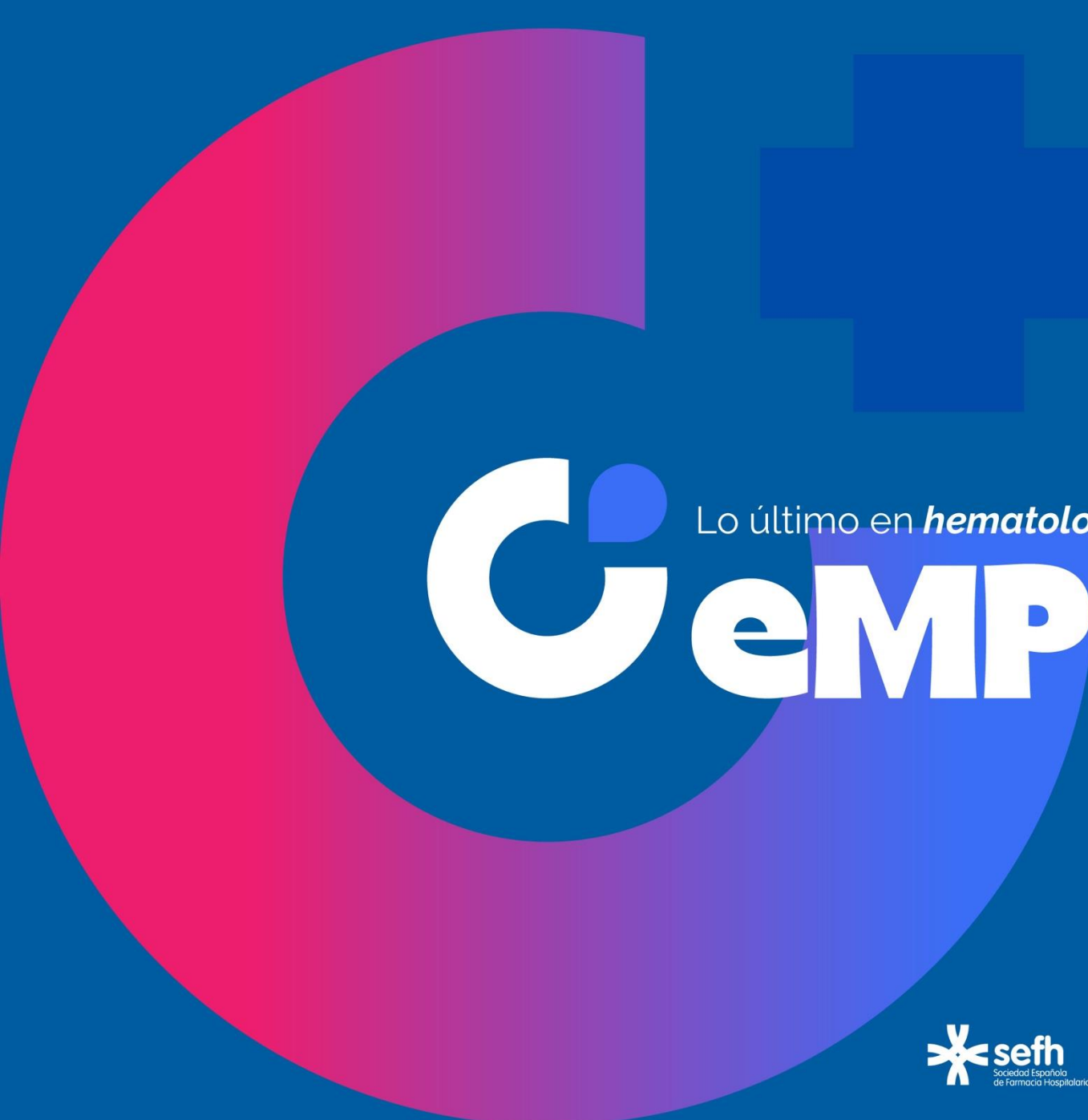




Lo último en *hematología* para *farmacia hospitalaria*

GemPhasis



Con el patrocinio de:
REGENERON*



Lo último en *hematología* para *farmacia hospitalaria*

eMPHasis

Míriam Merchante Andréu
Hospital Clínico Lozano Blesa Zaragoza

Viernes 12/06/2026: MM

Manejo de la enfermedad e impacto del tratamiento

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies

CHAIR: SHAJI KUMAR

Managing Disease and Treatment Burdens with Next Generation Therapies



Chair: Shaji Kumar, MD

**TREATMENT OPTIONS
FOR RELAPSED /
REFRACTORY MM
(RRMM) PATIENTS**

10:00-10:15
(15 min)



Xavier Leleu, MD, PhD

**CONSIDERATIONS
FOR USE OF
BISPECIFICS IN RRMM**

10:15-10:30
(15 min)



Paula Rodriguez-Otero, MD

**OPTIMIZING
BISPECIFIC THERAPY
TREATMENT IN RRMM**

10:30-10:45 (15 min)

PANEL DISCUSSION

10:45-11:00 (15 min)



Joseph Mikhael, MD

**MANAGING THE
BURDEN OF
MM TREATMENTS**

11:00-11:15 (15 min)

PANEL DISCUSSION

11:15-11:30 (15 min)



Shaji Kumar

Treatment Options for
Relapsed/Refractory MM (RRMM)
Patients

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BsAb-TCEs-Opciones disponibles

- OPCIONES DISPONIBLES: EFICACES....

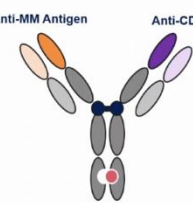
Pero NO podemos olvidar las complicaciones:

Nos preocupan las infecciones:

15-46% de infecciones G3-G4

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies
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Currently Available BsAb-TCEs: Efficacy, Safety, and Dosing



Representative BsAb-TCE Structure

	CD3 bsAb-TCEs
Dosing	Typically initiated at QW Patients with a sustained response may switch to Q2W or Q4W
Monotherapy patient population	RRMM ≥3 prior LOT, including an IMiD, PI, and anti-CD38
Initial administration	2 SUD
Location of administration	Inpatient
Duration of monitoring	24-48 hours hospitalization after each SUD and first full dose
Treatment duration	Until disease progression
CRS	46 - 79%
ICANS	3 - 11%
Infections (any grade)	59 - 76%
Infections (grade 3/4)	15- 45%
ORR	61 - 74%

Monotherapy safety:

Currently available bsAb-TCEs are efficacious treatment options for later lines of therapy, however, they require dosing and safety management due to inherent MOA risks.

