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EPICS

EPICS: Multiple Myeloma in 2022 and Beyond

September 23–24, 2022

FULL REPORT

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Meeting Snapshot

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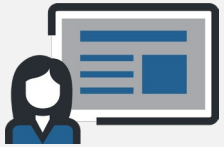
VIRTUAL CLOSED-DOOR ROUNDTABLE

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

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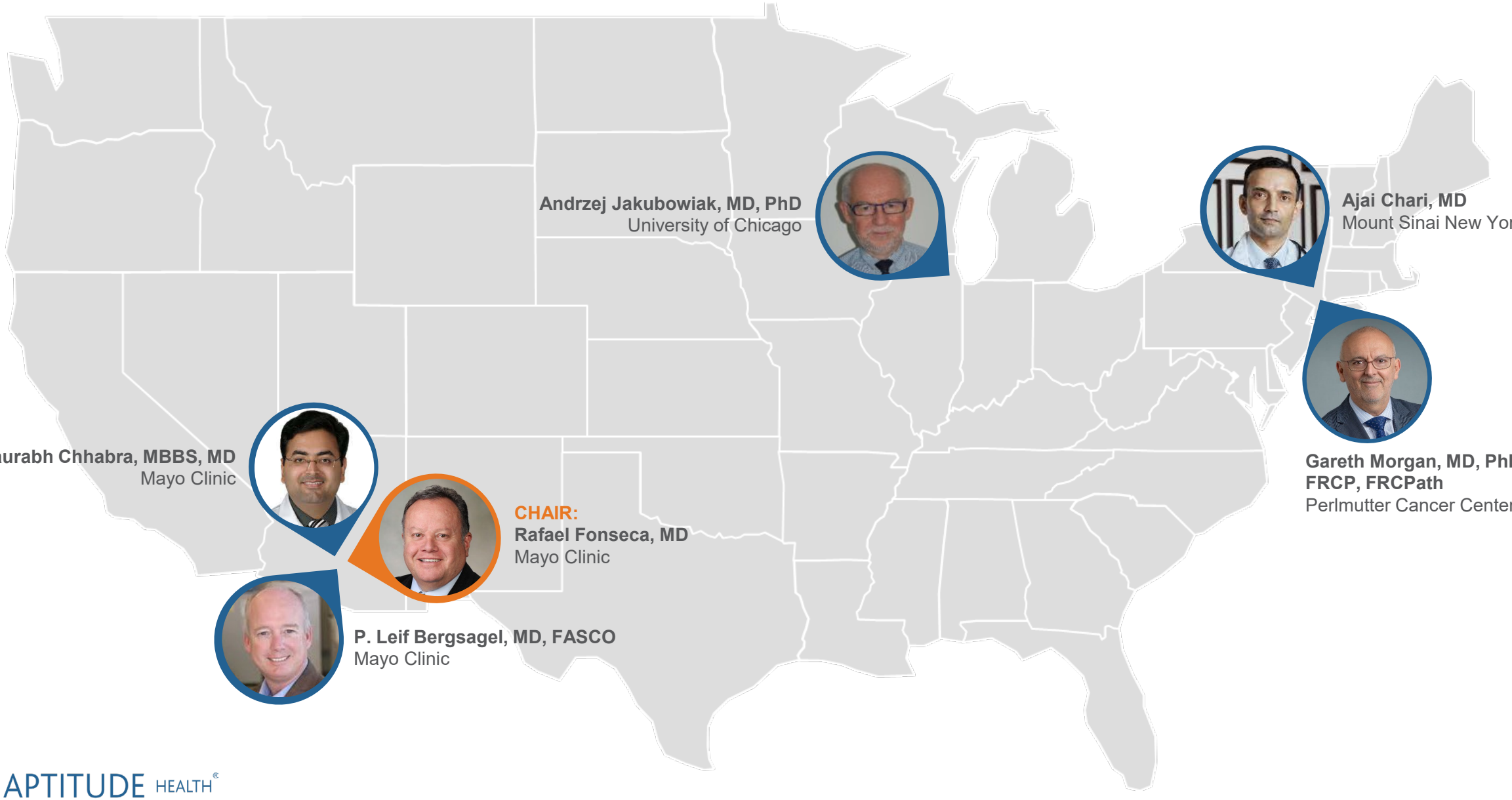

Andrzej Jakubowiak, MD, PhD
University of Chicago

Ajai Chari, MD
Mount Sinai New York

Saurabh Chhabra, MBBS, MD
Mayo Clinic

CHAIR:
Rafael Fonseca, MD
Mayo Clinic

P. Leif Bergsagel, MD, FASCO
Mayo Clinic

Gareth Morgan, MD, PhD, FRCP, FRCPath
Perlmutter Cancer Center

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Meeting Agenda (Day 1 – September 23, 2022)

