De la necesidad a la realidad en el paciente triple expuesto

Johnson&Johnson

Conflictos de interés

- He proporcionado asesoramiento científico a ...
- He participado en reuniones médicas organizadas por ...
- He recibido pagos por presentaciones y asesorías de ...
- Recibo honorarios por esta presentación

Definición del mieloma múltiple

El mieloma se diagnostica con mayor frecuencia en personas de **65-75 años.**[1]

La mediana de edad al diagnóstico es de **69 años.**[1]

Es, principalmente, una enfermedad de **la tercera edad.**[2]

Distribución de nuevos casos de MM por edad[1]

SEER 21 2018-2022. Todas las razas, ambos sexos

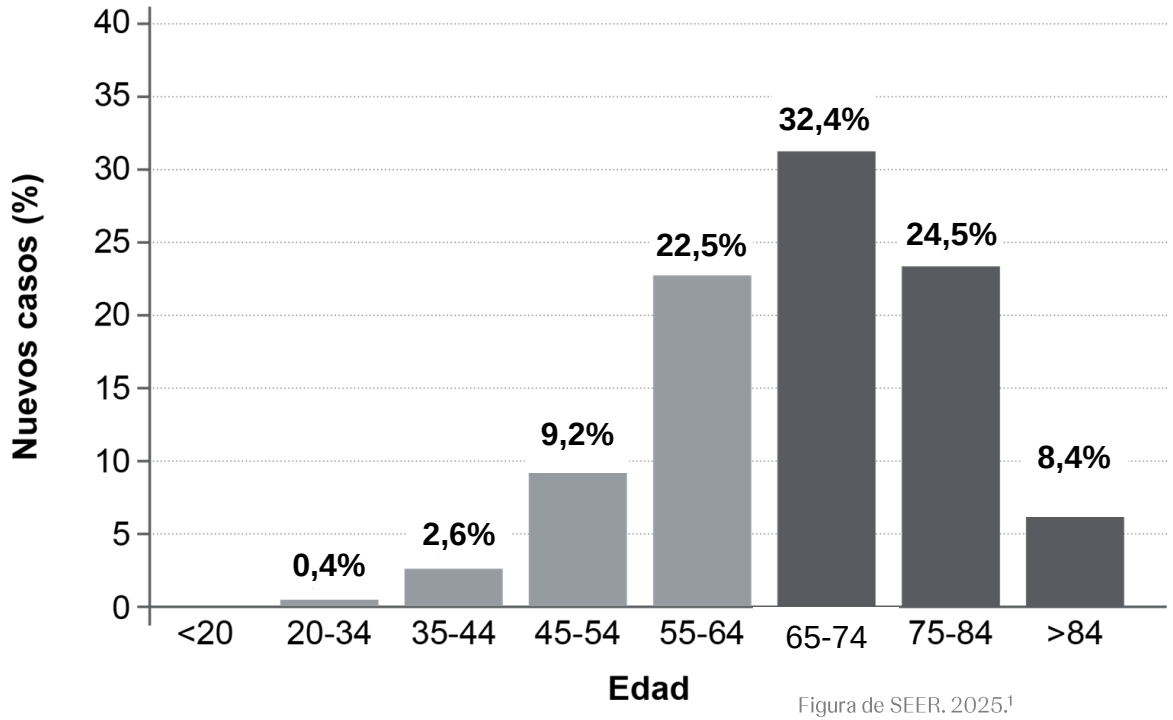


Figura de SEER. 2025.[1]

MM: mieloma múltiple.

1. SEER (Surveillance, Epidemiology, and End Results Program). Cancer Facts: Myeloma. U.S. Department of Health and Human Services. National Institutes of Health. National Cancer Institute. Disponible en: https://seer.cancer.gov/statfacts/html/mulmy.html Último acceso: abril 2025; 2. Larocca A, *et al.* Patient-centered practice in elderly myeloma patients: an overview and consensus from the European Myeloma Network (EMN) Leukemia. 2018;32(8):1697-1712.

Evolución del mieloma múltiple

El MM sigue siendo **incurable.**[1]

Con cada **recaída sucesiva,** la posibilidad de respuesta y la duración de la misma se reducen.[1]

Con cada **línea de tratamiento,** aumenta la carga de comorbilidad, las complicaciones y disminuye la eficacia del tratamiento.[2]

Representación esquemática del curso del MM[3]

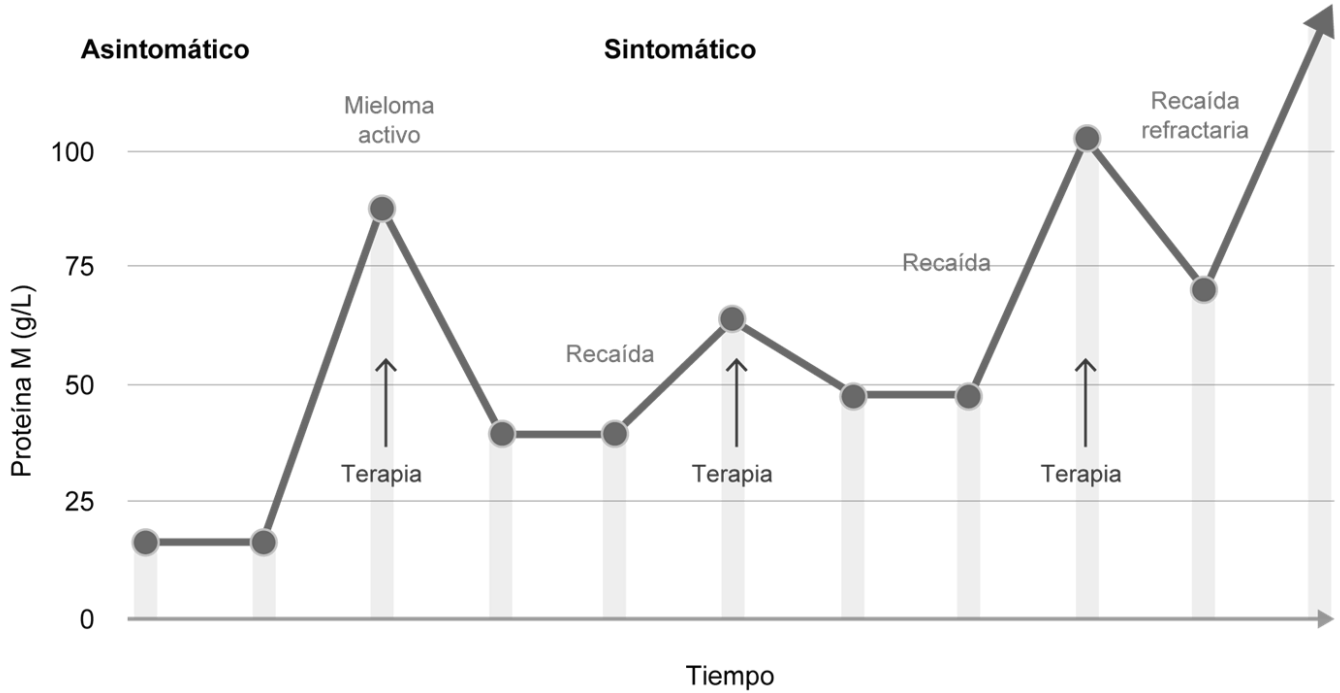
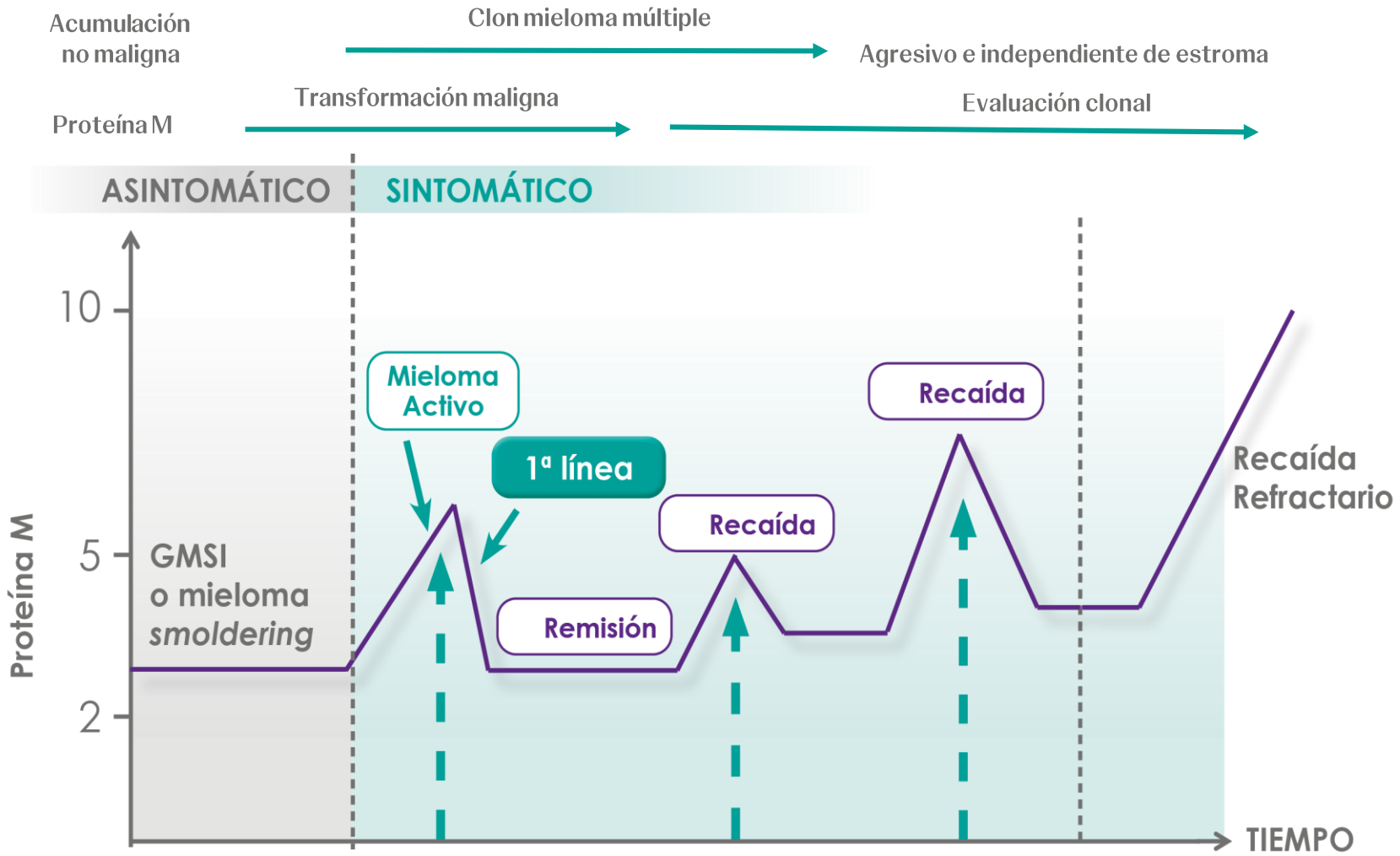


Figura adaptada de Kurtin et al. 2013.[3] Figura completa aquí.

MM: mieloma múltiple

1. Darzalex, assessment report. EMA/CHMP/22749/2020; 2. Yong K, *et al.* Multiple myeloma: patient outcomes in real-world practice. Br J Haematol. 2016;175(2):252-264, 3. Kurtin SE. Novel agents for the treatment of multiple myeloma: proteasome inhibitors and immunomodulatory agents. J Adv Pract Oncol. 2013;4 (Suppl 1):5–14



La cronología depende de los factores de riesgo individuales, incluidos los cambios genéticos y fenotípicos, la profundidad y duración de la respuesta a la terapia, la persistencia de una célula madre de MM maligna y la evolución de clones de MM competidores.[1]

Figura 2 de Kurtin SE, *et al.* 2013 . Trayectoria de la enfermedad del mieloma múltiple caracterizada por transformación maligna; ciclos seriados de respuesta, remisión y recaída en presencia de tratamiento; y evolución clonal con disminución de la profundidad y duración de la respuesta a lo largo del tiempo. Información de Agarwal & Ghobrial (2013), Borrello (2012), Durie *et al.* (2003), Keats *et al.* (2012).

GMSI: gammapatía monoclonal de significado incierto; **MM:** mieloma múltiple.

1. Kurtin SE, *et al.* Relapsed or Relapsed/Refractory Multiple Myeloma. J Adv Pract Oncol 2013;4(6)(supp 1):5-14.

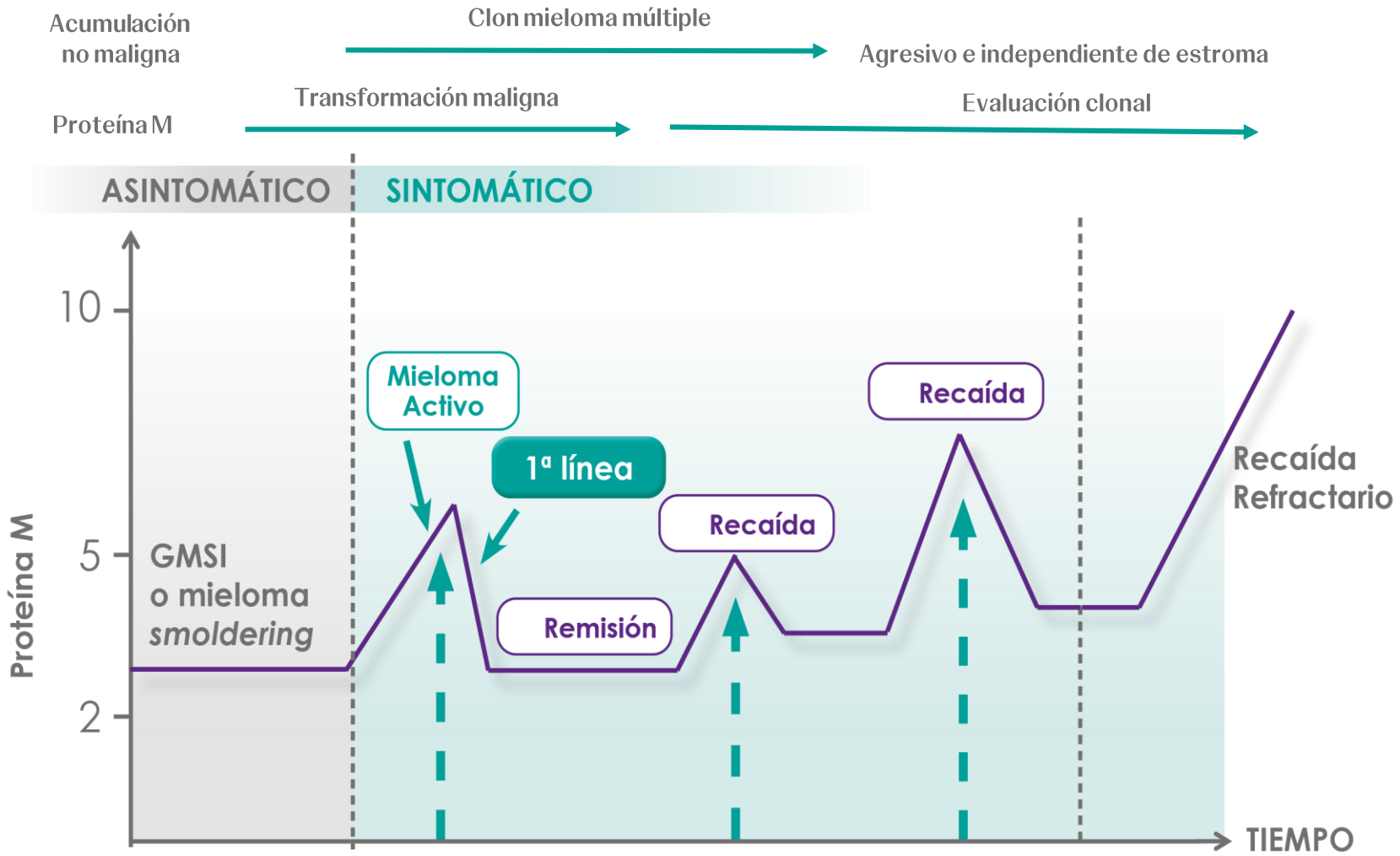
Importancia de una intervención temprana y eficaz en el tratamiento del MM

- Las nuevas combinaciones inducen **respuestas rápidas, profundas y sostenidas.**[1]
- La **remisión completa es más probable en pacientes con un nuevo diagnóstico de MM** que en aquellos con enfermedad en recaída/refractaria.[2]

Figura adaptada de Kurtin SE. 2013.[3] Figura completa aquí.

MM: mieloma múltiple.

1. Landgren O, *et al.* Modern multiple myeloma therapy: deep, sustained treatment response and good clinical outcomes. J Intern Med . 2017 Apr;281(4):365-382; **2.** Cejalvo MJ, *et al.* Which therapies will move to the front line for multiple myeloma? J. Expert Rev Hematol. 2017;10(5):383-392; **3.** Kurtin SE. Novel agents for the treatment of multiple myeloma: proteasome inhibitors and immunomodulatory agents. J Adv Pract Oncol. 2013;4 (Suppl 1):5–14.