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Treatment Options for Relapsed/Refractory MM (RRMM) Patients

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Treatment-Related Toxicities Associated with T-Cell Therapies

CRS

Engagement of immune cells by T-cell-engaging therapies triggers the release of cytokines. However, there is an increased risk of cytokine release syndrome (CRS), an acute systemic inflammatory reaction caused by a rapid release of proinflammatory cytokines into the blood.

If CRS occurs, events typically start within 1-2 days of a first full dose of a bisAb-TCE.

ICANS

Related to cytokine release, immune effector cell-associated neurotoxicity syndrome (ICANS) may develop due to increased levels of proinflammatory cytokines in central spinal fluid (CSF), which indicates loss of integrity of the blood-brain barrier (BBB).

If ICANS occurs, events typically start within 7 days of a first full dose of a bisAb-TCE.

Early Signs of CRS

- Fever
- Fatigue
- Headache
- Rash
- Diarrhea
- Arthralgia
- Myalgia

Late Symptoms of CRS

- Severe fever ($\geq 105^\circ\text{F}$; 40.5°C)
- Hypotension
- Circulatory collapse
- Capillary leak
- Pulmonary edema
- Cardiac dysfunction
- Multorgan system failure

T-cells Release Cytotoxic Cytokines When Triggered by Certain Therapies in Order to Destroy MM Cells

Lower Severity Symptoms of ICANS

- Tremor
- Orientation disorder

Medium Severity Symptoms of ICANS

- Aphasia
- Hallucinations

Higher Severity Symptoms of ICANS

- Disturbed consciousness
- Seizures
- Delirium



Xavier Leleu

Considerations for Use of Bispecifics in RMM

CRS e ICANS

- CRS: Importante reconocer aquellos signos tempranos vs tardíos.
 - Fiebre: En muchos pacientes dos horas tras infusión
 - Tardíos: Fiebre elevada, fuga capilar, edema pulmonar, insuficiencia cardiaca → fallo multiorgánico.
- Monitorización continua :Equipo formado
- Disponibilidad de IVIG

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies
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T-cell Therapy Treatment Facility Requirements

Approved Novel Therapy	EMA SmPC Language on Site Qualifications
Ciltacabtagene autoleucel ¹	Ciltacabtagene autoleucel must be administered in a qualified treatment center. Therapy should be initiated under the direction and supervision of a healthcare professional experienced in the treatment of hematological malignancies and trained for administration and management of patients treated with ciltacabtagene autoleucel.
Idecabtagene vicleucel ²	Idecabtagene vicleucel must be administered in a qualified treatment center. Idecabtagene vicleucel therapy should be initiated under the direction of and supervised by a healthcare professional experienced in the treatment of hematological malignancies and trained for the administration and management of patients treated with idecabtagene vicleucel.
Tecelismab ³	Tecelismab should be administered by a healthcare professional with adequately trained medical personnel and appropriate medical equipment to manage severe reactions, including CRS.
Etranatamab ⁴	Etranatamab should be administered via subcutaneous injection by a healthcare professional with adequately trained medical personnel and appropriate medical equipment to manage severe reactions, including CRS and ICANS.
Linvoseltamab ⁵	Linvoseltamab should be administered by a healthcare professional with immediate access to emergency equipment and appropriate medical support to manage severe reactions such as CRS, IRR, or ICANS if they occur.
Talquetamab ⁶	Talquetamab should be administered by a healthcare professional with adequately-trained medical personnel and appropriate medical equipment to manage severe reactions, including CRS and neurologic toxicity, including ICANS.



Requirements of Local Treatment Center

- ✓ CRS & ICANS management - trained personnel: HCPs/nurses
- ✓ ICU & emergency unit
- ✓ Tocilizumab in direct proximity
- ✓ Hematologist on-call 24/7
- ✓ Capabilities for IVIG supplementation



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Considerations for Use of Bispecifics in RMM

CRS=Cytokine Release Syndrome; EMA=European Medicines Agency; HCP=Health Care Professional; ICANS=Immune Effector Cell-Associated Neurotoxicity Syndrome; IRR=Immune Reaction; IVIG=Intravenous Immune Globulin; MM=Multiple Myeloma; RMM=Relapsed Multiple Myeloma; SmPC=Summary of Product Characteristics; 1. CARVYNT (ciltacabtagene autoleucel) EMA SmPC: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Dender, Belgium, Mar 2024. 2. IMYCAR (idecabtagene vicleucel) EMA SmPC: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Dender, Belgium, Mar 2024. 3. TECELISMAB (tecelismab) EMA SmPC: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Dender, Belgium, Mar 2024. 4. ETNATAMAB (etranatamab) EMA SmPC: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Dender, Belgium, Mar 2024. 5. LIVNOSELTAMAB (linvoseltamab) EMA SmPC: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Dender, Belgium, Mar 2024. 6. TALQUETAMAB (talquetamab) EMA SmPC: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Dender, Belgium, Mar 2024.

RECOMENDACIONES IMWG CRS e ICANS

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies
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IMWG Recommendations for CRS and ICANS Safety Risk Management

Prevention and Prophylaxis	Monitoring and Supportive Care	Treatment and Management
Step-up Dosing • Before full dose to mitigate occurrence and/or higher severity of CRS/ICANS Premedications (e.g., dex) • To reduce inflammation and blood pressure Prophylactic Toci (IL-6 Inhibitor) • Investigational; not recommended outside of clinical trials • Increasing evidence of use in real-world setting	Monitor for signs and symptoms • CRS: fever, headache, confusion, delirium, fatigue • ICANS: Headache, confusion, orientation disorder, apraxia, aphasia, delirium/hallucinations, tremor, hypertension, seizures, peripheral neuropathy Avoid G-CSF (CRS) • During periods of higher CRS risk Laboratory Investigations • CBC, comprehensive metabolic panels, inflammatory markers, coagulation tests Supportive Care • Acetaminophen, antihistamines, antipyretics, blood pressure medication, intravenous fluids (saline), oxygen, ventilation	Grade 1: Observation • CRS: Toci • ICANS: Dex Grade 2: Treatment • CRS: Toci + Dex • ICANS: Dex Grade 3: Treatment and hospitalization (ICU) • CRS: Toci + Dex • ICANS: Dex Grade 4: Treatment and hospitalization (ICU) • CRS: Toci + high-dose steroids (dex) • ICANS: Dex

IMWG published consensus guidelines and recommendations for the optimal use of bsAb-TCEs, including the prevention, monitoring, and management of CRS and ICANS. These include premedications, step-up dosing, hospitalization monitoring, and tocilizumab use.