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Time (MST)	Topic	Speaker/Moderator
2.00 PM – 2.10 PM (10 min)	**Welcome and Introductions**	Rafael Fonseca, MD
2.10 PM – 2.30 PM (20 min)	**Frontline Transplant-Eligible MM**	Leif Bergsagel, MD, FASCO
2.30 PM – 3.05 PM (35 min)	**Key Questions and Topics for Discussion**	
3.05 PM – 3.20 PM (15 min)	**Frontline Transplant-Ineligible MM**	Rafael Fonseca, MD
3.20 PM – 3.55 PM (35 min)	**Key Questions and Topics for Discussion**	
3.55 PM – 4.05 PM (10 min)	*BREAK*	
4.05 PM – 4.20 PM (15 min)	**MRD, Maintenance, and Consolidation Update**	Andrzej Jakubowiak, MD, PhD
4.20 PM – 5.00 PM (40 min)	**Key Questions and Topics for Discussion**	
5.00 PM – 5.20 PM (20 min)	**Summary Discussion: Key Takeaways on Multiple Myeloma**	Rafael Fonseca, MD
5.20 PM– 5.30 PM (10 min)	**Wrap-up and Overview**	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)	**Agenda Review**	Rafael Fonseca, MD
8.05 AM – 8.20 AM (15 min)	**The Continued Role of Immunomodulatory Agents (IMiDs) and Proteasome Inhibitors (PIs)**	Gareth Morgan, MD, PhD, FRCP, FRCPath
8.20 AM – 8.55 AM (35 min)	**Key Questions and Topics for Discussion**	
8.55 AM – 9.10 AM (15 min)	**Next-Generation Small Molecules: BCL2, XPO1, BCMA Inhibitors, and Beyond**	Rafael Fonseca, MD
9.10 AM – 9.45 AM (35 min)	**Key Questions and Topics for Discussion**	
9.45 AM – 10.00 AM (15 min)	**CAR T Therapies for the Treatment of MM**	Saurabh Chhabra, MBBS, MD
10.00 AM – 10.35 AM (35 min)	**Key Questions and Topics for Discussion**	
10.35 AM – 10.50 AM (15 min)	*BREAK*	
10.50 AM – 11.05 AM (15 min)	**Bispecific Agents for the Treatment of MM**	Ajai Chari, MD
11.05 AM – 11.40 AM (35 min)	**Key Questions and Topics for Discussion**	
11.40 AM – 11.55 AM (15 min)	**Summary Discussion: Key Takeaways on Multiple Myeloma**	Rafael Fonseca, MD
11.55 AM – 12.00 PM (5 min)	**Wrap-up and Overview**	Rafael Fonseca, MD

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Frontline Transplant-Eligible MM

Frontline Transplant-Eligible MM

Presented by Leif Bergsagel, MD

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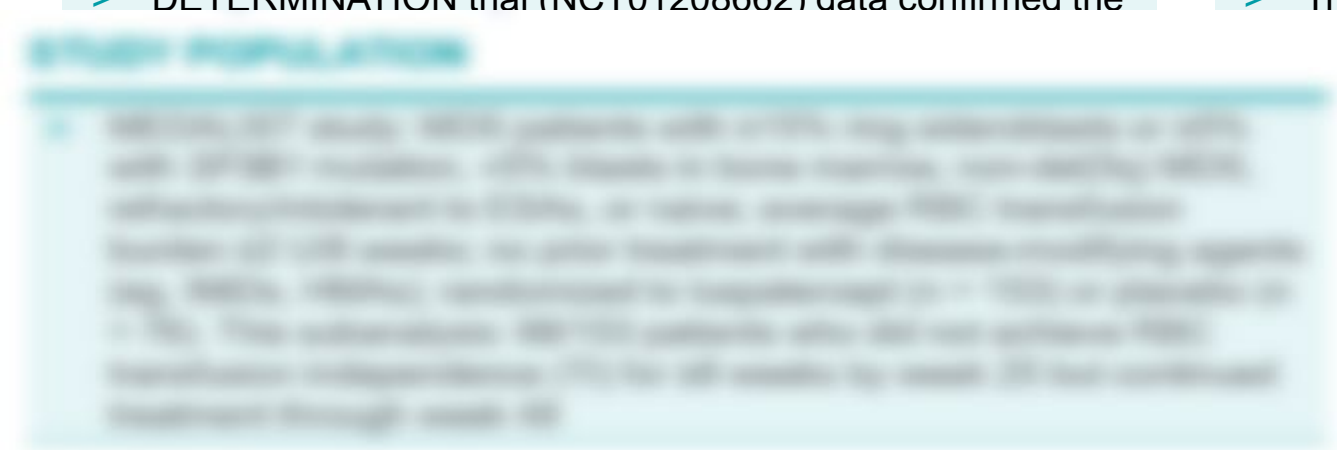
Genetic testing in BC