La cronología depende de los factores de riesgo individuales, incluidos los cambios genéticos y fenotípicos, la profundidad y duración de la respuesta a la terapia, la persistencia de una célula madre de MM maligna y la evolución de clones de MM competidores.[1]

Figura 2 de Kurtin SE, *et al.* 2013 . Trayectoria de la enfermedad del mieloma múltiple caracterizada por transformación maligna; ciclos seriados de respuesta, remisión y recaída en presencia de tratamiento; y evolución clonal con disminución de la profundidad y duración de la respuesta a lo largo del tiempo. Información de Agarwal & Ghobrial (2013), Borrello (2012), Durie *et al.* (2003), Keats *et al.* (2012).

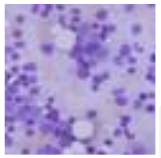
GMSI: gammapatía monoclonal de significado incierto; **MM:** mieloma múltiple.

1. Kurtin SE, *et al.* Relapsed or Relapsed/Refractory Multiple Myeloma. J Adv Pract Oncol 2013;4(6)(supp 1):5-14.

Criterios de progresión* (IMWG 2016)

Incremento > 25% (1 o +):

- CM sérico (incremento absoluto tiene que ser ≥0,5g/dl)
- Incremento del CM sérico ≥1 g/dl, si el valor del CM era ≥5g/dl
- CM urinario (incremento absoluto tiene que ser ≥200mg/24h)
- De la diferencia entre CLLs involucrada/no involucrada, en pacientes sin CM en suero u orina (incremento absoluto tiene que ser >10mg/dl)

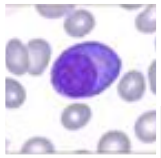


MO

- % CP en médula ósea independientemente de la cifra basal (incremento absoluto tiene que ser ≥10%), en pacientes sin CM en suero, orina ni CLLs medibles

Nuevas lesiones

- Aparición de lesiones nuevas (≥1), incremento ≥50% en la SDM en >1 lesión, o incremento ≥50% en el diámetro máximo de una lesión previa >1cm en el eje transversal



CP en sangre

- Incremento ≥50% en las CP circulantes en sangre (mínimo 200c/µl) si es la única expresión de la enfermedad medible

*La inmunofijación positiva por sí sola en un paciente previamente clasificado como que ha logrado una respuesta completa no se considerará progresión. Para calcular el tiempo transcurrido hasta la progresión y la supervivencia sin progresión, los pacientes que hayan logrado una respuesta completa y alcancen EMR- deben evaluarse utilizando los criterios enumerados para la enfermedad progresiva. Los criterios de recaída a partir de una respuesta completa o de recaída a partir de EMR deben utilizarse únicamente para calcular la supervivencia libre de enfermedad. En el caso de que un valor se considere un resultado espurio a criterio del médico (por ejemplo, un posible error de laboratorio), ese valor no se tendrá en cuenta al determinar el valor más bajo.[1]

Datos extraídos de la Tabla 4 de Kumar S, *et al.* Lancet Oncol 2016. Tabla completa disponible AQUÍ

CLL: cadenas ligeras libres; **CM:** componente monoclonal; **CP:** células plasmáticas; **EMR:** enfermedad mínima residual; **EMR-:** enfermedad mínima residual negativa; **IMWG:** *International Myeloma Working Group*; **MO:** médula ósea; **SDM:** suma de los productos de los diámetros perpendiculares máximos de las lesiones medidas.

1. Kumar S, *et al.* International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple mieloma. Lancet Oncol 2016;17:e328-46.

	Response criteria*
IMWG MRD criteria (requires a complete response as defined below)	
Sustained MRD-negative	MRD negativity in the marrow (NGF or NGS, or both) and by imaging as defined below, confirmed minimum of 1 year apart. Subsequent evaluations can be used to further specify the duration of negativity (eg, MRD-negative at 5 years)†
Flow MRD-negative	Absence of phenotypically aberrant clonal plasma cells by NGF‡ on bone marrow aspirates using the EuroFlow standard operation procedure for MRD detection in multiple myeloma (or validated equivalent method) with a minimum sensitivity of 1 in 10^5 nucleated cells or higher
Sequencing MRD-negative	Absence of clonal plasma cells by NGS on bone marrow aspirate in which presence of a clone is defined as less than two identical sequencing reads obtained after DNA sequencing of bone marrow aspirates using the LymphoSIGHT platform (or validated equivalent method) with a minimum sensitivity of 1 in 10^5 nucleated cells§ or higher
Imaging plus MRD-negative	MRD negativity as defined by NGF or NGS plus disappearance of every area of increased tracer uptake found at baseline or a preceding PET/CT or decrease to less mediastinal blood pool SUV or decrease to less than that of surrounding normal tissue¶
Standard IMWG response criteria‖	
Stringent complete response	Complete response as defined below plus normal FLC ratio** and absence of clonal cells in bone marrow biopsy by immunohistochemistry (κ/λ ratio ≤4:1 or ≥1:2 for κ and λ patients, respectively, after counting ≥100 plasma cells)††
Complete response	Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and <5% plasma cells in bone marrow aspirates
Very good partial response	Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥90% reduction in serum M-protein plus urine M-protein level <100 mg per 24 h
Partial response	≥50% reduction of serum M-protein plus reduction in 24 h urinary M-protein by ≥90% or to <200 mg per 24 h; If the serum and urine M-protein are unmeasurable, a ≥50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria; If serum and urine M-protein are unmeasurable, and serum-free light assay is also unmeasurable, ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma-cell percentage was ≥30%. In addition to these criteria, if present at baseline, a ≥50% reduction in the size (SPD)§§ of soft tissue plasmacytomas is also required
Minimal response	≥25% but ≤49% reduction of serum M-protein and reduction in 24-h urine M-protein by 50–89%. In addition to the above listed criteria, if present at baseline, a ≥50% reduction in the size (SPD)§§ of soft tissue plasmacytomas is also required
Stable disease	Not recommended for use as an indicator of response; stability of disease is best described by providing the time-to-progression estimates. Not meeting criteria for complete response, very good partial response, partial response, minimal response, or progressive disease
Progressive disease ¶¶,‖‖	Any one or more of the following criteria: Increase of 25% from lowest confirmed response value in one or more of the following criteria: Serum M-protein (absolute increase must be ≥0·5 g/dL); Serum M-protein increase ≥1 g/dL, if the lowest M component was ≥5 g/dL; Urine M-protein (absolute increase must be ≥200 mg/24 h); In patients without measurable serum and urine M-protein levels, the difference between involved and uninvolved FLC levels (absolute increase must be >10 mg/dL); In patients without measurable serum and urine M-protein levels and without measurable involved FLC levels, bone marrow plasma-cell percentage irrespective of baseline status (absolute increase must be ≥10%); Appearance of a new lesion(s), ≥50% increase from nadir in SPD§§ of >1 lesion, or ≥50% increase in the longest diameter of a previous lesion >1 cm in short axis; ≥50% increase in circulating plasma cells (minimum of 200 cells per μL) if this is the only measure of disease

(Table 4 and footnotes continue on the next page)

(Continued from previous page)

Clinical relapse	Clinical relapse requires one or more of the following criteria: Direct indicators of increasing disease and/or end organ dysfunction (CRAB features) related to the underlying clonal plasma-cell proliferative disorder. It is not used in calculation of time to progression or progression-free survival but is listed as something that can be reported optionally or for use in clinical practice; Development of new soft tissue plasmacytomas or bone lesions (osteoporotic fractures do not constitute progression); Definite increase in the size of existing plasmacytomas or bone lesions. A definite increase is defined as a 50% (and ≥1 cm) increase as measured serially by the SPD§§ of the measurable lesion; Hypercalcaemia (>11 mg/dL); Decrease in haemoglobin of ≥2 g/dL not related to therapy or other non-myeloma-related conditions; Rise in serum creatinine by 2 mg/dL or more from the start of the therapy and attributable to myeloma; Hyperviscosity related to serum paraprotein
Relapse from complete response (to be used only if the end point is disease-free survival)	Any one or more of the following criteria: Reappearance of serum or urine M-protein by immunofixation or electrophoresis; Development of ≥5% plasma cells in the bone marrow; Appearance of any other sign of progression (ie, new plasmacytoma, lytic bone lesion, or hypercalcaemia see above)
Relapse from MRD negative (to be used only if the end point is disease-free survival)	Any one or more of the following criteria: Loss of MRD negative state (evidence of clonal plasma cells on NGF or NGS, or positive imaging study for recurrence of myeloma); Reappearance of serum or urine M-protein by immunofixation or electrophoresis; Development of ≥5% clonal plasma cells in the bone marrow; Appearance of any other sign of progression (ie, new plasmacytoma, lytic bone lesion, or hypercalcaemia)

For MRD assessment, the first bone marrow aspirate should be sent to MRD (not for morphology) and this sample should be taken in one draw with a volume of minimally 2 mL (to obtain sufficient cells), but maximally 4–5 mL to avoid haemodilution. IMWG=International Myeloma Working Group. MRD=minimal residual disease. NGF=next-generation flow. NGS=next-generation sequencing. FLC=free light chain. M-protein=myeloma protein. SPD=sum of the products of the maximal perpendicular diameters of measured lesions. CRAB features=calcium elevation, renal failure, anaemia, lytic bone lesions. FCM=flow cytometry. SUV_{max}=maximum standardised uptake value. MFC=multiparameter flow cytometry. ^{18}F-FDG PET=^{18}F-fluorodeoxyglucose PET. ASCT=autologous stem cell transplantation.
*All response categories require two consecutive assessments made any time before starting any new therapy; for MRD there is no need for two consecutive assessments, but information on MRD after each treatment stage is recommended (eg, after induction, high-dose therapy/ASCT, consolidation, maintenance). MRD tests should be initiated only at the time of suspected complete response. All categories of response and MRD require no known evidence of progressive or new bone lesions if radiographic studies were performed. However, radiographic studies are not required to satisfy these response requirements except for the requirement of FDG PET if imaging MRD-negative status is reported. †Sustained MRD negativity when reported should also annotate the method used (eg, sustained flow MRD-negative, sustained sequencing MRD-negative). ‡Bone marrow MFC should follow NGF guidelines.[39] The reference NGF method is an eight-colour two-tube approach, which has been extensively validated. The two-tube approach improves reliability, consistency, and sensitivity because of the acquisition of a greater number of cells. The eight-colour technology is widely available globally and the NGF method has already been adopted in many flow laboratories worldwide. The complete eight-colour method is most efficient using a lyophilised mixture of antibodies which reduces errors, time, and costs. 5 million cells should be assessed. The FCM method employed should have a sensitivity of detection of at least 1 in 10^4 plasma cells. §DNA sequencing assay on bone marrow aspirate should use a validated assay such as LymphoSIGHT (Sequenta). ¶Criteria used by Zamagni and colleagues,[85] and expert panel (IMPetUs; Italian Myeloma criteria for PET Use).[86,87] Baseline positive lesions were identified by presence of focal areas of increased uptake within bones, with or without any underlying lesion identified by CT and present on at least two consecutive slices. Alternatively, an SUV_{max}=2·5 within osteolytic CT areas >1 cm in size, or SUV_{max}=1·5 within osteolytic CT areas ≤1 cm in size were considered positive. Imaging should be performed once MRD negativity is determined by MFC or NGS. ‖Derived from international uniform response criteria for multiple myeloma.[11] Minor response definition and clarifications derived from Rajkumar and colleagues.[14] When the only method to measure disease is by serum FLC levels: complete response can be defined as a normal FLC ratio of 0·26 to 1·65 in addition to the complete response criteria listed previously. Very good partial response in such patients requires a ≥90% decrease in the difference between involved and uninvolved FLC levels. All response categories require two consecutive assessments made at any time before the institution of any new therapy; all categories also require no known evidence of progressive or new bone lesions or extramedullary plasmacytomas if radiographic studies were performed. Radiographic studies are not required to satisfy these response requirements. Bone marrow assessments do not need to be confirmed. Each category, except for stable disease, will be considered unconfirmed until the confirmatory test is performed. The date of the initial test is considered as the date of response for evaluation of time dependent outcomes such as duration of response. **All recommendations regarding clinical uses relating to serum FLC levels or FLC ratio are based on results obtained with the validated Freelite test (Binding Site, Birmingham, UK). ††Presence/absence of clonal cells on immunohistochemistry is based upon the κ/λ/L ratio. An abnormal κ/λ ratio by immunohistochemistry requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting presence of an abnormal clone is κ/λ of >4:1 or <1:2. ‡‡Special attention should be given to the emergence of a different monoclonal protein following treatment, especially in the setting of patients having achieved a conventional complete response, often related to oligoclonal reconstitution of the immune system. These bands typically disappear over time and in some studies have been associated with a better outcome. Also, appearance of monoclonal IgG κ in patients receiving monoclonal antibodies should be differentiated from the therapeutic antibody. §§Plasmacytoma measurements should be taken from the CT portion of the PET/CT, or MRI scans, or dedicated CT scans where applicable. For patients with only skin involvement, skin lesions should be measured with a ruler. Measurement of tumour size will be determined by the SPD. ¶¶Positive immunofixation alone in a patient previously classified as achieving a complete response will not be considered progression. For purposes of calculating time to progression and progression-free survival, patients who have achieved a complete response and are MRD-negative should be evaluated using criteria listed for progressive disease. Criteria for relapse from a complete response or relapse from MRD should be used only when calculating disease-free survival. ‖‖In the case where a value is felt to be a spurious result per physician discretion (eg, a possible laboratory error), that value will not be considered when determining the lowest value.

Table 4: **IMWG criteria for response assessment including criteria for minimal residual disease**

Tabla 4 de Kumar S, *et al.* Lancet Oncol 2016.

Es el momento de nuevos enfoques

La **disponibilidad** de múltiples fármacos eficaces más allá del tratamiento de primera línea debería crear un marco para evaluar si los **criterios del IMWG** para iniciar el tratamiento en pacientes en recaída deberían ampliarse para incluir otras **condiciones clínicas** adversas que posiblemente puedan detectarse **antes de la progresión sintomática**[1].

La intervención con rescate temprano en contextos de progresión subclínica temprana y unas cinéticas de respuesta subóptimas o estancadas, **puede ofrecer nuevas oportunidades para mejorar los resultados en el MM**[1]

IMWG: *International Myeloma Working Group;* **MM:** mieloma múltiple

1. Lahuerta JJ, *et al.* Early detection of treatment failure and early rescue intervention in multiple myeloma: time for new approaches. Blood advances. 2021; 9;5(5):1340-1343. doi: 10.1182/bloodadvances.2020003996.