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Considerations for Use of Bispecifics in RRMM

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• PROFILAXIS:

- Asegurar no CRS antes de FD
- Uso profiláctico tocilizumab → Sigue en fase de EECC

• MONITORIZACIÓN:

- Evitar G durante alto riesgo de CRS

• MANEJO

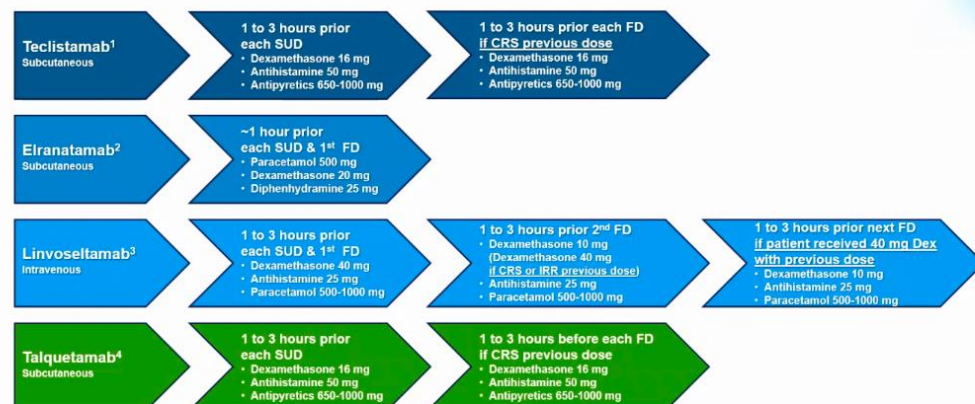
- Emperoamiento del ICANS tras uso de tocilizumab sin CRS.

PREMEDICACIÓN

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies

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Pre-Medications for BsAb-TCE Dosing Administration



BsAb-TCE= Bisppecific Antibody-T-Cell Engager. CRS=Cytokine Release Syndrome. FD=Full Dose. IRR=Infusion-Related Reaction. SUD=Step-up Dose.

1. TECVAYLI (teclistamab). EMA SmPC. Janssen-Cilag International NV. Beerse, Belgium. Jun 2024.

2. ELIXOIO (elranatamab). EMA SmPC. Pfizer Europe MA EEIG. Brussels, Belgium. Dec 2023.

3. LYNOSYTO (linvoseltamab). EMA SmPC. Biogenen Ireland Designated Activity Company (DAC). Dublin, Ireland. May 2025.

4. TALVEY (talquetamab). EMA SmPC. Janssen-Cilag International NV. Beerse, Belgium. Aug 2023.



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Considerations for Use of Bispecifics in RRMM

- Diferencia en el manejo de las premedicaciones

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NUEVA GENERACIÓN!!!

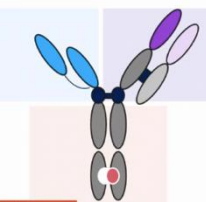
DIFERENTES EPITOPOS

POTENCIALMENTE PODRÍA MEJORAR LA AVIDEZ POR BCMA.

POTENCIALEMNTE MENOS CRS

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies
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Next Generation T-Cell Engaging Bispecific Antibody Design



Bivalent BCMA Binding

- ✓ Bivalent BCMA binding domain designed for high avidity to target myeloma cells

Differentiated BsAb Structural Design:

- Bivalent BCMA binding of etentamig is designed to promote T-cell-mediated killing and activation

Low Affinity CD3 Binding

- ✓ Low-affinity CD3 binding domain designed to reduce cytokine release

Differentiated BsAb Structural Design:

- The low-activating αCD3 moiety of etentamig is designed to retain cytotoxicity with lower levels of cytokines released

Silenced Fc Tail, Q4W Dosing

- ✓ Silenced Fc tail which retains FcRn binding, allowing for extended half-life and monthly dosing (Q4W)

Differentiated BsAb Structural Design:

- Structure is designed to allow for a longer half-life that enables longer intervals between doses

Non-Clinical Data

Clinical relevance of these structure activity relationships has not been established

Ententa is being developed as a differentiated, next-generation, BCMA x CD3 bsAb-TCE, composed of a high-avidity bivalent BCMA-binding domain, a present but silenced Fc tail, and a low-affinity CD3 binding domain.

BCMA=B-cell Maturation Antigen; BsAb=T-cell-Bispecific Antibody-T-Cell Engager; CD3=cluster of differentiation 3; FcRn=neonatal Fc receptor; Q4W=Every 4 Weeks.
1. Farnsworth DM, et al. submitted. 2023. 11/13-12/1 2023. 2. Buehler R, et al. ASCO Annual Meeting, June 1-5, 2018, Chicago, IL. 3. Buehler R, et al. Blood, 2017; 129(suppl. 1):551. 4. Shalunov D, et al. Poster #4695. ASH 2023. San Diego, CA. (Reused with permission from the American Society of Hematology. © 2023 The Authors. All rights reserved. Officially licensed by ASH for distribution via ASHNet). 5. Va R, et al. Poster #3378. ASH 2023. San Diego, CA. (Reused with permission from the American Society of Hematology. © 2023 The Authors. All rights reserved. Officially licensed by ASH for distribution via ASHNet). 6. Velasco A, et al. Poster #19165. ESHCT2024.

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Considerations for Use of Bispecifics in RRMM

- Unión bivalente a BCMA → ¿Mejorar la avidéz por la diana?
- Modificaciones estructurales → Mayor semivida → Administraciones mas espaciadas.
- Dominio de unión a CD3 de baja afinidad → ¿Disminuir CRS?