> 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)

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Frontline: Carfilzomib or bortezomib

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

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

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High-risk population and quad regimens

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

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

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MRD and transplant

Experts agreed that they would still transplant an MRD-negative patient, if they are young and fit

- Generally, the experts agreed this is a complex question; given that the patient is MRD-negative, the experts wondered if there is a need for

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Frontline Transplant-Ineligible MM

Frontline Transplant-Ineligible MM

Presented by Rafael Fonseca, MD

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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

Discussion: Frontline Transplant-Ineligible MM (1/2)

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MAIA: Treatment goals and transplant eligibility

The majority of experts prefer MAIA over VRd in transplant-ineligible patients

Discussion: Frontline Transplant-Ineligible MM (2/2)

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Isatuximab and quad regimens

In a frail patient, the experts would begin with anti-CD38 in combination with Rd and avoid proteasome inhibitors

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MRD, Maintenance, and Consolidation Update

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

Presented by Andrzej Jakubowiak, MD, PhD

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Maintenance

> There is a paucity of evidence for using the proteasome

Long-term lenalidomide maintenance

> Both the STAMINA and DETERMINATION trials reported longer

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

Presented by Andrzej Jakubowiak, MD, PhD

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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)

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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

Discussion: MRD, Maintenance, and Consolidation Update (2/3)

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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

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

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MRD negativity and trials

MRD has now become a surrogate endpoint but needs to 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

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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

EPICS

IMiD resistance

> Resistance can occur by mutation of the cereblon pathway,

IMiDs

> A comparison below shows minor groups added to IMiDs;

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

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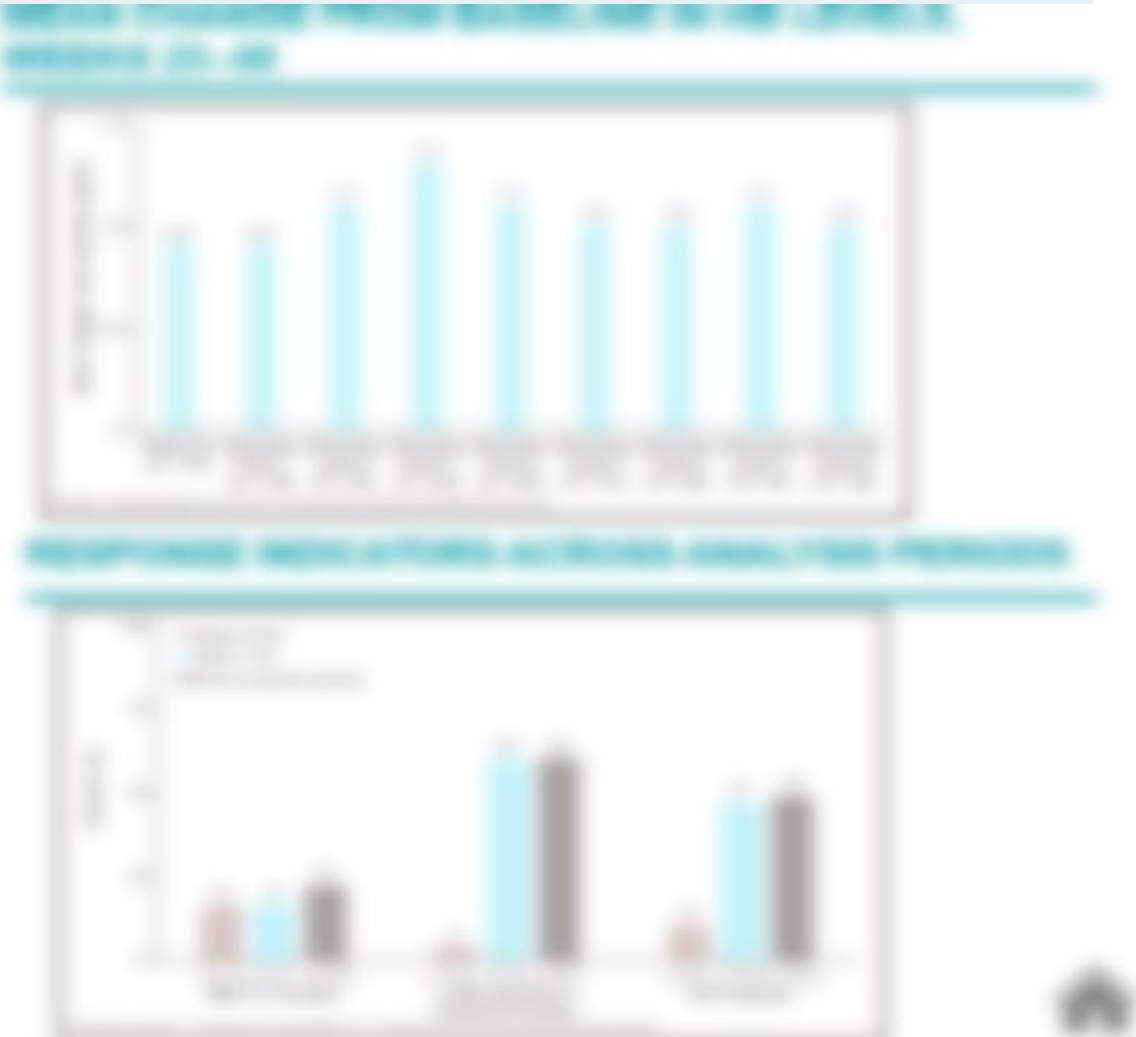
Mechanisms of resistance