10

Las altas tasas de abandono de pacientes con MMND subrayan la necesidad de utilizar regímenes de tratamiento adecuados en lugar de reservarlos para líneas posteriores[1]

PROPORCIÓN DE PACIENTES QUE ALCANZA CADA LÍNEA DE TRATAMIENTO (%) [2]

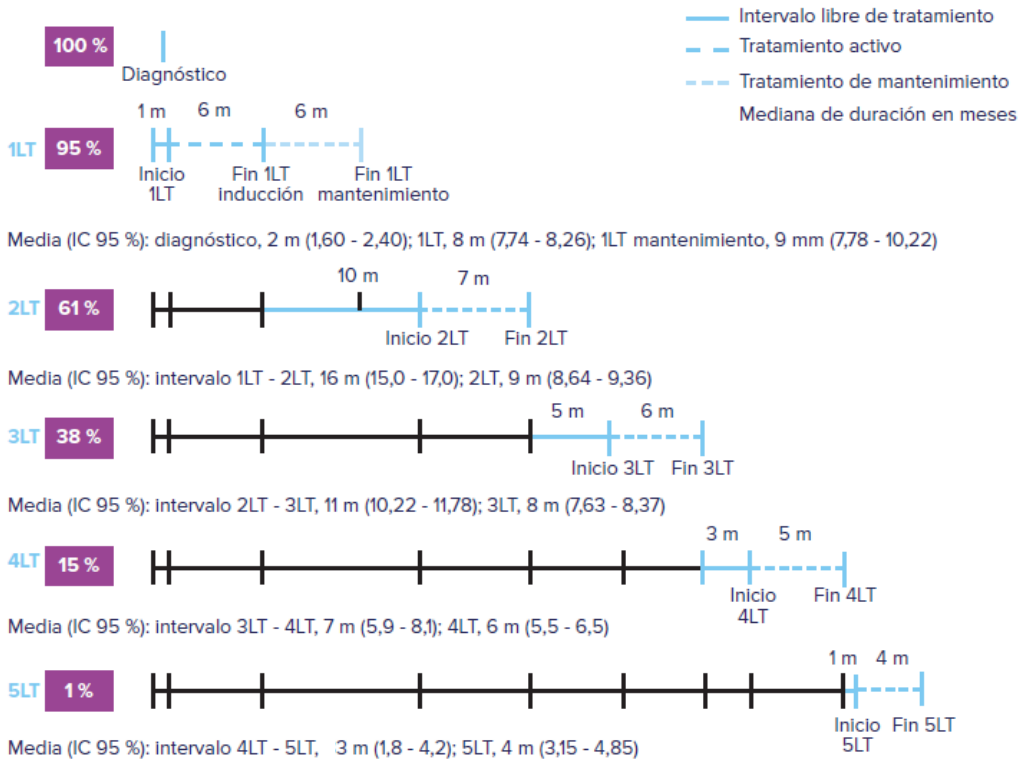
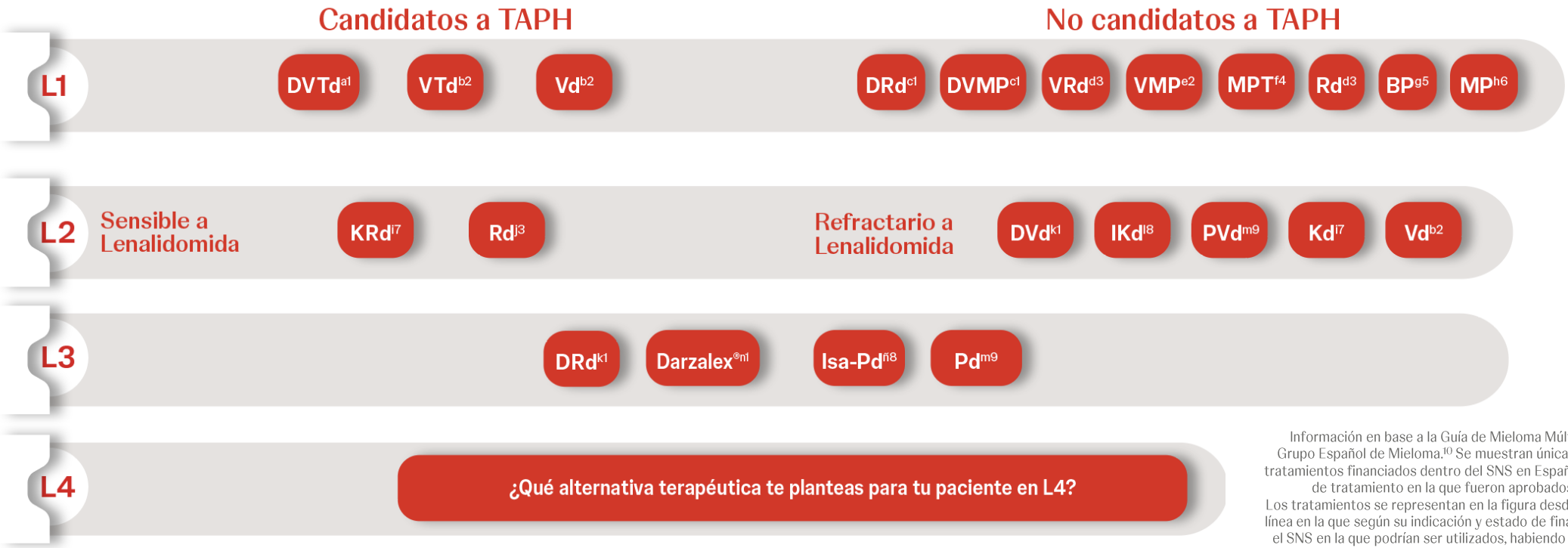


Figura 2 de Yong K, et al. 2016.[2]

MMND: mieloma múltiple de nuevo diagnóstico; LT: línea de tratamiento.

1. Fonseca R, *et al.* Frontline treatment patterns and attrition rates by subsequent lines of therapy in patients with newly diagnosed multiple myeloma. BMC Cancer. 2020;20:1087; 2. Yong K, et al. Multiple myeloma: patient outcomes in real-world practice. Br J Haematol. 2016;175(2):252-264.

¿En qué etapa de Mieloma Múltiple se encuentra su paciente?



Información en base a la Guía de Mieloma Múltiple del Grupo Español de Mieloma.[10] Se muestran únicamente los tratamientos financiados dentro del SNS en España en la línea de tratamiento en la que fueron aprobados[11-22]
Los tratamientos se representan en la figura desde la primera línea en la que según su indicación y estado de financiación en el SNS en la que podrían ser utilizados, habiendo regímenes que podrían ser utilizados en varias líneas de tratamiento.

Para mayor información acerca de los fármacos y combinaciones anteriormente mencionadas pulse AQUÍ

BP: bendamustina+prednisona; **DRd:** Darzalex®+lenalidomida+lenalidomida; **DVd:** Darzalex®+Velcade®+dexametasona; **DVMP:** Darzalex®+Velcade®+melfalán+prednisona; **DVTd:** Darzalex®+Velcade®+talidomida; **IKd:** isatuximab+carfilzomib+dexametasona; **Isa-Pd:** isatuximab+pomalidomida+dexametasona®; **Kd:** carfilzomib+dexametasona; **KRd:** carfilzomib+lenalidomida+dexametasona; **L1:** primera línea; **L2:** segunda línea; **L3:** tercera línea; **L4:** cuarta línea; **MPT:** melfalán+prednisona+talidomida; **Pd:** pomalidomida+dexametasona; **PVd:** pomalidomida+Velcade®+dexametasona; **P&R:** precio-reembolso; **Rd:** lenalidomida+dexametasona; **SNS:** Sistema Nacional de Salud; **TAPH:** trasplante autólogo de progenitores hematopoyéticos; **Vd:** Velcade+dexametasona; **VMP:** Velcade®+melanfalán+prednisona; **VRd:** Velcade®+lenalidomida+dexametasona; **VTd:** Velcade®+talidomida+dexametasona.

¿En qué etapa de Mieloma Múltiple se encuentra su

[a]Darzalex® está indicado en combinación con bortezomib, talidomida y dexametasona para el tratamiento de pacientes adultos con mieloma múltiple de nuevo diagnóstico que son candidatos a un trasplante autólogo de progenitores hematopoyéticos.[1]
[b]Velcade® está indicado en combinación con dexametasona o con dexametasona y talidomida, en el tratamiento de inducción de pacientes adultos con mieloma múltiple que no han sido previamente tratados y que sean candidatos a recibir tratamiento con altas dosis de quimioterapia previo a un trasplante de progenitores hematopoyéticos.[2]
[c]Darzalex® está indicado en combinación con lenalidomida y dexametasona o con bortezomib, melfalán y prednisona para el tratamiento de pacientes adultos con mieloma múltiple de nuevo diagnóstico que no son candidatos a un trasplante autólogo de progenitores hematopoyéticos.[1]
[d]Lenalidomida en terapia combinada con dexametasona, o bortezomib y dexametasona está indicado para el tratamiento de pacientes adultos con mieloma múltiple (MM) sin tratamiento previo que no son candidatos para un trasplante.[3]
[e]Velcade® está indicado en combinación con melfalán y prednisona, en el tratamiento de pacientes adultos con mieloma múltiple que no han sido previamente tratados y que no sean candidatos a recibir tratamiento con altas dosis de quimioterapia previo a un trasplante de progenitores hematopoyéticos. Velcade® en monoterapia, o en combinación con doxorubicina liposomal pegilada o con dexametasona, está indicado para el tratamiento de pacientes adultos con mieloma múltiple en progresión que han recibido previamente al menos 1 tratamiento y que han sido sometidos o no son candidatos a trasplante de progenitores hematopoyéticos.[2]
[f]Talidomida en combinación con melfalán y prednisona está indicado como tratamiento de primera línea de pacientes con mieloma múltiple no tratado de edad ≥ 65 años o no aptos para recibir quimioterapia a altas dosis.[4]
[g]Bendamustina está indicada en el tratamiento de primera línea del mieloma múltiple (estadio II con progresión o estadio III de Durie-Salmon) en combinación con prednisona, en pacientes mayores de 65 años que no son candidatos a un autotrasplante de células progenitoras y que tengan una neuropatía clínica en el momento del diagnóstico que impide el uso de tratamientos a base de talidomida o bortezomib.[5]
[h]Los comprimidos de melfalán están indicados en el tratamiento del mieloma múltiple.[6]
[i]Carfilzomib en combinación con lenalidomida y dexametasona o con dexametasona sola está indicado para el tratamiento de pacientes adultos con mieloma múltiple que han recibido como mínimo un tratamiento previo.[7]
[j]Lenalidomida en combinación con dexametasona está indicado en el tratamiento de los pacientes adultos con mieloma múltiple que hayan recibido al menos un tratamiento previo.[3]
[k]Darzalex® está indicado en combinación con lenalidomida y dexametasona, o bortezomib y dexametasona, para el tratamiento de pacientes adultos con mieloma múltiple que han recibido al menos un tratamiento previo.[1]
[l]Isatuximab en combinación con carfilzomib y dexametasona, para el tratamiento de pacientes adultos con mieloma múltiple que han recibido al menos un tratamiento previo.[8]
[m]Pomalidomida en combinación con bortezomib y dexametasona está indicado en el tratamiento de los pacientes adultos con mieloma múltiple que hayan recibido al menos un tratamiento previo, incluyendo lenalidomida. Pomalidomida en combinación con dexametasona está indicado en el tratamiento de los pacientes adultos con mieloma múltiple resistente al tratamiento o recidivante que hayan recibido al menos dos tratamientos previos, incluyendo lenalidomida y bortezomib, y que hayan experimentado una progresión de la enfermedad en el último tratamiento.[9]
[n]Darzalex® está indicado en monoterapia para el tratamiento de pacientes adultos con mieloma múltiple en recaída y refractario al tratamiento, que hayan recibido previamente un inhibidor del proteasoma y un agente inmunomodulador y que hayan presentado progresión de la enfermedad en el último tratamiento.[1]
[ñ]Isatuximab está indicado en combinación con pomalidomida y dexametasona, para el tratamiento de pacientes adultos con mieloma múltiple resistente al tratamiento o recidivante que han recibido al menos dos tratamientos previos, incluyendo lenalidomida y un inhibidor del proteosoma y han demostrado progresión de la enfermedad en el último tratamiento.[8]

BP: bendamustina+prednisona; **DRd:** Darzalex®+lenalidomida+dexametasona; **DVd:** Darzalex®+Velcade®+dexametasona; **DVMP:** Darzalex®+Velcade®+melfalán+prednisona; **DVTd:** Darzalex®+Velcade®+talidomida+dexametasona; **Isa-Pd:** isatuximab+prednisona+dexametasona; **KRd:** carfilzomib+lenalidomida+dexametasona; **L1:** primera línea; **L2:** segunda línea; **L3:** tercera línea; **L4:** cuarta línea; **IKd:** isatuximab+carfi lzomib+dexametasona; **Kd:** carfi lzomib+dexametasona; **MPT:** melfalán+prednisona+talidomida; **Pd:** pomalidomida+dexametasona; **PVd:** pomalidomida+Velcade®+dexametasona; **P&R:** precio y reembolso; **Rd:** lenalidomida+dexametasona; **TAPH:** trasplante autólogo de progenitores hematopoyéticos; **Vd:** Velcade®+dexametasona; **VMP:** Velcade®+melfalán+prednisona; **VRd:** Velcade®+lenalidomida+dexametasona; **VTd:** Velcade®+talidomida+dexametasona.

1. Ficha técnica de Darzalex®; **2.** Ficha Técnica de Velcade®. Disponible en: https://cima.aemps.es/cima/dochtml/ft/04274001/FT_04274001.html Último acceso abril 2025; **3.** Ficha Técnica de lenalidomida. Disponible en: https://cima.aemps.es/cima/dochtml/ft/07391004/FT_07391004.html Último acceso abril 2025; **4.** Ficha Técnica de talidomida. Disponible en: https://cima.aemps.es/cima/dochtml/ft/8443001/FT_8443001.html Último acceso abril 2025; **5.** Ficha Técnica de bendamustina. Disponible en: https://cima.aemps.es/cima/dochtml/ft/80644/FT_80644.html Último acceso abril 2025; **6.** Ficha Técnica de melfalán. Disponible en: https://cima.aemps.es/cima/pdfs/es/ft/83765/FT_83765.html.pdf Último acceso: abril 202; **7.** Ficha Técnica de carfilzomib. Disponible en: https://cima.aemps.es/cima/dochtml/ft/1151060003/FT_1151060003.html Último acceso abril 2025; **8.** Ficha Técnica de isatuximab. Disponible en: https://cima.aemps.es/cima/dochtml/ft/1201435001/FT_1201435001.html Último acceso abril 2025; **9.** Ficha Técnica de pomalidomida. Disponible en: https://cima.aemps.es/cima/dochtml/ft/113850004/FT_113850004.html Último acceso abril 2025; **10.** Grupo Español de Mieloma Múltiple. Guía de Mieloma Múltiple. 2021; **11.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos.do?metodo=verDetalle&cn=709152 Último acceso: abril 2025. **12.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https:// www.sanidad.gob.es/profesionales/medicamentos.do?metodo=verDetalle&cn=701016 Último acceso: abril 2025. **13.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos.do?metodo=verDetalle&cn=732577 Último acceso: abril 2025; **14.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos. do?metodo=verDetalle&cn=711285 Último acceso: abril 2025; **15.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos.do?metodo=verDetalle&cn=820910 Último acceso: abril 2025; **16.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www.sanidad.gob.es/profesionales/ medicamentos.do?metodo=verDetalle&cn=728515 Último acceso: abril 2025; **17.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos.do?metodo=verDetalle&cn=713555 Último acceso: abril 2025; **18.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www.sanidad.gob.es/ gl/profesionales/medicamentos.do?metodo=verDetalle&cn=652611 Último acceso: abril 2025; **19.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos.do?metodo=verDetalle&cn=724561 Último acceso: abril 2025; **20.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www. sanidad.gob.es/profesionales/medicamentos.do?metodo=verDetalle&cn=605789 Último acceso: abril 2025; **21.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos.do?metodo=verDetalle&cn=672240 Último acceso: abril 2025; **22.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos. Nomenclátor de ABRIL de 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos.do?metodo=verDetalle&cn=728802 Último acceso: abril 2025.

Importancia de una intervención temprana y eficaz en el tratamiento del MM

Los pacientes con MMRR que han recibido IPs, IMiDs y anticuerpo anti-CD38 tienen **mal pronóstico y limitadas opciones de tratamiento,** con una **baja probabilidad de respuesta** al tratamiento posterior[1]

LocoMMotion:

Estudio prospectivo en práctica clínica[2]

TRG	mSLP	mSG
31,9%*,[2]	4,6 meses*,[2]	13,8 meses*,[2]

LocoMMotion:

Estudio prospectivo en práctica clínica[3]

(Cohorte española)

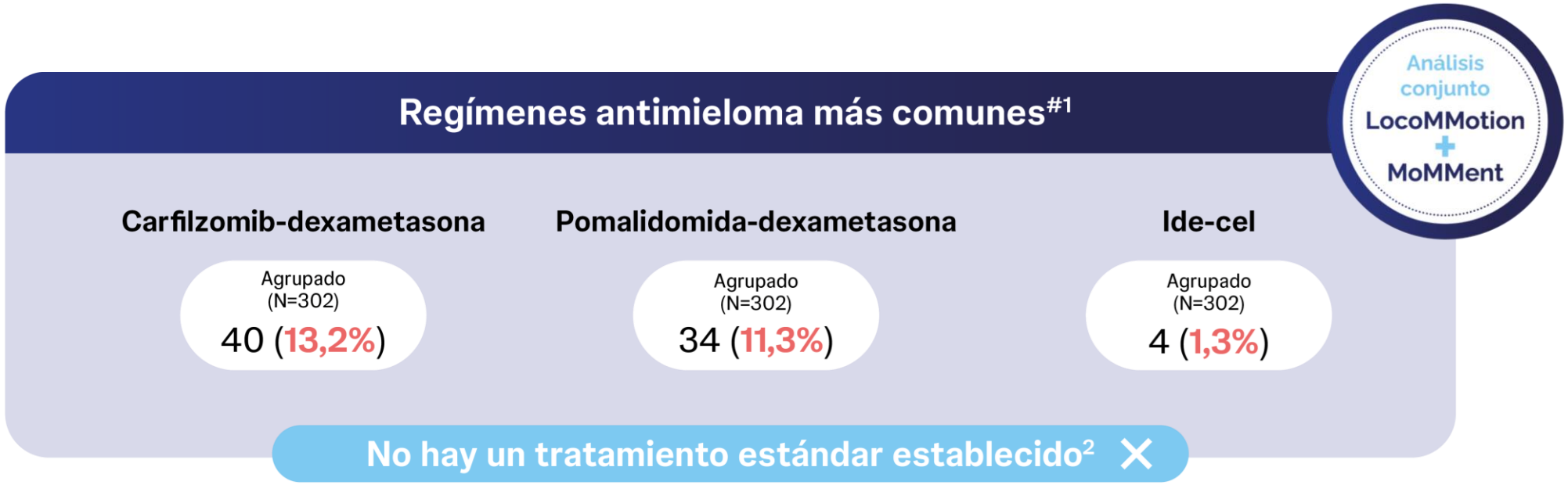
TRG	mSLP	mSG
29,2%^,[3]	4,6 meses^,[3]	11,6 meses^,[3]