- Dosis mensual desde el inicio.
- Brazo administración ambulatoria
- Endpoints:
 - Clinical impact differences: CRS/ICANS

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Infecciones

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies
CHAIR: SHAJI KUMAR

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**Optimizing
Bispecific Therapy
Treatment in RRMM**

Paula Rodriguez-Otero, MD

**Paula Rodríguez-
Otero**
Optimizing Bispecific Therapy
Treatment in RRMM

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Infecciones y BsAb-TCEs

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment
Burden with Next Generation Therapies
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Infection-Related Safety Risks with BsAb-TCEs

Immunosuppression
➤ T-cell activation, proliferation, & exhaustion

T-cell Exhaustion

Hypogammaglobulinemia (HGG)
➤ Normal plasma cells depleted
➤ Low serum IgG levels (immunoparesis)

Cytopenias
➤ Neutropenia
➤ Lymphopenia
➤ Anemia
➤ Thrombocytopenia

Death of Mature B Cells

Death of Plasma Cells (Malignant & Benign)

BsAb-TCE therapies are associated with distinct AE profiles that include CRS and ICANS risks, as well as AEs leading to increased infection risk such as cytopenias and HGG

AE=Adverse Event; BsAb-TCE= Bisppecific Antibody T-Cell Engager; CRS=Cytokine Release Syndrome; HGG=Hypogammaglobulinemia; ICANS=Immune effector Cell Associated Neurotoxicity Syndrome; IgG=Immunoglobulin G.
1. Raju N, et al. Blood Cancer J. 2020 Aug 4;13(8):115. 2. Friesch MJ, et al. Cancer Cell. 2020;110(1):115-25. 3. Lapanis M, et al. Front Immunol. 2020;11:702. Images created with BioRender.com

Paula Rodríguez-Otero
Optimizing Bispecific Therapy Treatment in RRMM

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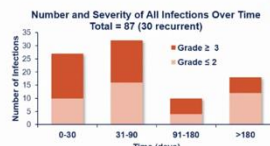
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• INFECCIONES:

- No sólo el F.
- También influyen:
 - Carga de la enfermedad.
 - Tratamientos previos
 - Agotamiento células T
- **Tener todos estos factores en cuenta.**

Single Center Experience: Real-World Infection Rates and Characterization in RRMM Patients Treated with BsAb-TCEs

Infection Characterization N=158	Tec N=77 (49%)	Elira N=24 (15%)	Tal N=57 (36%)
Median Follow-up, months	10.2	4.2	4.2
Any Grade Infections, n (%)	31 (40)	13 (54)*	13 (23)
Grade ≥ 3 Infections, n (%)	15 (19)	9 (38)	7 (12)
CMV Detection, n (%)	8 (18)	7 (29)	4 (8)
Any Grade CMV Reactions, n (%)	11 (24)	8 (33)	8 (15)
Grade 2 CMV Reactions, n (%)	3 (7)	3 (13)	1 (2)



- Any grade infections more frequent with BCMA-targeted agents vs GPRCSD
- Proactive CMV monitoring was implemented
- Infections became less frequent after initial months but accumulated with continued therapy
- Dose frequency reductions of bsAbs allowed per institutional protocol

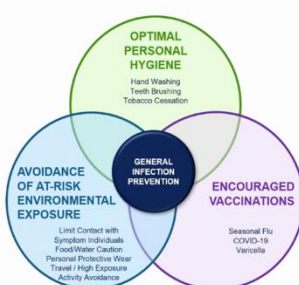
Higher rates of infection from Etx from this observational cohort were determined likely from less usage of IVIG, higher rates of prior BxAbx, smaller number of patients and shorter follow-up. ICMA-9 cell-inactivation antigen; EtxA5-TcT-specific antibody t-cell receptor; CMV-Cytomegalovirus; Etx-Encephalitis; GPR323Dip protein-coupled receptor class C group 5 member 9; Etx-Gade 100-invasive immunoglobulin; BxAbx-BxAbx-invasive myeloma; TcT-Tetanus; TcT-Tetanus; TcT-Tetanus.

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Treatment in RRMM

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Recommendations for Infection Safety Risk Management When Treating with BsAb-TCEs Beyond General Prevention



- ```

graph TD
 A[Prophylactic Measures] --> B[Management of AEs]
 B --> C[BsAb Dose Management]
 C --> D[BsAb-TCE Dosing]

```

**Prophylactic Measures**

  - Screenings
  - Prophylactic Anti-Microbials
  - Vaccinations

**Management of AEs**

  - IgG / HGG Monitoring
  - Heme AE Monitoring / Neutropenia Management
  - BsAb Dose Management

**BsAb-TCE Dosing**

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Optimizing Bispecific Therapy  
Treatment in RRMM

AE=Adverse Event; BSA=Body Surface Area; TCE=Tricarballycic Acid; TCE-1 Cell Engager; IgG=Immunoglobulin G; Heme-Hematological; HGG=Hypergammaglobulinemia; TCE-1 Cell Engager

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- RWE: En vida real generalmente menos infecciones grado  $\frac{3}{4}$  → Papel de la profilaxis
- Generalmente: Incidencia infecciones en los primeros seis meses del tratamiento → Pero MONITORIZACIÓN continua
- VACUNACION: ANTES DE BCMA
- Profilaxis antiviral

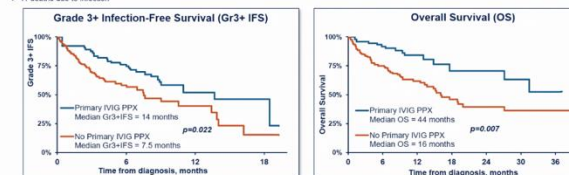
- **USO PROFILACTICO DE IGIV. Desde C1**

- **Pautas menos intensivas. ¿PERIODOS LIBRES DE TRATAMIENTO?**

### Primary IVIG Supplementation Reduced the Risk of High-Grade Infections in MM Patients Receiving Teclistamab

**Retrospective Analysis of 225 RRMM Patients Treated with Teclistamab [133 (41%) received primary rVIG PPX]**

- 288 infections were recorded in 136 patients (Median time to infection = 97 days)
- Majority of patients hospitalized for infectious complications (n=175, 81%)
- 11 deaths due to infection



- IVIG use for infection management may lead to better survival, however, poses additional burden of MM care

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Optimizing Bispecific Therapy  
Treatment in RRMM