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



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

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Lenalidomide-refractory patients

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

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

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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)

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IMiDs and PIs

Experts discussed the various factors that affect choice of triplet vs

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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

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Belantamab mafodotin

> Like many other agents in multiple myeloma,

Selinexor

> In R/R MM, selinexor has been

Venetoclax

> Venetoclax is a generally well-tolerated drug

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

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Selinexor

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

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

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Venetoclax

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

personally less [frequently] observing the toxicities which were so detrimental in the BELLINI study.

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

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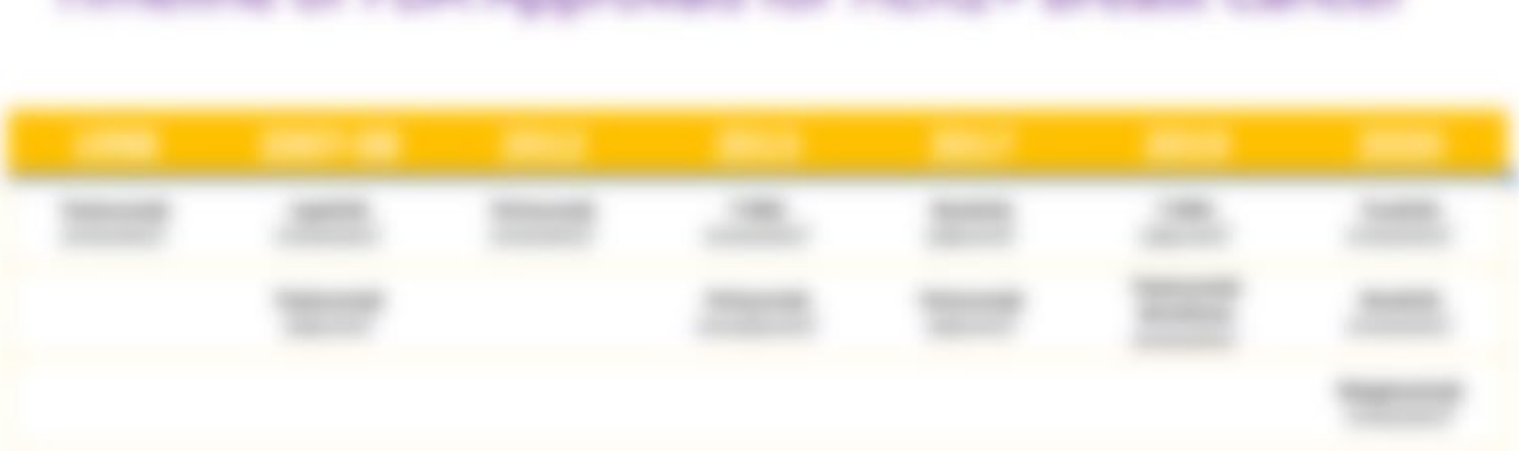
Belantamab

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



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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

EPICS

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

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

Presented by Saurabh Chhabra, MBBS, MD

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CAR T-Cell Toxicities	KarMMa: Idecabtagene Vicleucel (N = 128)	CARTITUDE-1: Ciltacabtagene Autoleucel (N = 97)

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

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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

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

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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

[CAR T] always going to be transplant centers.

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

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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

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

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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

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Should patients be treated with bispecifics until progression?

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

Presented by Ajai Chari, MD

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

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

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

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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

should take a break [from treatment].

”

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

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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

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

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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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