En el estudio prospectivo, no intervencionista y multinacional LocoMMotion (NCT04035226) participaron 248 pacientes que habían recibido ≥3 líneas de tratamiento previas, incluidos un IP, un IMiD y un anticuerpo anti-CD38, con progresión de la enfermedad durante o después de su última línea de tratamiento. El criterio de valoración principal fue la TRG. Los criterios secundarios de valoración fueron la SLP y la SG. Algunas terapias utilizadas en la población general del estudio LocoMMotion no se utilizaron en la cohorte española. Esto puede atribuirse a un acceso más limitado a los tratamientos en España o a un menor tamaño de la muestra. Además, la ausencia de un tratamiento estándar claro en esta población fuertemente pretratada complica el diseño de ensayos clínicos aleatorizados o las comparaciones indirectas de los nuevos tratamientos con las terapias existentes.[3]

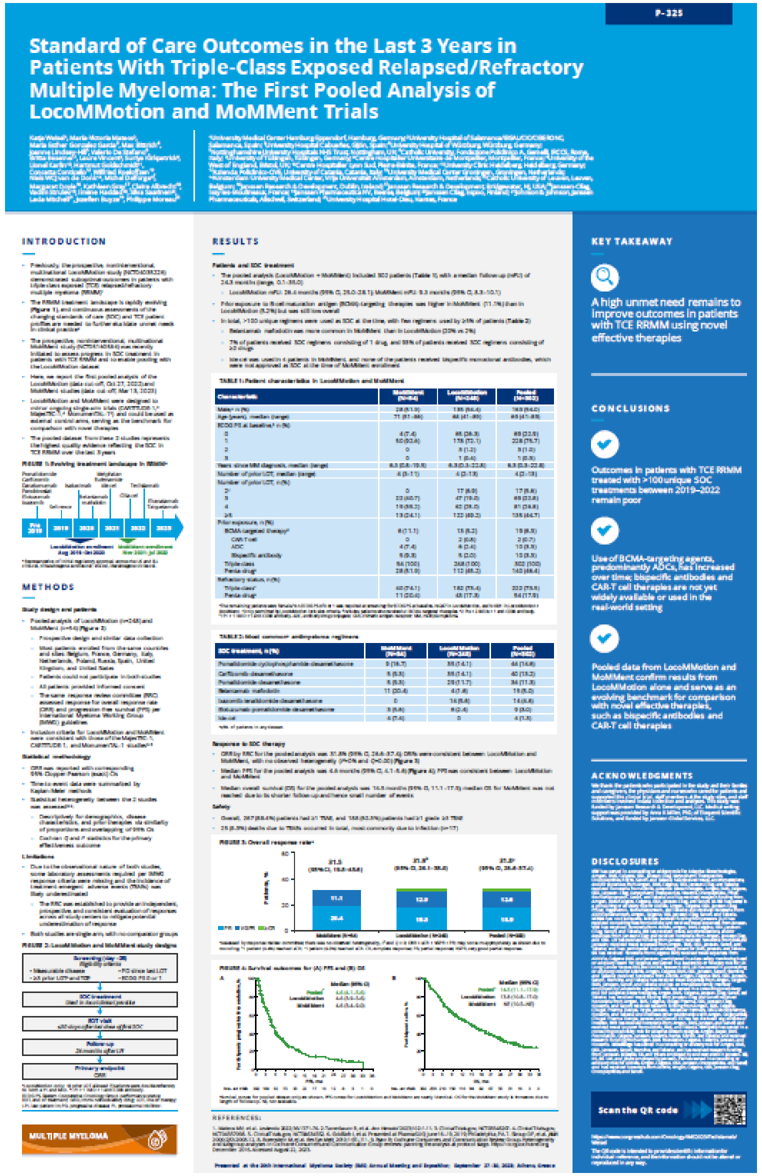
*Con una mediana de seguimiento de 26,4 meses: (IC 95%, 26,1-38,0), (IC 95%, 3,9-5,6), y (IC 95%, 10,8-17,0), respectivamente para TRG, mSLP y mSG.[2]
^Con una mediana de seguimiento de 29,2 meses: (IC 95%, 12,6-51,1), (IC 95%, 1,2-6,3), y (IC 95%, 6,4-24,5), respectivamente para TRG, mSLP y mSG.[3]
IC: intervalo de confianza**; IMiD:** inmunomodulador**; IP:** inhibidor del proteasoma**; MMRR:** mieloma múltiple en recaída/refractario**; mSG:** mediana de la supervivencia global**; mSLP:** mediana de la supervivencia libre de progresión**; SG:** supervivencia global; **SLP:** supervivencia libre de progresión; **TRG:** tasa de respuesta global.

1. Moreau P, *et al.* Adv Ther. 2023;40(5):2412-2425. 2. Mateos MV, *et al.* Leukemia. 2024;38(12):2554-2560. 3. Mateos MV, *et al.* Clin Lymphoma Myeloma Leuk. 2024 Apr;24(4):224-231.e2.

LocoMMotion y MoMMent registran >100 esquemas de tratamiento diferentes (2019-2022), con unos pocos regímenes usados en >5 % de los pacientes:[1]



Regímenes financiados en España. Extraído de la Tabla 2 de Weisel K, *et al.* IMS 2023. Póster completo disponible AQUÍ
Para mayor información acerca de los tratamientos anteriormente mencionados, consultar sus respectivas fi chas técnicas disponibles en CIMA.
El análisis conjunto (LocoMMotion + MoMMent) incluyó 302 pacientes, con una mediana de seguimiento de 24,3 meses (intervalo, 0,1-35,0).[1]
*LocoMMotion y MoMMent son estudios prospectivos, no intervencionistas, multinacionales con el objetivo de evaluar el estándar de tratamiento en práctica clínica habitual en pacientes con MMRR TCE. Reclutamiento del estudio LocoMMotion agosto 2019- octubre 2020. Reclutamiento del estudio MoMMent noviembre 2021- julio 2022.[1]
Debido a la naturaleza observacional de ambos estudios, faltaron algunas evaluaciones de laboratorio requeridas por los criterios de respuesta del IMWG y es probable que se subestimara la incidencia de acontecimientos adversos emergentes del tratamiento. Ambos estudios son de un solo brazo, sin grupos de comparación.[1]
#≥5 % de los pacientes de cualquier conjunto de datos.[1]
CIMA: Centro de Información de Medicamentos; **Ide-cel:** idecabtagén vicleucel; **IMWG:** *International Myeloma Working Group;* **MMRR:** mieloma múltiple en recaída y refractario; **TCE:** triple expuestos.
1. Weisel K, *et al.* Standard of Care Outcomes in the Last 3 Years in Patients With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma: The First Pooled Analysis of LocoMMotion and MoMMent Trials Póster P-325 presentado en 20th International Myeloma Society (IMS) Annual Meeting and Exposition; 27-30 septiembre 2023; Atenas, Grecia; **2.** Moreau P, *et al.* Comparative Efficacy of Teclistamab Versus Current Treatments in Real-World Clinical Practice in the Prospective LocoMMotion Study in Patients with Triple-Class-Exposed Relapsed and/or Refractory Multiple Myeloma. Adv Ther. 2023;40(5):2412-2425.



P-325
Standard of Care Outcomes in the Last 3 Years in Patients With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma: The First Pooled Analysis of LocoMMotion and MoMMent Trials
INTRODUCTION
RESULTS
KEY TAKEAWAY
A high unmet need remains to improve outcomes in patients with TCE RRMM using novel effective therapies
CONCLUSIONS
Outcomes in patients with TCE RRMM treated with >100 unique SOC treatments between 2019–2022 remain poor
Use of BCMA-targeting agents, predominantly ADCs, has increased over time; bispecific antibodies and CAR-T cell therapies are not yet widely available or used in the real-world setting
Pooled data from LocoMMotion and MoMMent confirm results from LocoMMotion alone and serve as an evolving benchmark for comparison with novel effective therapies, such as bispecific antibodies and CAR-T cell therapies
METHODS
ACKNOWLEDGMENTS
DISCLOSURES
MULTIPLE MYELOMA
Scan the QR code

Los pacientes con MMRR TCE siguen demostrando resultados subóptimos[1]

Nos enfrentamos a un reto en el paciente con MMRR expuesto a triple clase[1]

MMRR: mieloma múltiple en recaída y refractario; **TCE:** triple expuestos.

1. Weisel K, *et al.* Standard of Care Outcomes in the Last 3 Years in Patients With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma: The First Pooled Analysis of LocoMMotion and MoMMent Trials Póster P-325 presentado en 20th International Myeloma Society (IMS) Annual Meeting and Exposition; 27-30 septiembre 2023; Atenas, Grecia.

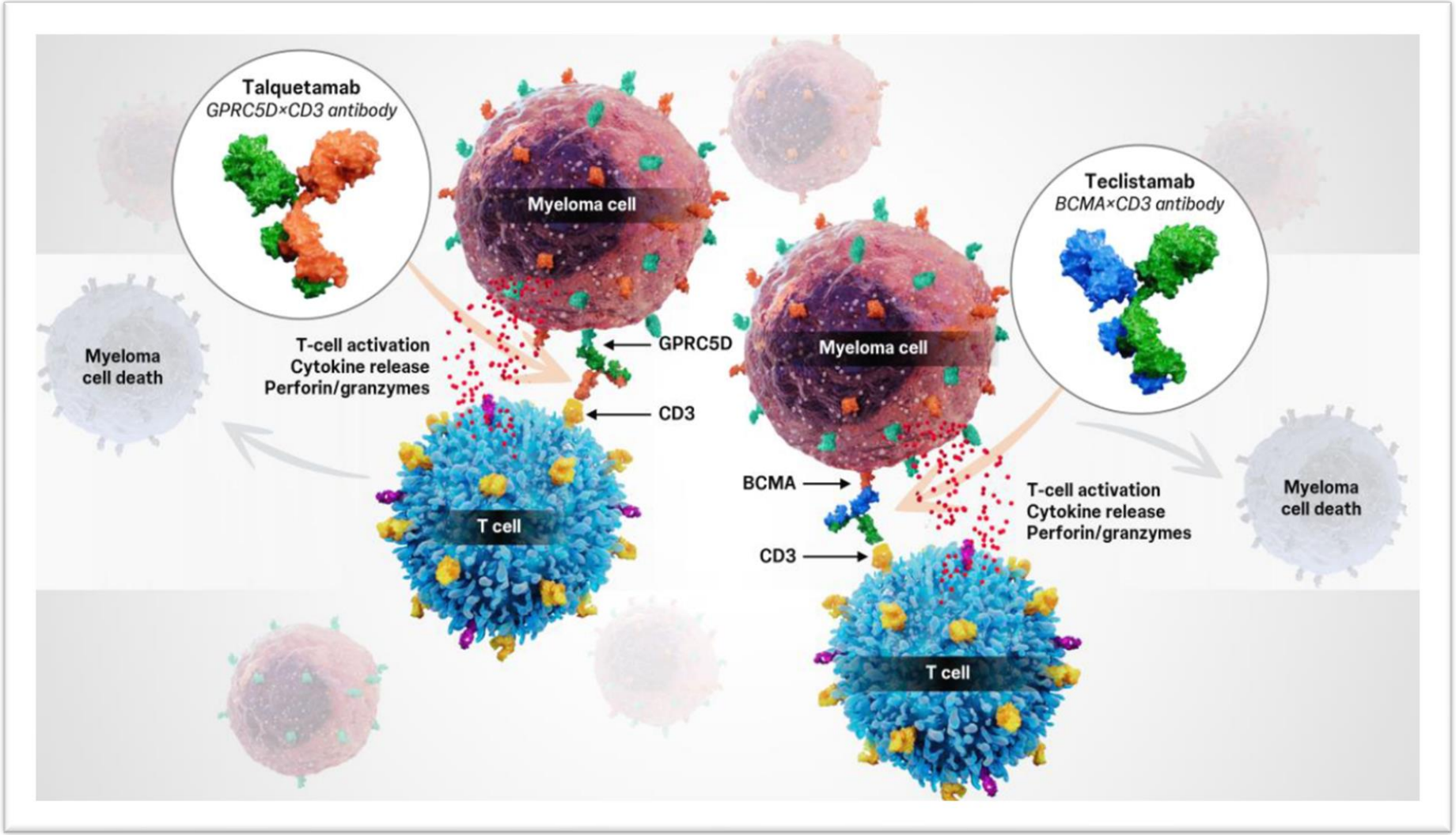
Indicación de teclistamab y talquetamab autorizada en Ficha Técnica

Teclistamab^¶ está indicado en monoterapia para el tratamiento de pacientes adultos con **mieloma múltiple en recaída y refractario,** que han recibido al menos **3 tratamientos previos,** incluidos un agente inmunomodulador, un inhibidor del proteasoma y un anticuerpo anti CD38, y han presentado progresión de la enfermedad al último tratamiento.[1]

Talquetamab*§ está indicado en monoterapia para el tratamiento de pacientes adultos con **mieloma múltiple en recaída y refractario,** que han recibido al menos **3 tratamientos previos,** incluyendo un agente inmunomodulador, un inhibidor del proteasoma y un anticuerpo anti-CD38 y han presentado progresión de la enfermedad al último tratamiento.[2]

*Autorizado por la Comisión Europea el 21 de agosto de 2023.[3]
§TALVEY® está disponible para su uso en España desde el 1 de diciembre de 2024.[4]
^Autorizado por la Comisión Europea el 23 de agosto de 2022.[5]
¶TECVAYLI® está disponible para su uso en España desde el 1 de mayo de 2024.[6]
CD38: *cluster of differentiation* 38; **GPRC5D:** miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; **MMRR:** mieloma múltiple en recaída y refractario.
1. Ficha Técnica de teclistamab **2.** Ficha Técnica de TALVEY®; **3.** EMA. TALVEY®.European Commission Decision. Disponible en: https://www.ema.europa.eu/en/medicines/human/EPAR/talvey#authorisation-details Último acceso: abril 2025; **4.** Nomenclator. TALVEY®. Disponible en: https://www.sanidad.gob.es/va/profesionales/nomenclator.do? Último acceso abril 2025. **5.** EPAR TECVAYLI®. Disponible en: https://www.ema.europa.eu/en/medicines/human/EPAR/tecvayli Consultado por última vez en abril de 2025. 6. Nomenclator. TECVAYLI®. Disponible en: https://www.sanidad.gob.es/va/profesionales/nomenclator.do? Último acceso abril 2025.

Mecanismos de acción: anti-BCMA y anti-GPRC5D[1]



BCMA: antígeno de maduración de células B; **CD:** *cluster of differentiation;* **GPRC5D:** miembro D del grupo 5 de la familia C del receptor acoplado a proteína G.

1. Cohen, Y. C., *et al.* (2024). Talquetamab + Teclistamab in patients with relapsed/refractory multiple myeloma: Updated Phase 1b results from RedirecTT-1 with >1 year of follow-up. Presentado en el 21st International Myeloma Society (IMS) Annual Meeting, septiembre 25–28, Río de Janeiro, Brasil.

TECVAYLI®
(teclistamab-cqyv) Injection for subcutaneous use
10 mg/mL and 90 mg/mL

De la necesidad a la realidad en el paciente triple expuesto

TECVAYLI® está indicado en monoterapia para el tratamiento de pacientes adultos con mieloma múltiple en recaída y refractario, que han recibido al menos tres tratamientos previos, incluidos un agente inmunomodulador, un inhibidor del proteasoma y un anticuerpo anti-CD38 y han presentado progresión de la enfermedad al último tratamiento.[4]
‡ Autorizado por la Comisión Europea el 23 de agosto de 2022. EPAR Tecvayli®.[5]
*Desde el primer paciente en ensayo clínico, a nivel global.[2]

▼ Este medicamento está sujeto a seguimiento adicional, es prioritaria la notificación de sospechas de reacciones adversas asociadas a este medicamento.