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# Impacto del tratamiento

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment  
Burdens with Next Generation Therapies  
CHAIR: SHAJI KUMAR

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**Managing the Burden of MM Treatments**

Joseph Mikhael, MD

**Joseph Mikhael**  
Managing the Burden of MM Treatments

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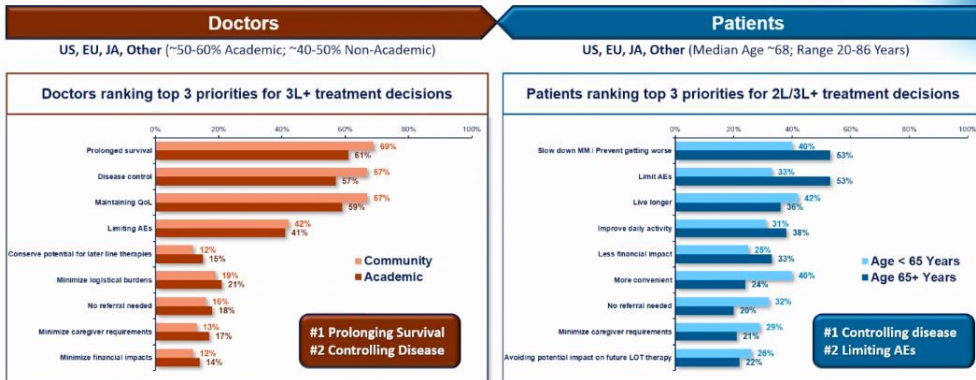
# Prioridades

## Preferencias:

- Visión médico versus visión paciente :
- Supervivencia versus independencia, control de la enfermedad, efectos secundarios, hospitalizaciones...
- Los pacientes quieren seguir con sus vidas y sus rutinas
- Pacientes acaban exhaustos.

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies  
CHAIR: SHAJI KUMAR

### Doctor Versus Patient Priorities for Treatment Decisions



**Joseph Mikhael**  
Managing the Burden of MM Treatments



Whilst doctors and patients choose disease control and limiting AEs as high priorities, other burdens including convenience, financial impact, and independence are important priorities for MM patients.

AE=Adverse Event; 2L/3L=Line of Therapy; EU=European Union; JA=Japan; QoL=Quality of Life; RRM=Relapsed/Refractory Multiple Myeloma; US=United States.  
1. Alseidi S, et al. 2025;19:1009-1104

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# Nuevas terapias: ¿Mejorar el impacto del tratamiento?

## 10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies

CHAIR: SHAJI KUMAR

### AIMM: How may newer therapies further improve MM treatment burden?

| Novel Therapy in Development | Anticabtagene Autoleucel (Anito-cel)                                              | Arlocabtagene Autoleucel (Arlo-cel)                                                                                                        | AZD0120 (FasTCAR-T)                                                                                                  | Ramantamig (JNJ-5322)                                                               | ABBV-2001 (ISB 2001)                   |
|------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------|
|                              |                                                                                   |                                                                                                                                            |                                                                                                                      |                                                                                     |                                        |
| MOA                          | CAR T                                                                             | CAR T                                                                                                                                      | Dual CAR T                                                                                                           | Trispecific T-cell Engager                                                          | Trispecific T-cell Engager             |
| Antigen                      | BCMA                                                                              | GPRC5D                                                                                                                                     | BCMA & CD19                                                                                                          | BCMA x GPRC5D x CD3                                                                 | BCMA x CD38 x CD3                      |
| Novelty / Differentiation    | Expedited Manufacturing                                                           | Non-BCMA CAR T                                                                                                                             | Dual Antigen CAR T                                                                                                   | Dual Antigen TsAb-TCE                                                               | Dual Antigen TsAb-TCE                  |
| Key Trials                   | Ph 2 IMMagine-1 (NCT05396885) 4L+ RRMM<br>Ph 3 IMMagine-3 (NCT06413498) 2-4L RRMM | Ph 1 CC-95266-MM-001 (NCT04674813) 2-4L RRMM<br>Ph 2 QUINTESSENTIAL (NCT06297226) 3L+ RRMM<br>Ph 3 QUINTESSENTIAL-2 (NCT06615479) 1-3 RRMM | Ph 1b/2 DURGA-1 (NCT05850234) 4L+ RRMM<br>Ph 1 DURGA-2 (NCT07073547) HR NDMM<br>Ph 3 DURGA-4 (NCT07391657) 2-4L RRMM | Ph 1 CR109234 (NCT05652335) 4L+ RRMM & ALA<br>Ph 3 TRilogy-4 (NCT07258511) 4L+ RRMM | Ph 1 TRIgnite-1 (NCT05862012) 3L+ RRMM |

This slide illustrates data from different studies. It is not intended to suggest or imply comparison between products or regimens without supportive data.  
ALA=light chain amyloidosis. BCMA=b-cell maturation antigen. CAR T=chimeric antigen receptor T-cell. CD3/CD19/CD38=cluster of differentiation 3/19/38. GPRC5D=g protein-coupled receptor class C group 5 member D. HR=high risk. L=line of therapy. MM=multiple myeloma. MOA=mechanism of action. NDMM=newly diagnosed multiple myeloma. Ph=phase. RRMM=relapsed/refractory multiple myeloma. scFv=single-chain variable fragment. TsAb-TCE=trispecific antibody T-cell engager.  
1. <https://clinicaltrials.gov>. 2. Patel K, et al. Oral #256. ASH 2025. 3. Bai S, et al. Poster #PA-080. IMS2025. Toronto, Canada. 4. Du J, et al. ASH 2025, abstract #258. 5. Richard S, et al. ASH 2025, abstract #269. 6. Popel R, et al. Oral #S100. EHA2025. Milan, Italy. 7. Krishnan A, et al. Poster #4042. ASH2025. Orlando, FL. 8. Lichtman E, et al. Oral #7514. ASCO2025. Chicago, IL. 9. Quach, et al. Oral #GA-035. IMS 2025. Toronto, Canada.



