Blurred text block]*

*[Blurred text block]*

*[Blurred text block]*

# Discussion: Bispecific Agents for the Treatment of MM (2/3)

## CAR T vs bispecifics

**There was consensus that CAR T efficacy is superior to that of bispecifics, but bispecifics will have a greater impact for the wider patient population, as there will be fewer access**



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# Discussion: Bispecific Agents for the Treatment of MM (3/3)

## CAR T vs bispecifics

**Experts debated whether the response rate is higher with CAR T compared with bispecifics**

> The response rate can be associated with patient selection; with limited availability of CAR T,



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