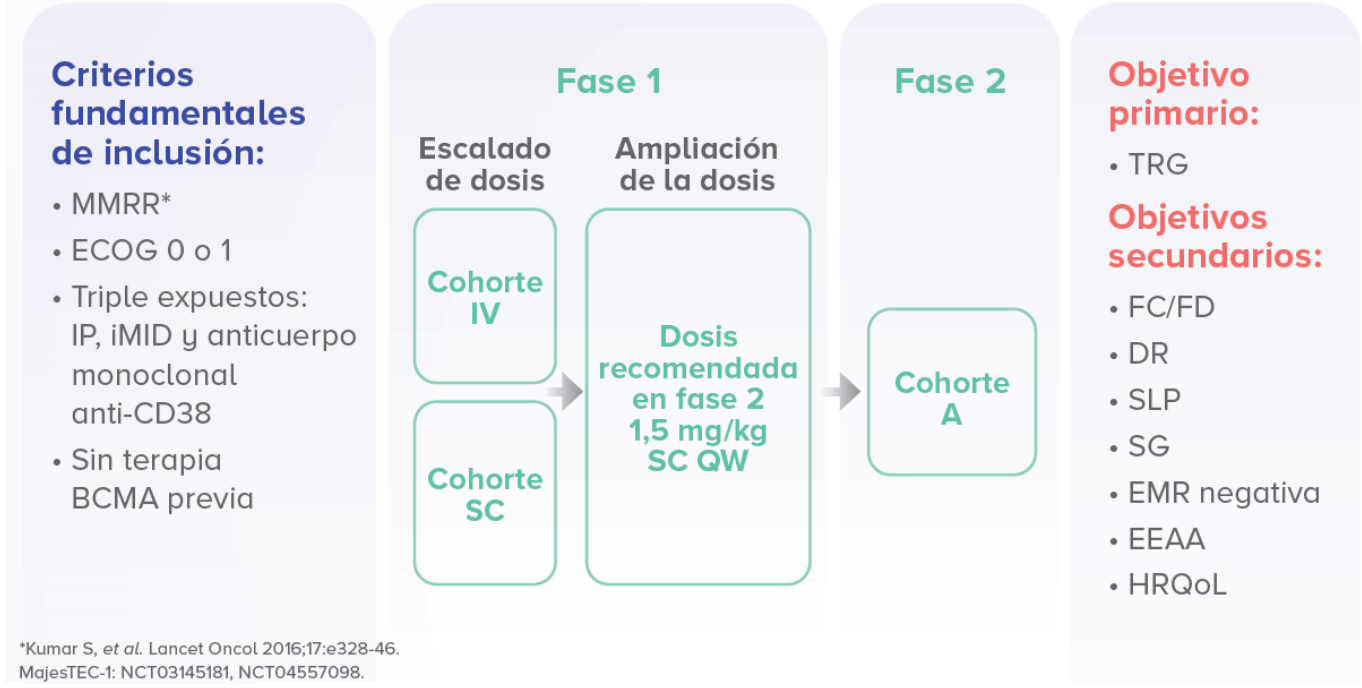
1. Nomenclátor. Disponible en: https://www.sanidad.gob.es/profesionales/nomenclator.do Consultado por última vez en abril 2025. 2. Martin TG, *et al.* Póster 3331. Presentado en el Congreso anual de ASH, 7-10 diciembre 2024, San Diego, California, EEUU. 3. Zhao J, *et al.* J Hematol Oncol. 2023;16(1):92. 4. Ficha Técnica de TECVAYLI®. 5. EPAR TECVAYLI®. Disponible en: https://www.ema.europa.eu/en/medicines/human/EPAR/tecvayli Consultado por última vez en abril 2025

Estudio MAJESTEC-1

En el estudio MAJESTEC-1 se evaluaron 165 pacientes[1]

MajesTEC-1 es un estudio de fase I/II, que evalúa la eficacia y seguridad de teclistamab en monoterapia en pacientes con MMRR[1]

Diseño del estudio[2]



*Kumar S, *et al.* Lancet Oncol 2016;17:e328-46.
MajesTEC-1: NCT03145181, NCT04557098.

Fecha de reclutamiento: marzo 2020 - agosto 2021[1]
Figura 1 de Sidana *et al.* 2023[2]

BCMA: antígeno de maduración de linfocitos B; **DR:** duración de la respuesta; **EA:** evento adverso; **ECOG:** *Eastern Cooperative Oncology Group*; **EMR:** enfermedad mínima residual; **FC:** farmacocinética; **FD:** farmacodinámica; **HRQoL:** calidad de vida relacionada con la salud; **IMiD:** inmunomodulador; **IP:** inhibidor del proteosoma; **IV:** intravenosa; **MMRR:** mieloma múltiple en recaída/refractario; **QW:** una vez a la semana; **SC:** subcutánea; **SG:** supervivencia global; **SLP:** supervivencia libre de progresión; **TRG:** tasa de respuesta global.

1. Moreau P, *et al.* N Engl J Med. 2022;387(6):495-505. 2. Sidana S, *et al.* P879. Presented at the (EHA) 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany.

Se incluyó un amplio espectro de pacientes triple expuestos con MMRR[1]

Características basales de los pacientes[1]

Características	N=165
Edad (años), mediana (rango)	64,0 (33,0–84,0)
Género masculino, n (%)	96 (58,2)
Etnia - n (%)	
Blanca	134 (81,2)
Negra/afroamericana	21 (12,7)
Asiática	3 (1,8)
Otra	7 (4,2)
EMD,[a] n (%)	28 (17,0)
Perfil citogenético de alto riesgo, n/N (%)	38/148 (25,7)
Estadio ISS - n/N (%)	
I	85/162 (52,5)
II	57/162 (35,2)
III	20/162 (12,3)

Características	N=165
Tiempo desde el diagnóstico (años), mediana (rango)	6,0 (0,8–22,7)
N° de líneas previas de tratamiento, mediana (rango)	5 (2–14)
Trasplante previo de células madre - n (%)	135 (81,8)
Estado de exposición - n (%)	
Triple expuesto[b]	165 (100)
Penta expuesto[c]	116 (70,3)
Estado de refractariedad - n (%)	
Anticuerpo monoclonal anti CD38	148 (89,7)
Triple-refractario[b]	128 (77,6)
Penta-refractario[c]	50 (30,3)

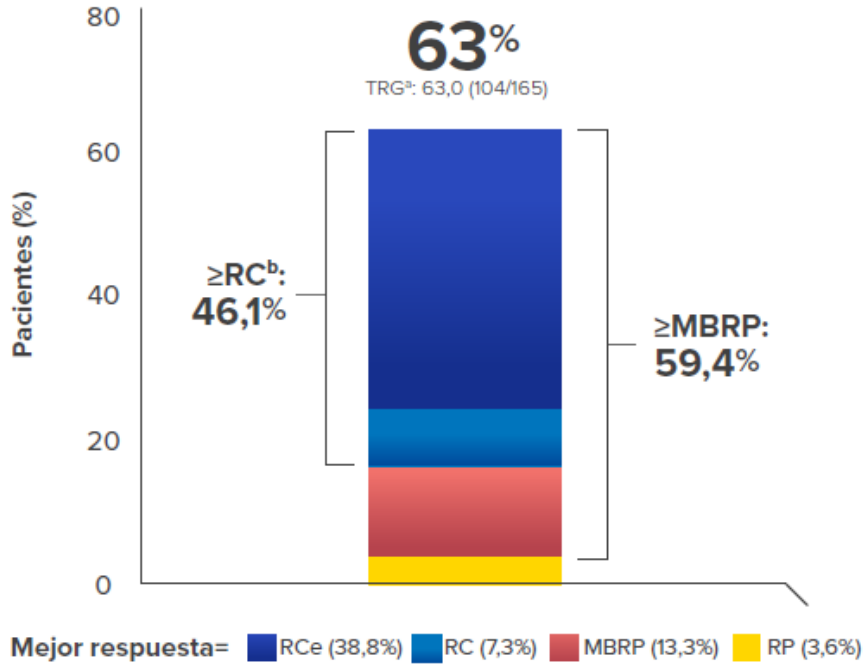
[a]Incluye pacientes que tenían ≥1 plasmocitoma de tejidos blandos no asociado a hueso.
[b]≥1 IP, ≥1 IMiD, 1 anticuerpo anti-CD38.
[c]≥2 IP, ≥2 IMiD, 1 anticuerpo anti-CD38.
Tabla 1 de Sidana *et al.* 2023[1]

EMD: enfermedad extramedular; **IMiD:** inmunomodulador; **IP:** inhibidor del proteasoma; **ISS:** *International Staging System;* **MMRR:** mieloma múltiple en recaída/refractario.
1. Sidana S, *et al.* P879. Presented at the (EHA) 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany.

Aproximadamente la mitad de los pacientes alcanzaron ≥RC[1]

Tras 30,4 meses de mediana de seguimiento, teclistamab ofrece respuestas profundas y duraderas[1]

Tasa de respuesta global[1]



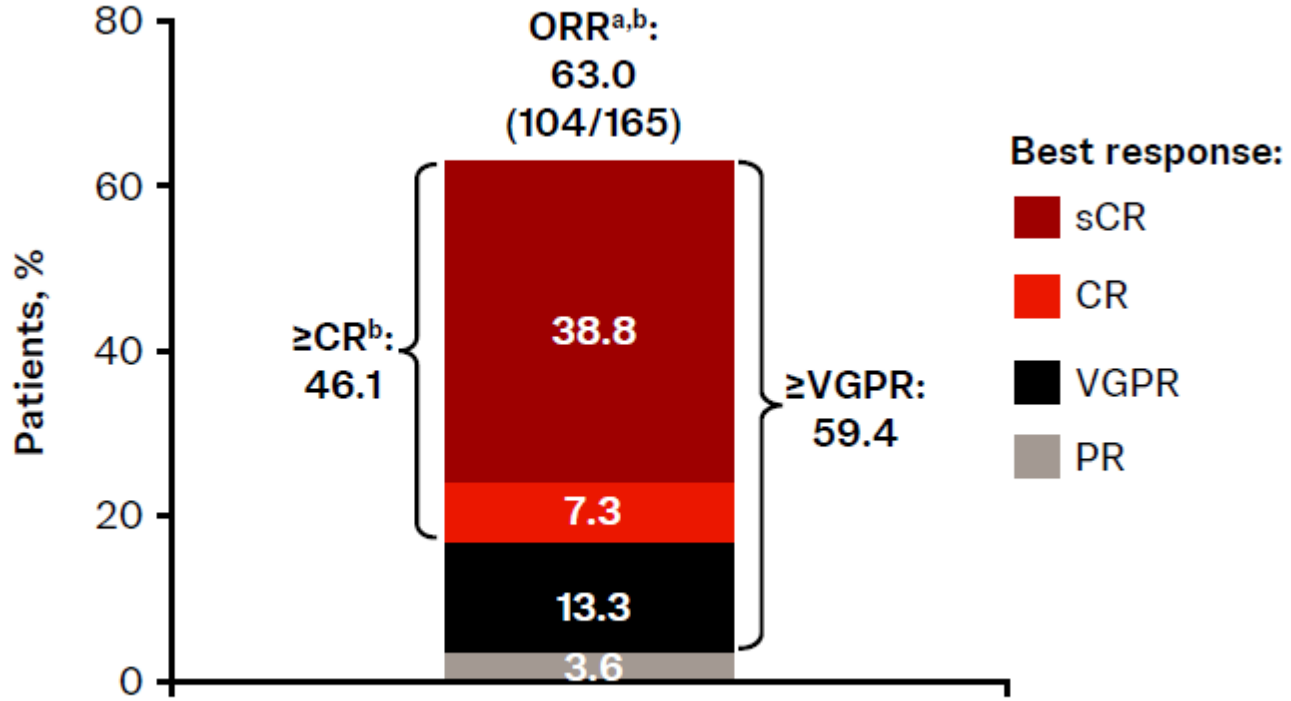
[a]TRG evaluada por un comité de revisión independiente.
[b]A los 30 meses de mediana de seguimiento de la población de fase 2 de eficacia (pacientes inscritos en la cohorte A el 18 de marzo de 2021 o antes; n=110 pacientes de acuerdo con la ficha técnica de EE. UU.): TRG, 61,8%; ≥RC, 46,4% (n=51).
Gráfica modificada en base a la figura 2 de Garfall *et al.* 2024.[1]
Figura 2 completa disponible aquí.

Casi el 85% de las RC son RC estrictas*,[1]

De los pacientes con EMR evaluable, el 85,7% fueron EMR- en cualquier momento[1]

*Cálculo realizado en base al porcentaje de pacientes con RCe (38,8%) respecto al total de pacientes con ≥RC 46,1%.[1]
EMR: enfermedad mínima residual; **MBRP:** muy buena respuesta parcial; **RC:** respuesta completa; **RCe:** respuesta completa estricta; **RP:** respuesta parcial; **TRG:** tasa de respuesta global.
1. Garfall AL, *et al.* Presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA & Virtual. (Poster 7540).

Figure 2: ORR



[a]Response assessed by independent review committee. [b]At 30-month mFU of the phase 2 efficacy population (patients enrolled in cohort A on or before March 18, 2021; n=110 patients supporting the USPI[1]): ORR, 61.8%; ≥CR, 46.4% (n=51).
sCR, stringent complete response; USPI, United States prescribing information.

La importancia de que sus pacientes lleguen antes a ≥RC[1]

La RC es un objetivo importante y clínicamente significativo en el tratamiento del MM, que demuestra un beneficio para la supervivencia en todas las fases del tratamiento[1]

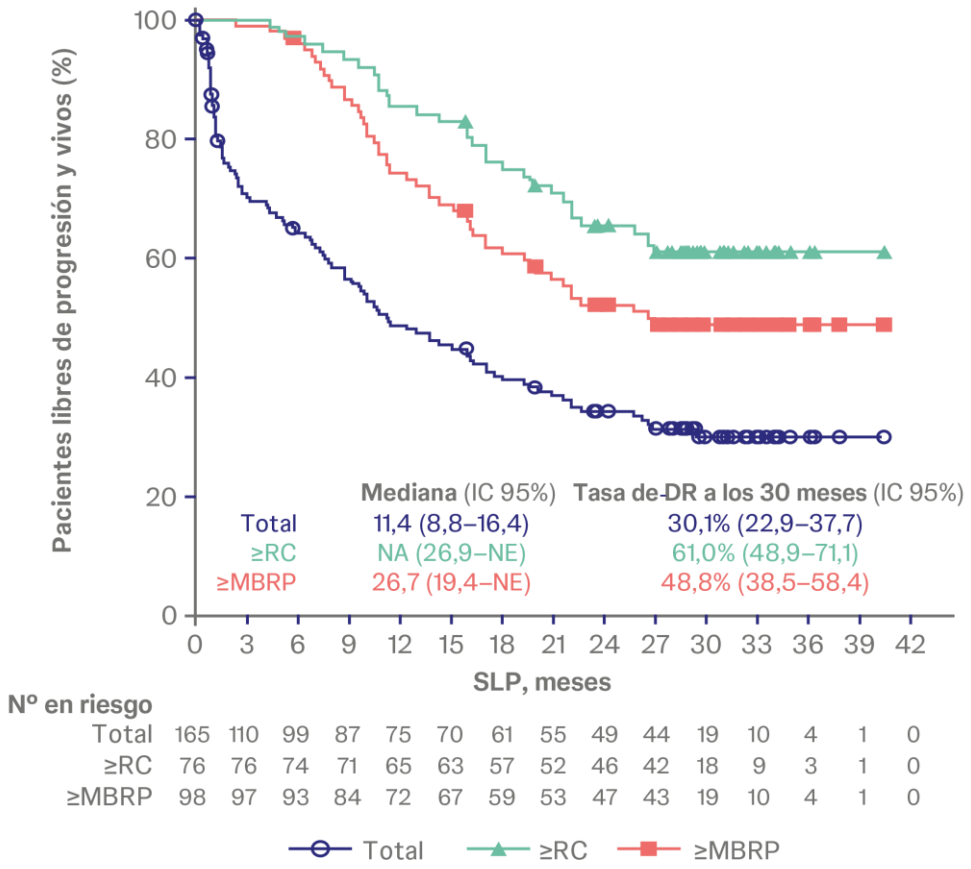
Mediana de tiempo a primera respuesta:[2]	Mediana de tiempo hasta ≥RC[3]
1,2 meses (intervalo: 0,2-5,5)	**4,6 meses** (intervalo: 1,6-18,5)

MM: mieloma múltiple; RC: respuesta completa.

1. Chanan-Khan AA, Giralt S. J Clin Oncol. 2010 May 20;28(15):2612-24. 2. Moreau P, *et al.* N Engl J Med. 2022;387(6):495-505. 3. Sidana S, *et al.* P879. EHA 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany.12

mSLP no alcanzada para los pacientes con ≥RC[1]

Supervivencia libre de progresión



≈3 de cada 5* pacientes tratados con teclistamab alcanzaron una mSLP >26 meses[1]

Gráfica modificada en base a la figura 4 de Garfall *et al.* 2024.[1]
Figura 4 completa disponible aquí.
Mediana de seguimiento de los datos: 30,4 meses.

*≥MBRP 59,4%.[1]

IC: intervalo de confianza; **MBRP:** muy buena respuesta parcial; **mSLP:** mediana de la supervivencia libre de progresión; **NA:** no alcanzada; **NE:** no estimable; **RC:** respuesta completa; **SLP:** supervivencia libre de progresión.