**Joseph Mikhael**  
Managing the Burden of MM Treatments

10:00 - 11:30 AIMM : An Interactive Multiple Myeloma (MM) Journey- Managing Disease and Treatment Burdens with Next Generation Therapies  
CHAIR: SHAJI KUMAR

ABBV-2001 (CD38×BCMA×CD3) Trispecific Antibody T-cell Engager

**Joseph Mikhael**  
Managing the Burden of MM Treatments

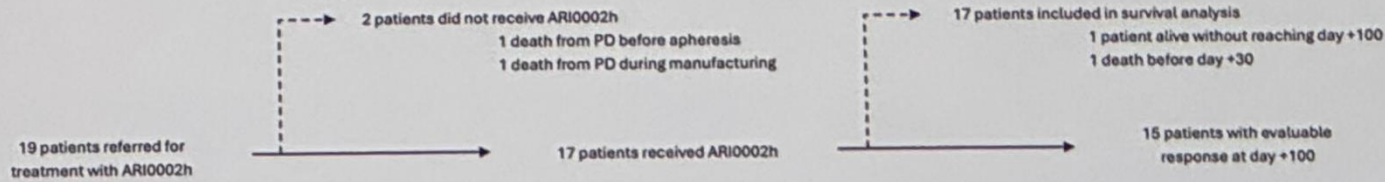
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# DISCUSIÓN

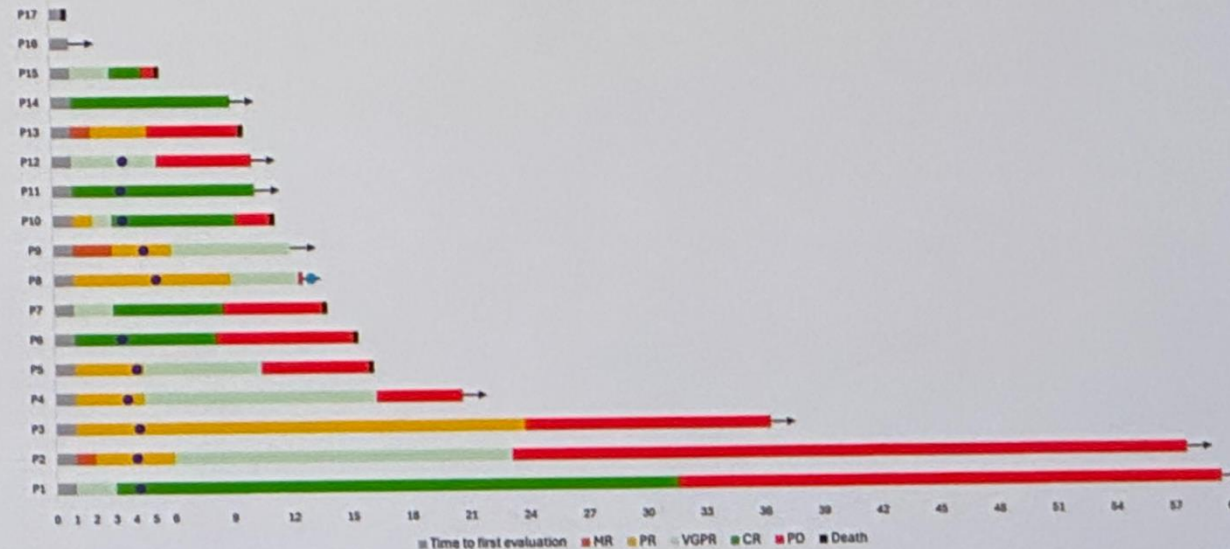
- **TOCILIZUMAB PROFILÁCTICO** con biespecíficos ( Off label) :
  - No en biespecíficos si ingresado, SI en paciente ambulatorio.
  - Tocilizumab: Acción dura 4-6 días,. Usar sólo en primera dosis del step up..
  - Si no se usa → Recomendación usarlo ya desde CRS G1.
- Importancia de la **evolución en el manejo** de los tratamientos
- **IVIG**: Sistemáticamente de forma mensual desde C1.
- **DEXAMETASONA 10mg** en profilaxis debería ser suficiente, recordar pararla a tiempo para evitar agotamiento células T.
- Revacunación antes de biespecíficos. Revacunación periódica (neumococo, VRS...)-→ **Importancia de vacunación de FAMILIA y CUIDADORES**
- **DURACIÓN DEL TRATAMIENTO**: Importancia de la profundidad de respuesta → No está claro el punto en el que podríamos plantear suspender el tratamiento.
- RECHALLENGE → Parece improbable. Hay que asegurar cuando parar el tratamiento...
  - Riesgo de infección → Relacionado claramente con la duración del tratamiento.
- Ideal: Poder identificar que terapia dirigir a cada paciente → NO respuesta

# Cesni-cel (ARI 0002h) in Ultra-high Risk Myeloma with PCL and/or CNS Involvement

12 had PCL, 5 had CNS-MM and 2 had dual involvement



- 15/17 (88%) had evaluable response at day +100: 10 with PCL, 4 with CNS-MM and 1 with PCL/CNS-MM.
- **ORR at day +100 was 88%.**
- 8/15 (53%) achieved a vgPR or better;
- 5/15 (33%) improved responses after day +100.
- **BM-MRD negativity rate was 100%** in all patients with available information at day +100 (14/15; one case not assessed).



# Muchas Gracias

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## EHA 2026

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Más conocimiento,  
**más opciones,**  
mejores decisiones  
para cada paciente.

**NO TRATAR  
MIELOMAS, TRATAR  
PERSONAS**



Personalización



Innovación



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Esperanza

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# Eficacia comparativa de linvoseltamab frente a teclistamab en pacientes con mieloma múltiple triple clase expuesto en recaída/refractario: análisis ajustado por comparación indirecta (MAIC).

## Comparative efficacy of linvoseltamab versus teclistamab in triple-class exposed relapsed/refractory multiple myeloma: updated matching-adjusted indirect comparison with longer follow-up

Masuda, T., Hara, T., Nishida, T., et al. J Clin Oncol. 2024;42(15):2155-2163. doi:10.1200/JCO.2023.42.15.2155

### BACKGROUND

Linvoseltamab is a first-in-class, anti-CD38 monoclonal antibody (mAb) approved for the treatment of relapsed and refractory multiple myeloma (RRMM). Teclistamab is a first-in-class, anti-CD38 mAb approved for the treatment of RRMM. Both mAbs are CD38-targeting antibodies that bind to CD38 on the surface of plasma cells, leading to cell death. Linvoseltamab is a humanized mAb, while teclistamab is a murine mAb. Both mAbs are administered intravenously. Linvoseltamab is administered as a 30-minute infusion, while teclistamab is administered as a 90-minute infusion. Both mAbs are administered every 2 weeks for the first 8 weeks, followed by every 4 weeks thereafter. The efficacy of both mAbs has been evaluated in phase 1 and phase 2 clinical trials. In this study, we compared the efficacy of linvoseltamab and teclistamab in patients with RRMM using a matching-adjusted indirect comparison (MAIC) with longer follow-up.

### OBJECTIVE

To compare the efficacy of linvoseltamab versus teclistamab in patients with RRMM using a MAIC with longer follow-up.

### METHODS

We conducted a MAIC with longer follow-up to compare the efficacy of linvoseltamab and teclistamab in patients with RRMM. The study included patients from the LINTOX and TELLURIO phase 2 clinical trials. The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), time to next treatment (TTNT), and best response rate (BRR). The MAIC was conducted using the R package 'MatchIt'. The results of the MAIC are presented in Table 1.

### RESULTS

The MAIC with longer follow-up showed that linvoseltamab had a significantly higher OS compared to teclistamab in patients with RRMM. The hazard ratio (HR) for OS was 0.65 (95% CI, 0.45-0.95). The PFS, TTNT, and BRR were also significantly higher in the linvoseltamab group compared to the teclistamab group.

### CONCLUSIONS

Our results suggest that linvoseltamab may be a more effective treatment option than teclistamab for patients with RRMM. Further studies are needed to confirm these findings.

### KEYWORDS

linvoseltamab, teclistamab, multiple myeloma, relapsed and refractory, matching-adjusted indirect comparison, MAIC, overall survival, progression-free survival, time to next treatment, best response rate.

### INTRODUCTION

Multiple myeloma (MM) is a hematologic malignancy characterized by the proliferation of plasma cells in the bone marrow. It is the second most common hematologic malignancy in adults. The standard of care for MM has evolved over time, with the introduction of novel agents and combination therapies. In recent years, CD38-targeting antibodies have emerged as a promising class of drugs for the treatment of MM. Linvoseltamab and teclistamab are two such antibodies that have been evaluated in clinical trials.

Linvoseltamab is a humanized anti-CD38 mAb that binds to CD38 on the surface of plasma cells, leading to cell death. It is administered intravenously every 2 weeks for the first 8 weeks, followed by every 4 weeks thereafter. Teclistamab is a murine anti-CD38 mAb that also binds to CD38 on the surface of plasma cells, leading to cell death. It is administered intravenously every 2 weeks for the first 8 weeks, followed by every 4 weeks thereafter.

Both mAbs have been evaluated in phase 1 and phase 2 clinical trials. In the LINTOX phase 2 trial, linvoseltamab was compared to a control group in patients with RRMM. The results showed that linvoseltamab had a significantly higher OS compared to the control group. In the TELLURIO phase 2 trial, teclistamab was compared to a control group in patients with RRMM. The results showed that teclistamab had a significantly higher OS compared to the control group.

Given the promising results of both mAbs in clinical trials, it is important to compare their efficacy in a head-to-head trial. However, a direct comparison between linvoseltamab and teclistamab has not been conducted. Therefore, we conducted a MAIC with longer follow-up to compare the efficacy of linvoseltamab and teclistamab in patients with RRMM.

The MAIC with longer follow-up showed that linvoseltamab had a significantly higher OS compared to teclistamab in patients with RRMM. The HR for OS was 0.65 (95% CI, 0.45-0.95). The PFS, TTNT, and BRR were also significantly higher in the linvoseltamab group compared to the teclistamab group.

Our results suggest that linvoseltamab may be a more effective treatment option than teclistamab for patients with RRMM. Further studies are needed to confirm these findings.

### TAKEAWAYS

- In the absence of head-to-head trials, MAICs following well-established methods offer benefits in understanding the relative efficacy of treatment options while adjusting for differences in trial populations and outcomes.
- Results from the updated MAIC with longer follow-up are consistent with prior analyses, demonstrating statistically significant improvements for linvoseltamab versus teclistamab in OS, PFS, OS, and TTNT.
- These findings, with the longest available follow-up, suggest continued greater efficacy for linvoseltamab versus teclistamab, highlighting its potential as a highly effective treatment option for patients with TCR RRMM.

### POSTER PFB30

FIGURE 1. DOR per IRC before and after matching on the six most important predefined prognostic factors\*

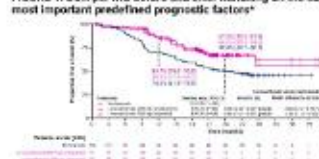


FIGURE 2. PFS per IRC before and after matching on the six most important predefined prognostic factors

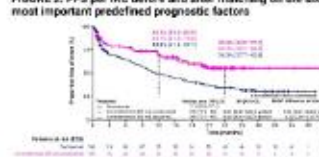


FIGURE 3. OS before and after matching on the six most important predefined prognostic factors



FIGURE 4. TTNT before and after matching on the six most important predefined prognostic factors

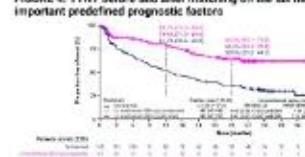


TABLE 1. Comparison of efficacy outcomes before and after matching on the six most important predefined prognostic factors

| Outcome      | Linvoseltamab    | Teclistamab      | HR (95% CI)      | P-value | Linvoseltamab    | Teclistamab      | HR (95% CI)      | P-value |
|--------------|------------------|------------------|------------------|---------|------------------|------------------|------------------|---------|
| OS per IRC   | 53.0 (31.2-74.8) | 71.6 (50.2-93.0) | 0.65 (0.45-0.95) | <0.01   | 53.0 (31.2-74.8) | 71.6 (50.2-93.0) | 0.65 (0.45-0.95) | <0.01   |
| PFS per IRC  | 38.0 (18.5-57.5) | 60.0 (40.0-80.0) | 0.63 (0.43-0.93) | <0.01   | 38.0 (18.5-57.5) | 60.0 (40.0-80.0) | 0.63 (0.43-0.93) | <0.01   |
| TTNT per IRC | 56.1 (38.8-73.4) | 62.0 (42.0-82.0) | 0.91 (0.61-1.32) | 0.15    | 56.1 (38.8-73.4) | 62.0 (42.0-82.0) | 0.91 (0.61-1.32) | 0.15    |

### LIMITATIONS

- This study was a retrospective MAIC and therefore subject to the limitations of retrospective studies. The results of the MAIC should be interpreted with caution.
- The study included patients from two phase 2 clinical trials, which may have introduced selection bias.
- The MAIC with longer follow-up was conducted using the R package 'MatchIt', which may have introduced some bias.
- The study did not include a head-to-head trial, which would have provided more definitive results.
- The study did not include a larger number of patients, which would have increased the statistical power.