1. Garfall AL, *et al.* Presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA & Virtual. (Poster 7540).

7540

Long-Term Follow-Up From the Phase 1/2 MajesTEC-1 Trial of Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma

Alfred L Garfall[1], Ajay K Nooka[2], Niels WCJ van de Donk[3], Philippe Moreau[4], Manisha Bhutani[5], Albert Oriol[6], Thomas G Martin[7], Laura Rosiñol[8], María-Victoria Mateos[9], Nizar J Bahlis[10], Rakesh Popat[11], Britta Besemer[12], Joaquín Martínez-López[13], Amrita Y Krishnan[14], Michel Delforge[15], Lin Huang[16], Deeksha Vishwamitra[16], Tara Stephenson[16], Katherine Chastain[17], Surbhi Sidana[18]

Key Takeaway

With the longest follow-up of any bispecific antibody in multiple myeloma (median 30.4 months), teclistamab continues to demonstrate deep and durable responses, including in patients who transition to less frequent dosing

Conclusions

- Teclistamab ORR was 63.0%, with 46.1% of patients achieving ≥CR
- Of MRD-evaluable patients, 85.7% were MRD-negative at any point, sustained for ≥6 months in 56.1% and ≥12 months in 38.9%
- Teclistamab mDOR increased to 24 months overall, and was NR for patients in ≥CR (30-month DOR rate, 60.8%)
- Teclistamab offers an effective treatment for patients with TCE RRMM, with a manageable safety profile and no new safety signals

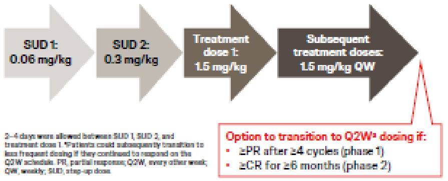
Introduction

- Teclistamab is the first approved B-cell maturation antigen (BCMA) × CD3 bispecific antibody for the treatment of triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM), with weight-based dosing[1-3]
- At 22.8-month median follow-up (mFU) in the MajesTEC-1 study, rapid, deep, and durable responses were observed in patients treated with teclistamab[4]
  - Overall response rate (ORR), 63.0%; complete response or better (≥CR) rate, 45.5%
  - Median duration of response (DOR), 21.6 months; median progression-free survival (PFS), 11.3 months; median overall survival (OS), 21.9 months
- Here, we present longer-term results from MajesTEC-1 at 30.4-month mFU

Methods

- The MajesTEC-1 study design has been previously described (NCT03145181, NCT04557098)[3]
  - Eligible patients had TCE RRMM with no prior BCMA-directed therapy
  - Primary endpoint: ORR
  - Patients received teclistamab at the recommended phase 2 dose (RP2D), with the option to transition to less frequent dosing (Figure 1)

Figure 1: Teclistamab dosing schedule



Results

Study population

- At 30.4-month mFU (data cut-off: Aug 22, 2023), 165 patients had received teclistamab at the RP2D
  - Baseline characteristics have been previously presented[3,4]
  - 65 patients had transitioned to less frequent dosing (eg, Q2W)
- 38 patients remain on treatment (37 on a less frequent dosing schedule)

Efficacy

- ORR was 63.0% (≥CR, 46.1%); responses continued to deepen and remained durable (Figures 2 and 3)
- 85.7% (48/56) of minimal residual disease (MRD)-evaluable patients achieved MRD negativity (10^{-5} threshold), sustained for ≥6 months in 56.1% (23/41) and for ≥12 months in 38.9% (14/36) (Table 1 and Supplemental Figure 2)
- DOR, PFS, and OS were further improved for patients who achieved very good partial response (VGPR) or better, ≥CR, or MRD negativity, and for those with ≤3 vs >3 prior lines of therapy (LOT) (Figure 4 and Table 1)
  - No notable differences in baseline characteristics were observed between patients with ≤3 vs >3 prior LOT

Figure 2: ORR

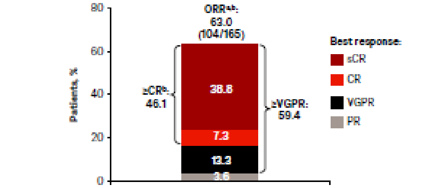


Table 1: DOR, PFS, and OS in patient subgroups

	mDOR, mo (95% CI)	mPFS, mo (95% CI)	mOS, mo (95% CI)
All RP2D (N=165)[a]	24.0 (17.0–NE)	11.4 (8.8–16.4)	22.2 (15.1–29.9)
≥CR (n=76)[a]	NR (26.7–NE)	NR (26.9–NE)	NR (35.5–NE)
≥VGPR (n=98)[a]	25.6 (18.1–NE)	26.7 (19.4–NE)	NR (31.0–NE)
MRD-neg (n=48)[b]	NR (19.2–NE)	NR (21.0–NE)	NR (29.9–NE)
≤3 pLOT (n=43)	24.0 (14.0–NE)	21.7 (13.8–NE)	NR (18.3–NE)
>3 pLOT (n=122)	22.4 (14.9–NE)	9.7 (6.4–13.1)	17.7 (12.2–29.7)
Phase 2 efficacy (USPI) (n=110)[c]	22.4 (14.9–NE)	10.8 (7.4–16.4)	21.7 (12.7–29.9)
≥CR (n=51)[c]	NR (21.6–NE)	NR (22.8–NE)	NR (NE–NE)

[a]Supplemental Figure 1. [b]Supplemental Figure 2. [c]Supplemental Figure 3.
mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; MRD-neg, MRD negative; NE, not estimable; NR, not reached; pLOT, prior line of therapy.

Figure 3: DOR

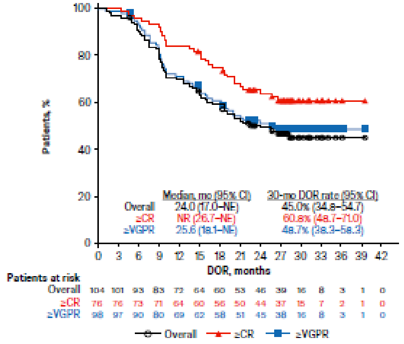
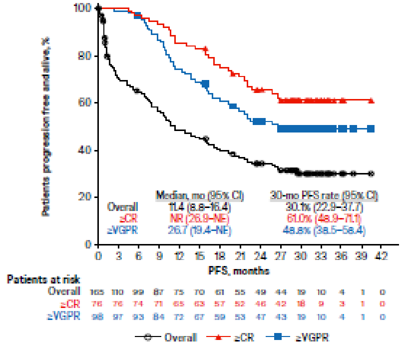


Figure 4: PFS



Safety

- The most common treatment-emergent adverse event (TEAEs) remained cytopenias and infections (Table 2)
- No changes in cytokine release syndrome (CRS) or immune effector cell–associated neurotoxicity syndrome at 30.4-month mFU
- Infections occurred in 78.8% of patients (grade 3/4, 55.2%)
  - Of grade 5 infections, 18/22 were due to COVID-19
    - No new grade 5 COVID-19 TEAEs at 30.4-month mFU
  - Onset of new grade ≥3 infections continued to generally decline over time
    - Factors such as transitioning to Q2W dosing and increasing use of immunoglobulin replacement may contribute to this trend
- TEAEs leading to dose reduction (n=1 [0.6%]) or discontinuation (n=8 [4.8%]; 5 due to infection) were infrequent
- No new safety signals were reported

Table 2: TEAEs occurring in ≥20% of patients in MajesTEC-1

TEAEs, n (%)	N=165 Any Grade	N=165 Grade 3/4
Any TEAE	165 (100)	156 (94.5)
Hematologic		
Neutropenia	118 (71.5)	108 (65.5)
Anemia	91 (55.2)	62 (37.6)
Thrombocytopenia	69 (41.8)	38 (23.0)
Lymphopenia	60 (36.4)	57 (34.5)
Leukopenia	33 (20.0)	15 (9.1)
Nonhematologic		
Infections	130 (78.8)	91 (55.2)
COVID-19	48 (29.1)	35 (21.2)
CRS	119 (72.1)	1 (0.6)
Diarrhea	57 (34.5)	6 (3.6)
Pyrexia	51 (30.9)	1 (0.6)
Fatigue	50 (30.3)	4 (2.4)
Cough	46 (27.9)	0
Nausea	45 (27.3)	1 (0.6)
Injection site erythema	44 (26.7)	0
Arthralgia	42 (25.5)	2 (1.2)
Headache	40 (24.2)	1 (0.6)
Constipation	37 (22.4)	0
Hypogammaglobulinemia	36 (21.8)	3 (1.8)
Back pain	33 (20.0)	4 (2.4)

Multiple Myeloma

Please scan QR code

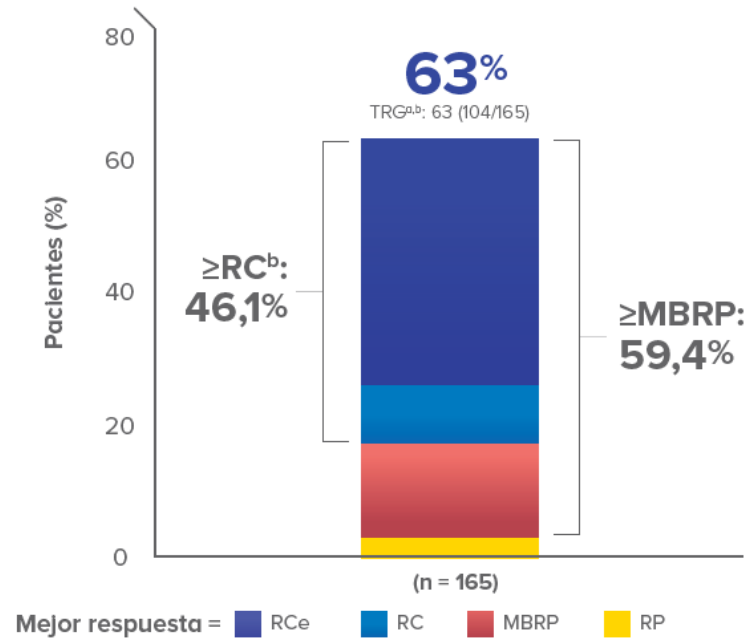
Poster

Supplementary material

¿Es posible optimizar los resultados del tratamiento?

En el estudio MajesTEC-1, tras 30,4 meses de mediana de seguimiento:[1,2]

Tasa de respuesta global



[a]TRG evaluada por un comité de revisión independiente.
[b]A los 30 meses de mediana de seguimiento de la población de fase 2 de eficacia (pacientes inscritos en la cohorte A el 18 de marzo de 2021 o antes; n=110 pacientes de acuerdo con la ficha técnica de EE. UU.): TRG, 61,8%; ≥RC, 46,4% (n=51).
Figura adaptada de la figura 2 de Garfall *et al.* 2024.[1]
Figura original disponible aquí.

Población MajesTEC-1:

- **Casi la mitad de los pacientes alcanzan ≥RC**[1]
- De los pacientes con EMR evaluable, **el 85,7% fueron EMR-** 10^{-5} en cualquier momento[1]
- Mediana de tiempo hasta ≥RC: **4,6 meses** (intervalo: 1,6-18,5)[3]

Utilizado en líneas tempranas, teclistamab ofrece:[2]

- **6 de cada 10** pacientes alcanzan ≥RC[§]
- De los pacientes con EMR evaluable, el **94,1%** fueron EMR- 10^{-5} en cualquier momento
- Estos resultados se alcanzan más rápido: 3 **meses para alcanzar la mejor respuesta** (vs. 5,7 meses)

Tasa de respuesta global

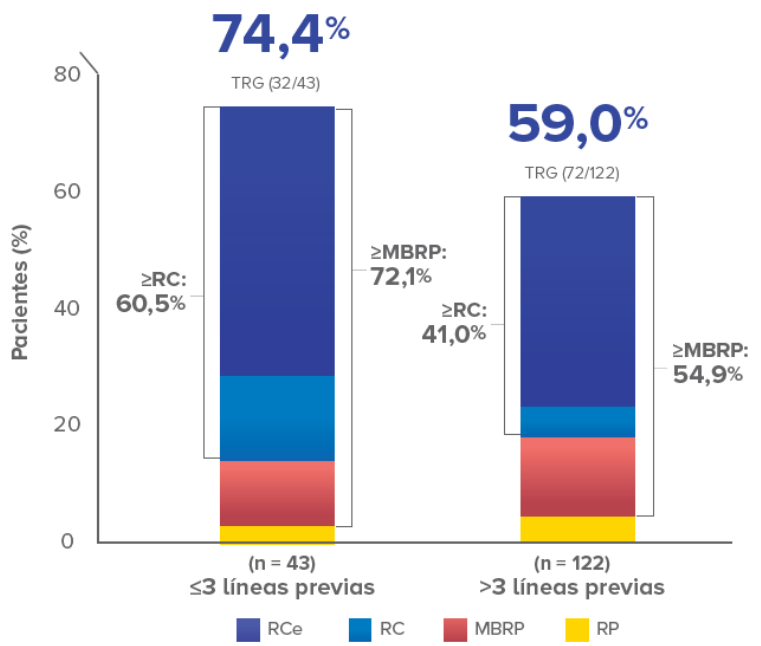
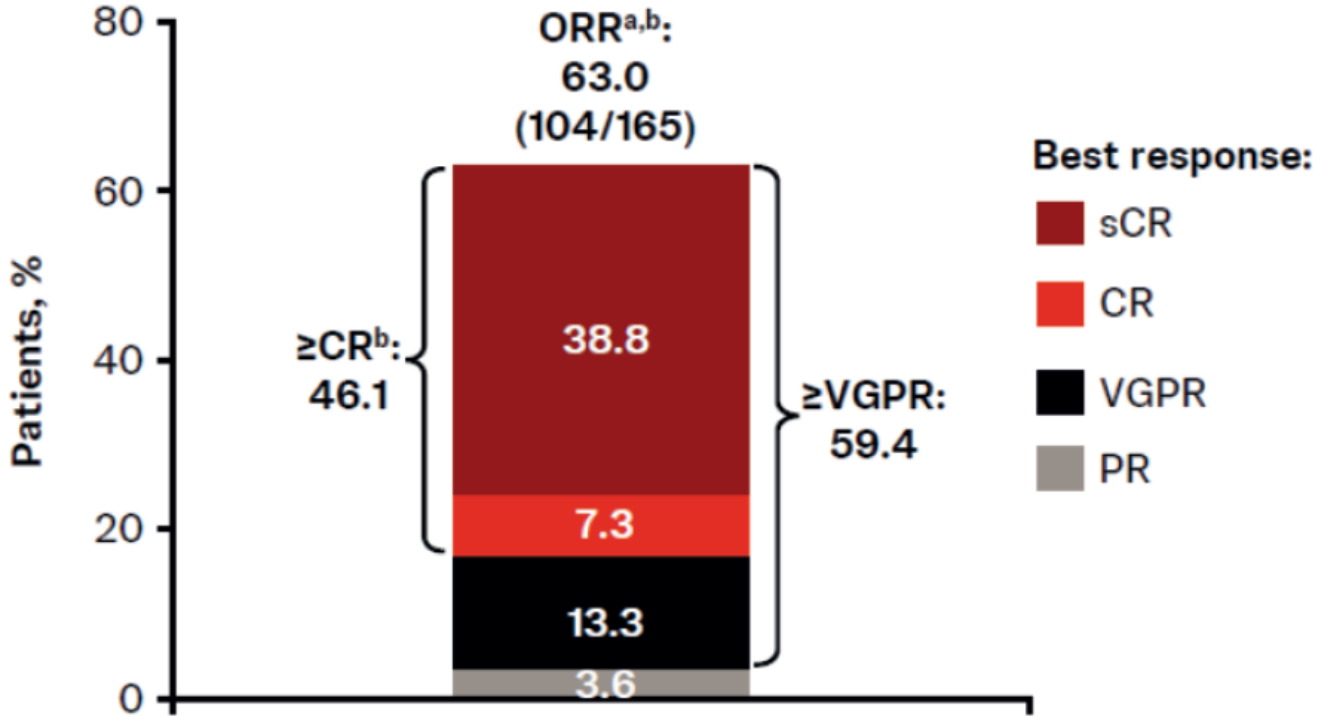


Figura adaptada de la figura 2 de Costa *et al.* 2024.[2]
Figura original disponible aquí.

[§]60,5%.
El 100% de los pacientes de este subanálisis eran triple clase expuestos (IP, IMID, antiCD38).* De los 165 pacientes del MajesTEC-1, 122 pacientes habían recibido >3 líneas previas (mediana de líneas previas 5 (rango: 4-14)) y 43 pacientes ≤3 líneas previas (mediana de líneas previas 3 (rango: 2-3)).* 38/43 pacientes recibió teclistamab en 4L, 5/43 pacientes en 3L y ninguno en 2L.[#] *Datos extraídos de la Tabla 1 de Costa,[2] tabla completa disponible aquí. [#]Datos extraídos de la Tabla 14 de Tecvayli EMA assessment report,[4] tabla completa disponible aquí.
EMR: enfermedad mínima residual; **MBRP:** muy buena respuesta parcial; **RC:** respuesta completa; **RCe:** respuesta completa estricta; **RP:** respuesta parcial; **TRG:** tasa de respuesta global.
1. Garfall AL, *et al.* Presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA & Virtual. (Poster 7540). 2. Costa LJ, *et al.* Póster 912. Presentado en el Congresso Brasileiro de Hematologia, Hemoterapia e Terapia Celular (HEMO 2024) – São Paulo. 3. Sidana S, *et al.* Presented at the European Hematology Association (EHA) 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany. (Poster P879). 4. EPAR TECVAYLI®. Disponible en: https://www.ema.europa.eu/en/medicines/human/EPAR/tecvayli Consultado por última vez en abril de 2025

Figure 2: ORR



[a]Response assessed by independent review committee. [b]At 30-month mFU of the phase 2 efficacy population (patients enrolled in cohort A on or before March 18, 2021; n=110 patients supporting the USPI[1]): ORR, 61.8%; ≥CR, 46.4% (n=51). sCR, stringent complete response; USPI, United States prescribing information.

Figura 2 de Garfall *et al*. 2024.

Figure 2: Response rates.

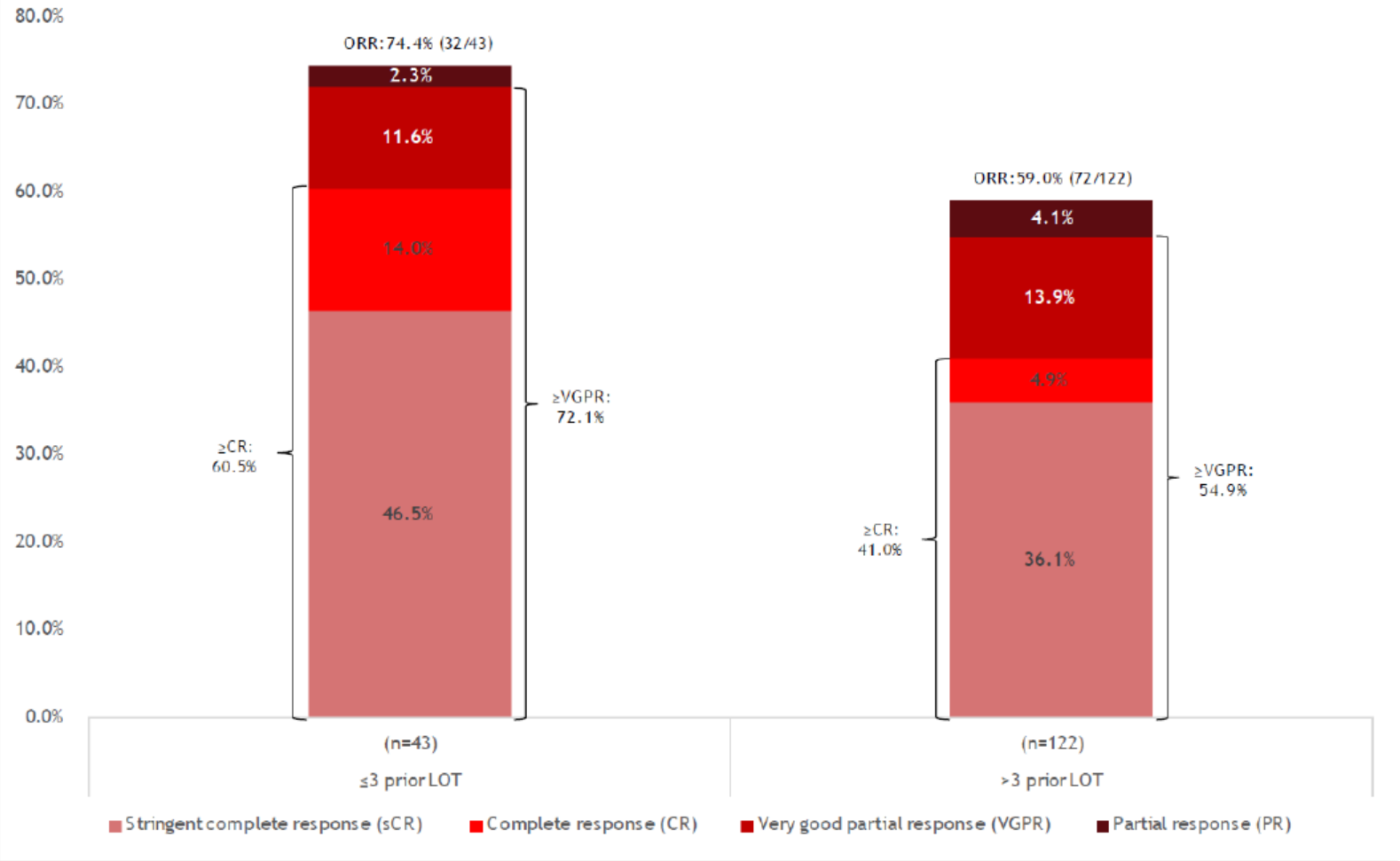


Figura 2 de Costa *et al*. 2024.

En el estudio MajesTEC-1, tras 30,4 meses de mediana de seguimiento:[1,2]

Población MajesTEC-1:

- **Casi la mitad de los pacientes alcanzan ≥RC**[1]
- De los pacientes con EMR evaluable, **el 85,7% fueron EMR-** 10^{-5} en cualquier momento[1]
- Mediana de tiempo hasta ≥RC:

4,6 meses (intervalo: 1,6-18,5)[3]

Utilizado en líneas tempranas, Tecvayli® ofrece:[2]

- **6 de cada 10** pacientes alcanzan **≥RC**§
- De los pacientes con EMR evaluable, el **94,1%** fueron **EMR-** 10^{-5} en cualquier momento
- Estos resultados se alcanzan más rápido: **3 meses para alcanzar la mejor respuesta** (vs. 5,7 meses)

§60,5%.

El 100% de los pacientes de este subanálisis eran triple clase expuestos (IP, IMID, antiCD38).* De los 165 pacientes del MajesTEC-1, 122 pacientes habían recibido >3 líneas previas (mediana de líneas previas 5 (rango: 4-14)) y 43 pacientes ≤3 líneas previas (mediana de líneas previas 3 (rango: 2-3)).* 38/43 pacientes recibió teclistamab en 4L, 5/43 pacientes en 3L y ninguno en 2L.# *Datos extraídos de la Tabla 1 de Costa,[2] tabla completa disponible aquí. #Datos extraídos de la Tabla 14 de Tecvayli EMA assessment report,[4] tabla completa disponible aquí.

EMR: enfermedad mínima residual; **MBRP:** muy buena respuesta parcial; **RC:** respuesta completa; **RCe:** respuesta completa estricta; **RP:** respuesta parcial; **TRG:** tasa de respuesta global.

1. Garfall AL, *et al.* Presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA & Virtual. (Poster 7540). 2. Costa LJ, *et al.* Póster 912. Presentado en el Congresso Brasileiro de Hematologia, Hemoterapia e Terapia Celular (HEMO 2024) – São Paulo. 3. Sidana S, *et al.* Presented at the European Hematology Association (EHA) 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany. (Poster P879). 4. EPAR TECVAYLI®. Disponible en: https://www.ema.europa.eu/en/medicines/human/EPAR/tecvayli Consultado por última vez en abril de 2025.

Table 1: Prior treatment exposure by number of prior LOT.

Characteristic	≤3 prior LOT (n=43)	>3 prior LOT (n=122)
Number of prior LOT, median (range)	3 (2-3)	5 (4-14)
Triple-class exposed, n (%)	43 (100.0)	122 (100.0)
Penta-drug exposed, n (%)	20 (46.5)	96 (78.7)
Refractory status		
Any anti-CD38 antibody, n (%)	39 (90.7)	109 (89.3)
Double-class,[a] n (%)	25 (58.1)	108 (88.5)
Triple-class,[b] n (%)	25 (58.1)	103 (84.4)
Penta-drug,[c] n (%)	5 (11.6)	45 (36.9)
Last LOT, n (%)	40 (93.0)	108 (88.5)
Drug-specific refractory status		
Bortezomib, n (%)	15 (34.9)	68 (55.7)
Carfilzomib, n (%)	22 (51.2)	73 (59.8)
Lenalidomide, n (%)	32 (74.4)	101 (82.8)
Pomalidomide, n (%)	25 (58.1)	102 (83.6)

[a]PI + IMiD. [b]PI + IMiD + anti-CD38 antibody. [c]2 PIs + 2 IMiDs + anti-CD38 antibody.

Tabla 1 de Costa *et al.* 2024.

Table 14. Prior Anti-Cancer Medications for MM (MajesTEC-1study, RP2D, phase 1 and Cohort A, phase 2)

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Total number of subjects with any prior therapies for multiple myeloma	40 (100.0%)	125 (100.0%)	165 (100.0%)
Number of prior lines of therapy[a]			
N	40	125	165
Category			
2	3 (7.5%)	2 (1.6%)	5 (3.0%)
3	9 (22.5%)	29 (23.2%)	38 (23.0%)
4	4 (10.0%)	31 (24.8%)	35 (21.2%)
5	9 (22.5%)	25 (20.0%)	34 (20.6%)
> 5	15 (37.5%)	38 (30.4%)	53 (32.1%)
Mean (SD)	5.1 (2.19)	5.1 (2.17)	5.1 (2.17)
Median	5.0	5.0	5.0
Range	(2; 11)	(2; 14)	(2; 14)
Prior PI	40 (100.0%)	125 (100.0%)	165 (100.0%)
Bortezomib	39 (97.5%)	123 (98.4%)	162 (98.2%)
Carfilzomib	32 (80.0%)	87 (69.6%)	119 (72.1%)
Ixazomib	9 (22.5%)	31 (24.8%)	40 (24.2%)
Prior IMiD	40 (100.0%)	125 (100.0%)	165 (100.0%)
Lenalidomide	39 (97.5%)	122 (97.6%)	161 (97.6%)
Pomalidomide	31 (77.5%)	108 (86.4%)	139 (84.2%)
Thalidomide	12 (30.0%)	48 (38.4%)	60 (36.4%)
Prior anti-CD38	40 (100.0%)	125 (100.0%)	165 (100.0%)
Daratumumab	40 (100.0%)	112 (89.6%)	152 (92.1%)
Isatuximab	0	21 (16.8%)	21 (12.7%)
Prior Selinexor	1 (2.5%)	5 (4.0%)	6 (3.6%)
Prior Melphalan Flufenamide	1 (2.5%)	0	1 (0.6%)
Prior PI+IMiD	40 (100.0%)	125 (100.0%)	165 (100.0%)
Prior PI+IMiD+anti-CD38	40 (100.0%)	125 (100.0%)	165 (100.0%)
Prior penta-exposed	26 (65.0%)	90 (72.0%)	116 (70.3%)

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Prior transplantation	34 (85.0%)	101 (80.8%)	135 (81.8%)
Autologous	34 (85.0%)	101 (80.8%)	135 (81.8%)
1	28 (70.0%)	84 (67.2%)	112 (67.9%)
≥ 2	6 (15.0%)	17 (13.6%)	23 (13.9%)
Allogenic	4 (10.0%)	4 (3.2%)	8 (4.8%)
Prior radiotherapy	18 (45.0%)	49 (39.2%)	67 (40.6%)
Prior cancer-related surgery/procedure	5 (12.5%)	19 (15.2%)	24 (14.5%)

Key: PI=proteasome inhibitor; IMiD=Immunomodulatory agent; RP2D=recommended Phase 2 dose

[a] Based on data recorded on prior systemic therapy eCRF page.

Note: PI includes bortezomib, carfilzomib, ixazomib; IMiD includes thalidomide, lenalidomide, and pomalidomide; anti-CD38 includes daratumumab and isatuximab. Penta includes at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.

Note: Percentages calculated with the number of all treated subjects as denominator.

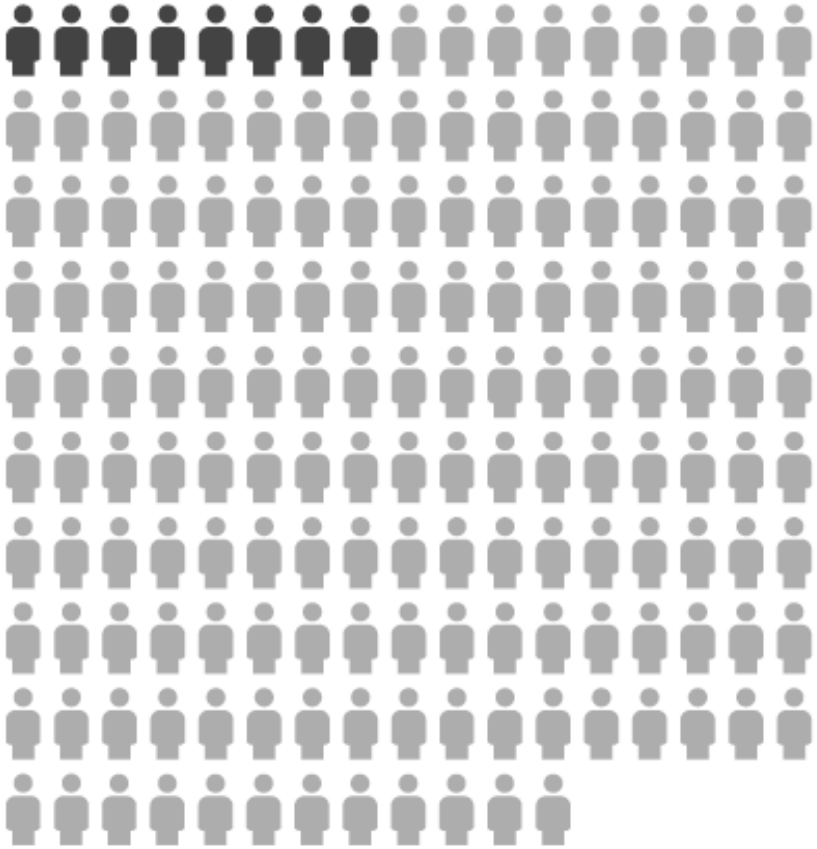
Tabla 14 del Tecvayli® EMA assessment report.

¿Qué podemos esperar del perfil de seguridad*?

*Para mayor información acerca del perfil de seguridad de Tecvayli® consultar sección 4.4 y 4.8 de la Ficha Técnica.

Con 30,4 meses de mediana de seguimiento, teclistamab mantiene un perfil de seguridad predecible y manejable[1]

<5%* de interrupciones por EEAA[1]



30,4 meses de mediana de seguimiento
*La interrupción del tratamiento debido a EEAA (n=8 [4,8%]; incluidas 5 debidas a infecciones) fueron infrecuentes. La infografía representa los 8 pacientes sobre 165 que interrumpieron definitivamente el tratamiento[1]
Tabla de efectos adversos que ocurrieron en ≥20% de los pacientes del MajesTEC-1 disponible aquí.
EEAA: eventos adversos; **MM:** mieloma múltiple.
1. Garfall AL, *et al.* Presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA & Virtual. (Poster 7540).

Table 2: TEAEs occurring in ≥20% of patients in MajesTEC-1

TEAEs, n (%)	N=165	
	Any Grade	Grade 3/4
Any TEAE	**165 (100)**	**156 (94.5)**
Hematologic		
Neutropenia	118 (71.5)	108 (65.5)
Anemia	91 (55.2)	62 (37.6)
Thrombocytopenia	69 (41.8)	38 (23.0)
Lymphopenia	60 (36.4)	57 (34.5)
Leukopenia	33 (20.0)	15 (9.1)
Nonhematologic		
Infections	130 (78.8)	91 (55.2)
COVID-19	48 (29.1)	35 (21.2)
CRS	119 (72.1)	1 (0.6)
Diarrhea	57 (34.5)	6 (3.6)
Pyrexia	51 (30.9)	1 (0.6)
Fatigue	50 (30.3)	4 (2.4)
Cough	46 (27.9)	0
Nausea	45 (27.3)	1 (0.6)
Injection site erythema	44 (26.7)	0
Arthralgia	42 (25.5)	2 (1.2)
Headache	40 (24.2)	1 (0.6)
Constipation	37 (22.4)	0
Hypogammaglobulinemia	36 (21.8)	3 (1.8)
Back pain	33 (20.0)	4 (2.4)

Tabla 2 de Garfall *et al*. 2024.

CRS, neurotoxicidad, infecciones

CRS: síndrome de liberación de citoquinas, por sus siglas en inglés.

La mayoría de los CRS se produjeron durante la pauta de escalado, requiriendo vigilancia durante el inicio del tratamiento[1]

Incidencia global de CRS con teclistamab en MajesTEC-1 (N=165)

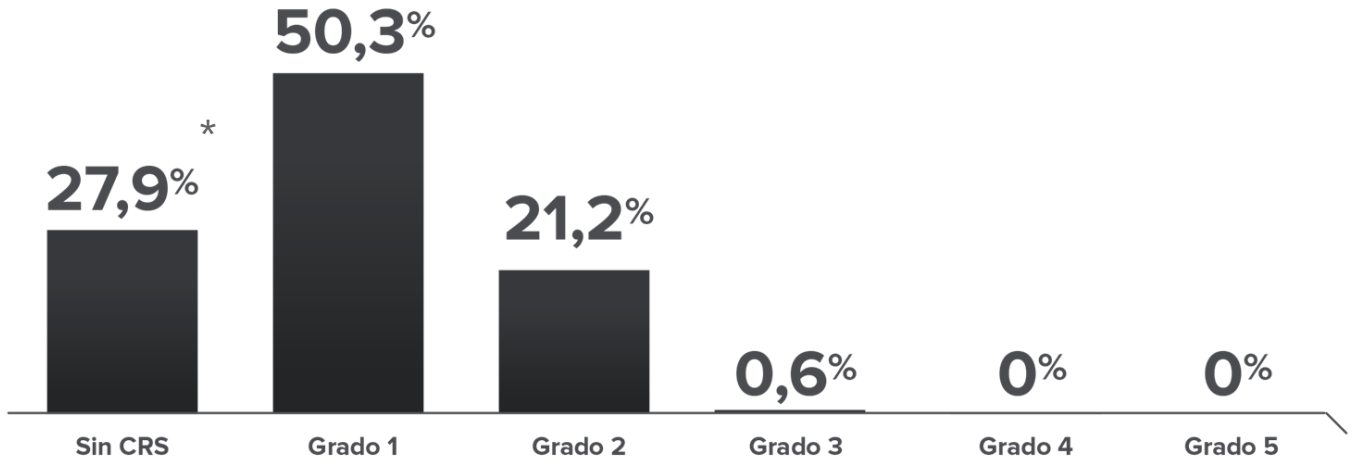


Figura construida en base a la tabla 1 de Martin *et al.* 2023.[1]
Tabla completa disponible aquí

Mediana de tiempo hasta el inicio del CRS[1]

2 días
(rango: 1-6)

Mediana de duración del CRS[1]

2 días
(rango: 1-9)

Mediana de seguimiento de 14,1 meses.[1]
*El 27,9% proviene de restar al 100% de pacientes el 72,1% que tuvieron CRS.[1]
CRS: síndrome de liberación de citoquinas, por sus siglas en inglés.
1. Martin TG, *et al.* Cancer. 2023;129(13):2035-2046.