### APPENDICES

Supplemental appendices are available at <https://doi.org/10.1200/JCO.2023.42.15.2155>.

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- Estudio retrospectivo de comparación indirecta ajustada utilizando datos individuales del ensayo LINKER-MM1 (linvoseltamab) frente a datos publicados de MajesTEC-1 (teclistamab).
- Conclusiones:** Tras el ajuste por los principales factores pronósticos, **linvoseltamab demostró una mayor TRG y una duración de respuesta más prolongada, con una tendencia a mejorar la SLP y el tiempo hasta el siguiente tratamiento frente a teclistamab.**
- Estos resultados sugieren que linvoseltamab podría ofrecer una eficacia superior en pacientes con mieloma múltiple triple clase expuesto, **aunque deben interpretarse con cautela por tratarse de una comparación indirecta y no aleatorizada.**

**Multiple myeloma**

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1 of 1

Appendix

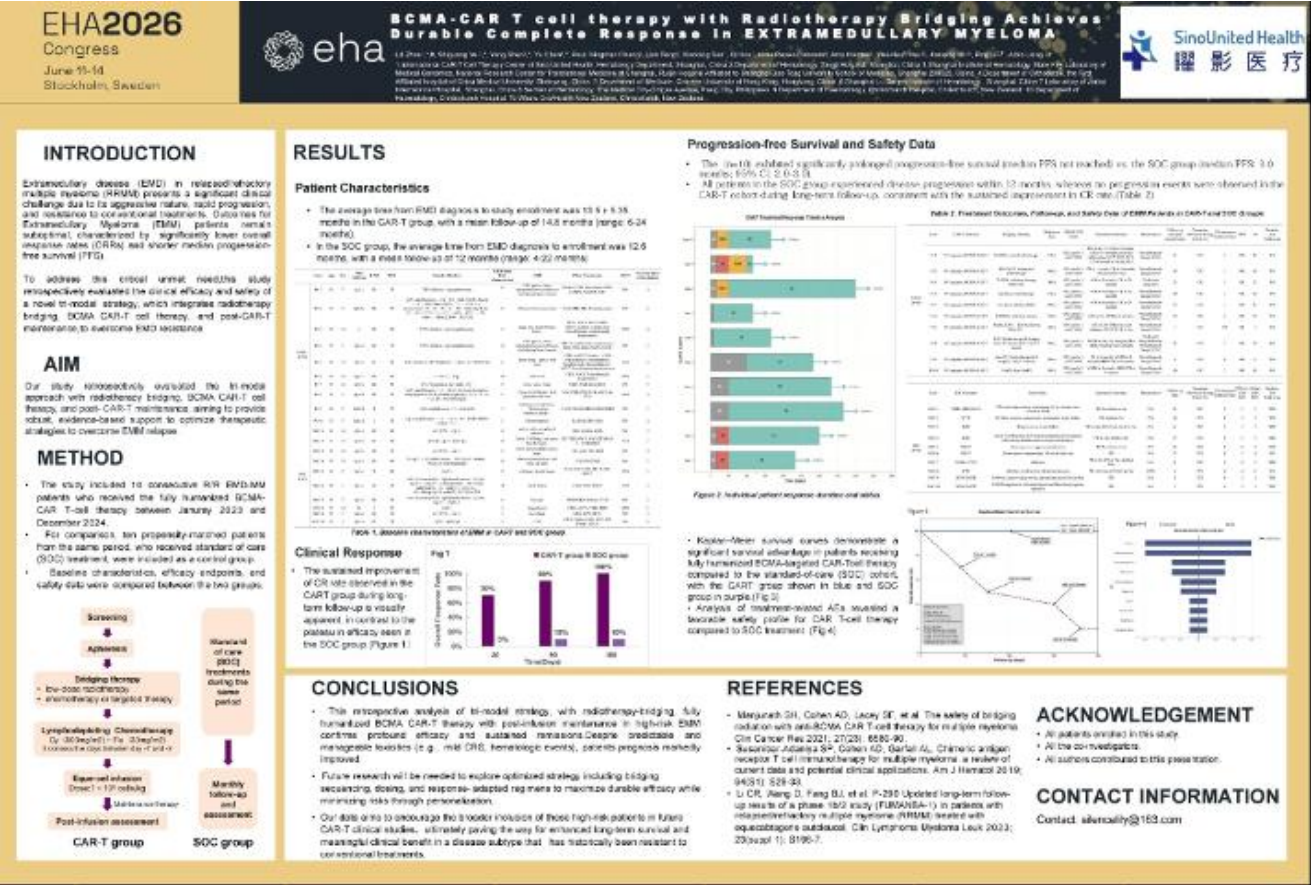
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Presented at American Society of Hematology (ASH) 2023, December, December 1-5, 2023, and at International Myeloma Workshop (IMW) 2023, December 1-5, 2023, both in Chicago, IL, USA.

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# La terapia con células CAR-T anti-BCMA con radioterapia como tratamiento puente logra una respuesta completa duradera en el mieloma múltiple extramedular.



Estudio retrospectivo que evaluó a pacientes con MM y enfermedad extramedular tratados con CAR-T anti-BCMA y que recibieron radioterapia como tratamiento puente frente a una cohorte sin enfermedad extramedular.

**Conclusiones:** La incorporación de radioterapia como terapia puente antes del CAR-T anti-BCMA se asoció con respuestas profundas y duraderas, alcanzándose una elevada proporción de RC en pacientes con enfermedad extramedular.

Además, la **SLP y el perfil de seguridad fueron comparables** a los observados en pacientes sin enfermedad extramedular, lo que sugiere que esta estrategia puede mitigar el mal pronóstico tradicional de este subgrupo de alto riesgo.