TABLE 1 Overall incidence of CRS with teclistamab in MajesTEC-1.

Patients with CRS events, No. (%)	Overall patients in MajesTEC-1 (*N* = 165)	First CRS event (*N* = 165)
Total patients with CRS	119 (72.1)	119 (72.1)
Maximum toxicity grade		
Grade 1	83 (50.3)	87 (52.7)
Grade 2	35 (21.2)	32 (19.4)
Grade 3	1 (0.6)	0
Grade 4	0	0
Grade 5	0	0
Timing of CRS[a]		
Step-up dose 1	72 (43.6)	72 (43.6)
Step-up dose 2	58 (35.2)	32 (19.4)
Repeat step-up[b]	1 (0.6)	1 (0.6)
Cycle 1 day 1	40 (24.2)	10 (6.1)
Cycle 1 day 8	8 (4.8)	2 (1.2)
Cycle 1 day 15	4 (2.4)	0
Cycle 1 day 22	2 (1.2)	2 (1.2)
Cycle 2+[c]	6 (3.6)	0
Patients with multiple events	55 (33.3)	–
Worse grade at any subsequent event	4 (2.4)	–
Discontinuation due to CRS	0	–

Note: CRS was graded according to American Society for Transplantation and Cellular Therapy criteria.[6]

Abbreviation: CRS, cytokine release syndrome.

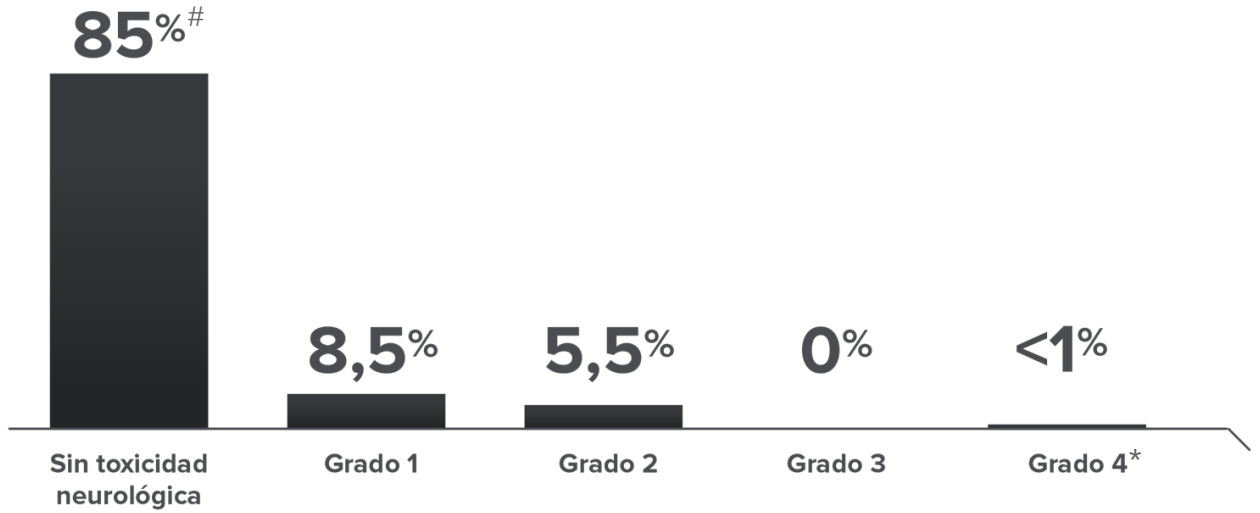
[a]Patients may appear in more than one category. Occurrence was based on the last treatment visit on or before the day in which the event occurred.

[b]Before cycle 1.

[c]One patient had grade 1 CRS after a repeat step-up dose in cycle 6; one patient had grade 2 CRS after a repeat step-up dose in cycle 2.

El 15% de los pacientes presentaron algún evento de neurotoxicidad[1]

Incidencia global de toxicidades neurológicas en MajesTEC-1 (N=165)



Datos extraídos de la Ficha Técnica de Tecvayli®.[1]

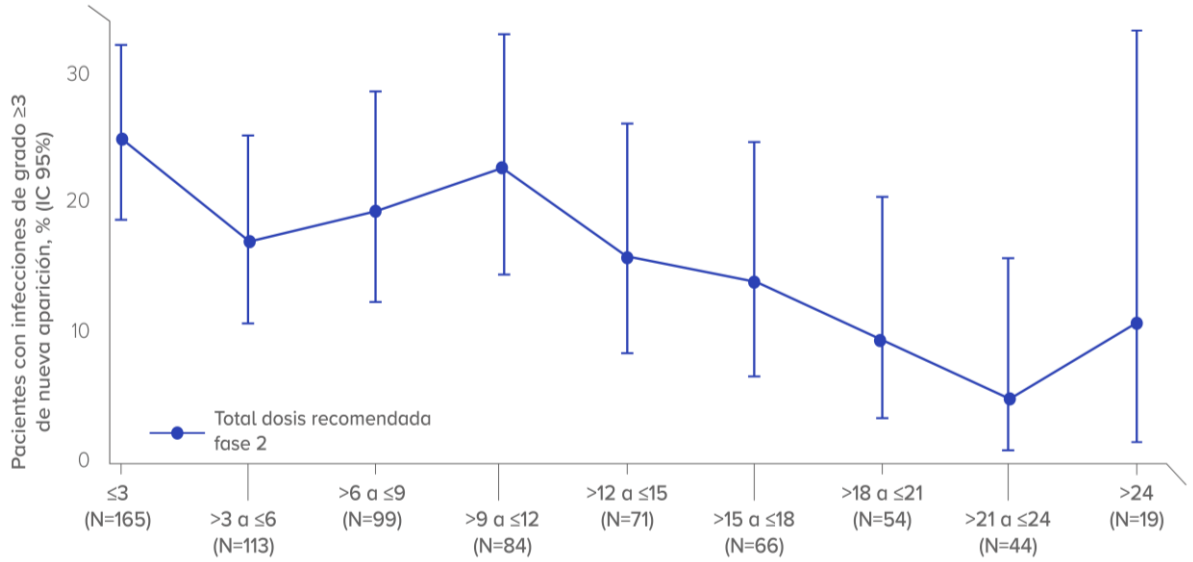
Pacientes que presentaron ICANS[1,^]	Mediana de tiempo hasta la aparición del ICANS desde la última dosis de teclistamab[2,^]	Mediana de duración del ICANS[2,^]
3% (n=5)	**4 días** (rango: 2-8)	**3 días** (rango: 1-20)

#El 85% proviene de restar al 100% de pacientes el 15% que tuvieron neurotoxicidad.[1]
*Evento convulsivo grado 4 reportado en un paciente con meningitis bacteriana.[3]
^Mediana de seguimiento de 14,1 meses.[2]
ICANS: síndrome de neurotoxicidad asociada a células inmunoefectoras.
1. Ficha técnica de TECVAYLI®. **2.** Hua G, *et al.* J Adv Pract Oncol. 2023 Mar;14(2):163-171. **3.** Moreau P, *et al.* N Engl J Med. 2022;387(6):495-505.

Se reportaron un 3% de discontinuaciones en el manejo de infecciones[1,*]

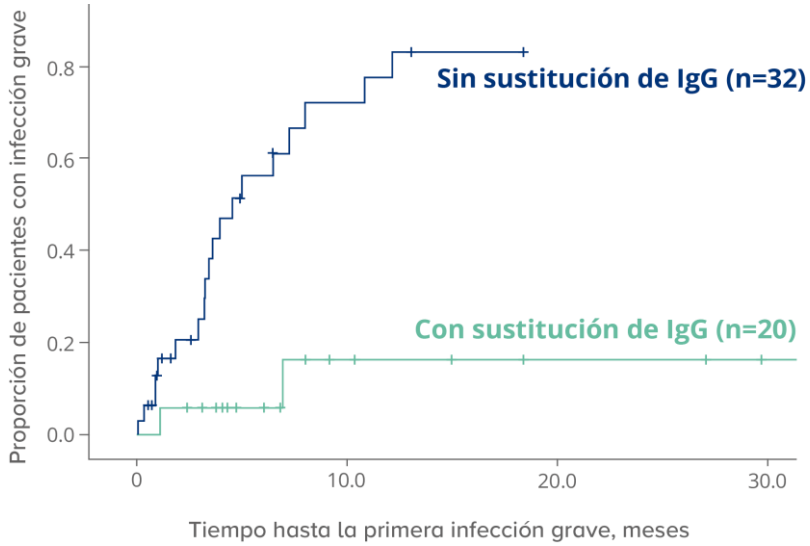
La aparición de nuevas infecciones de grado ≥3 disminuyó con el tiempo, en consonancia con el momento en que se pasó a una **dosificación menos frecuente**[2,^]

Nuevas infecciones de grado ≥3 a lo largo del tiempo



Mediana de seguimiento de 23 meses.
Figura 5 de van de Donk *et al.* 2023.[3]

La IVIG protege frente infecciones graves (grado ≥3)[3]



Mediana de seguimiento de 23 meses.
Figura de van de Donk *et al.* 2023.[4]

*5 casos entre 165 pacientes totales.[1] Un 78,8% de pacientes presentaron infecciones de cualquier grado (55,2% de grado 3/4), con un 29,1% de COVID-19 de cualquier grado (21,2% de grado 3/4). Tabla completa disponible aquí.
^Para más información consultar sección 4.4 y 4.8 de la Ficha Técnica.
IVIG: inmunoglobulina intravenosa; **Q2W:** cada 2 semanas.

1. Garfall AL, *et al.* Presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA & Virtual. (Poster 7540). **2.** Sidana S, *et al.* P879. Presented at the (EHA) 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany. **3.** van de Donk, NWJS; *et al.* P8011. Presented at the 2023 ASCO Annual Meeting; June 2–6, 2023; Chicago, IL, USA & Virtual. **4.** Van de Donk NWJS, *et al.* Oral presentation. Presented at the 20th IMS Annual Meeting; September 27-30, 2023; Athens, Greece.

Table 2: TEAEs occurring in ≥20% of patients in MajesTEC-1

TEAEs, n (%)	N=165	
	Any Grade	Grade 3/4
Any TEAE	**165 (100)**	**156 (94.5)**
Hematologic		
Neutropenia	118 (71.5)	108 (65.5)
Anemia	91 (55.2)	62 (37.6)
Thrombocytopenia	69 (41.8)	38 (23.0)
Lymphopenia	60 (36.4)	57 (34.5)
Leukopenia	33 (20.0)	15 (9.1)
Nonhematologic		
Infections	130 (78.8)	91 (55.2)
COVID-19	48 (29.1)	35 (21.2)
CRS	119 (72.1)	1 (0.6)
Diarrhea	57 (34.5)	6 (3.6)
Pyrexia	51 (30.9)	1 (0.6)
Fatigue	50 (30.3)	4 (2.4)
Cough	46 (27.9)	0
Nausea	45 (27.3)	1 (0.6)
Injection site erythema	44 (26.7)	0
Arthralgia	42 (25.5)	2 (1.2)
Headache	40 (24.2)	1 (0.6)
Constipation	37 (22.4)	0
Hypogammaglobulinemia	36 (21.8)	3 (1.8)
Back pain	33 (20.0)	4 (2.4)

Tabla 2 de Garfall *et al*. 2024.

TECVAYLI® digital

Posología
y forma de administración

Con un esquema de dosis personalizado, basado en peso y flexible*,[1]

Escalado de dosis 1
Dosis de 0,06 mg/kg SC de TECVAYLI®
Primer día de tratamiento

Escalado de dosis 2
Dosis de 0,3 mg/kg SC de TECVAYLI®
**2-7 días después de la escalada de dosis 1*

Primera dosis de mantenimiento
Dosis de 1,5 mg/kg SC de TECVAYLI®
§2-7 días después de la escalada de dosis 2

↓

Continuar una vez por semana hasta la progresión de la enfermedad o toxicidad inaceptable^

Dosis quincenal con teclistamab:
En pacientes que presentan ≥RC durante al menos de 6 meses, se puede considerar una reducción en la frecuencia de dosis a 1,5 mg/kg SC cada dos semanas[2]

*Para más información acerca de la pauta posológica autorizada, consultar sección 4.2 de la Ficha Técnica.
^Dejar transcurrir un mínimo de cinco días entre las dosis de mantenimiento semanales.
RC: respuesta completa; SC: subcutánea.
1. Sidana S, *et al.* P879. Presented at the (EHA) 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany. 2. Ficha técnica de TECVAYLI®.

Conclusiones

Casi la mitad de los pacientes alcanzan respuesta completa*,[1]

- **mSLP no alcanzada** para estos pacientes[1]

Usado en líneas tempranas:[2]

- **Más del doble de mSLP** vs. líneas más tardías^
- Las tasas de **infecciones** de grado ≥3 fueron numéricamente **más bajas**§
- **3 meses para alcanzar la mejor respuesta** (vs. 5,7 meses)

<5%¶ de interrupciones por EEAA[2]

Manteniendo la dosis semanal basada en peso durante 6 meses desde ≥RC[3]

Más de 14.000 pacientes tratados‖,[4]

*46,1%.[1]
^mSLP ≤ 3 líneas de tratamiento previas fue de 21,7 meses (IC 95%, 13,8-NA) vs. 9,7 meses.[2]
§Respecto a líneas de tratamiento más tardías: ≤ 3 líneas de tratamiento previas (46,5%) vs. > 3 líneas de tratamiento previas (58,2%).[2]
¶Eventos adversos surgidos durante el tratamiento que condujeron a la interrupción del tratamiento (n=8 [4,8%]).[2]
‖Desde el primer paciente en ensayo clínico, a nivel global.[4]

1. Garfall AL, *et al.* Presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA & Virtual. (Poster 7540). **2.** Costa LJ, *et al.* Presented at European Hematology Association (EHA) Hybrid Congress; 13-16 June 2024; Madrid, Spain (Poster P923). **3.** Ficha Técnica de TECVAYLI®. **4.** Martin TG, *et al.* Póster 3331. Presentado en el Congreso anual de ASH, 7-10 diciembre 2024, San Diego, California, EEUU.

Ficha técnica

Ficha Técnica disponible en el siguiente link:

https://static.janssen-emea.com/sites/default/files/Spain/SMPC/ES-PL-0220.pdf

Para más información, acceda a
la Ficha Técnica a través del QR

TALVEY® (talquetamab-tgvs) Injection for subcutaneous use 2 mg/mL and 40 mg/mL

▼ TALVEY®

EVOLUCIONA TU ESTRATEGIA

ACTÚA CONTRA EL GPRC5D[1]

Para tus pacientes con mieloma múltiple en recaída y refractario triple expuestos*

TALVEY® es el primer y único anticuerpo biespecífico dirigido contra el GPRC5D aprobado para el MMRR[2]

*TALVEY® está indicado en monoterapia para el tratamiento de pacientes adultos con mieloma múltiple en recaída y refractario, que han recibido al menos 3 tratamientos previos, incluyendo un agente inmunomodulador, un inhibidor del proteasoma y un anticuerpo anti-CD38 y han presentado progresión de la enfermedad al último tratamiento.[1]

▼ Este medicamento está sujeto a seguimiento adicional, es prioritaria la notificación de sospechas de reacciones adversas asociadas a este medicamento.

CD38: *cluster of differentiation* 38; **GPRC5D:** miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; **MMRR:** mieloma múltiple en recaída y refractario.

1. Ficha Técnica TALVEY®; **2.** Jakubowiak A, *et al.* Updated Results of Talquetamab, a GPRC5DxCD3 Bispecific Antobody, in Patients With Relapsed/Refractory Multiple Myeloma With Prior Exposure to T-Cell Redirecting Therapies: Results of the Phase 1/2 MonumenTAL-1 Study. Poster 3377 presentado en 65th American Society of Hematology (ASH) Annual Meeting; 9-12 diciembre 2023; San Diego, CA. EEUU.

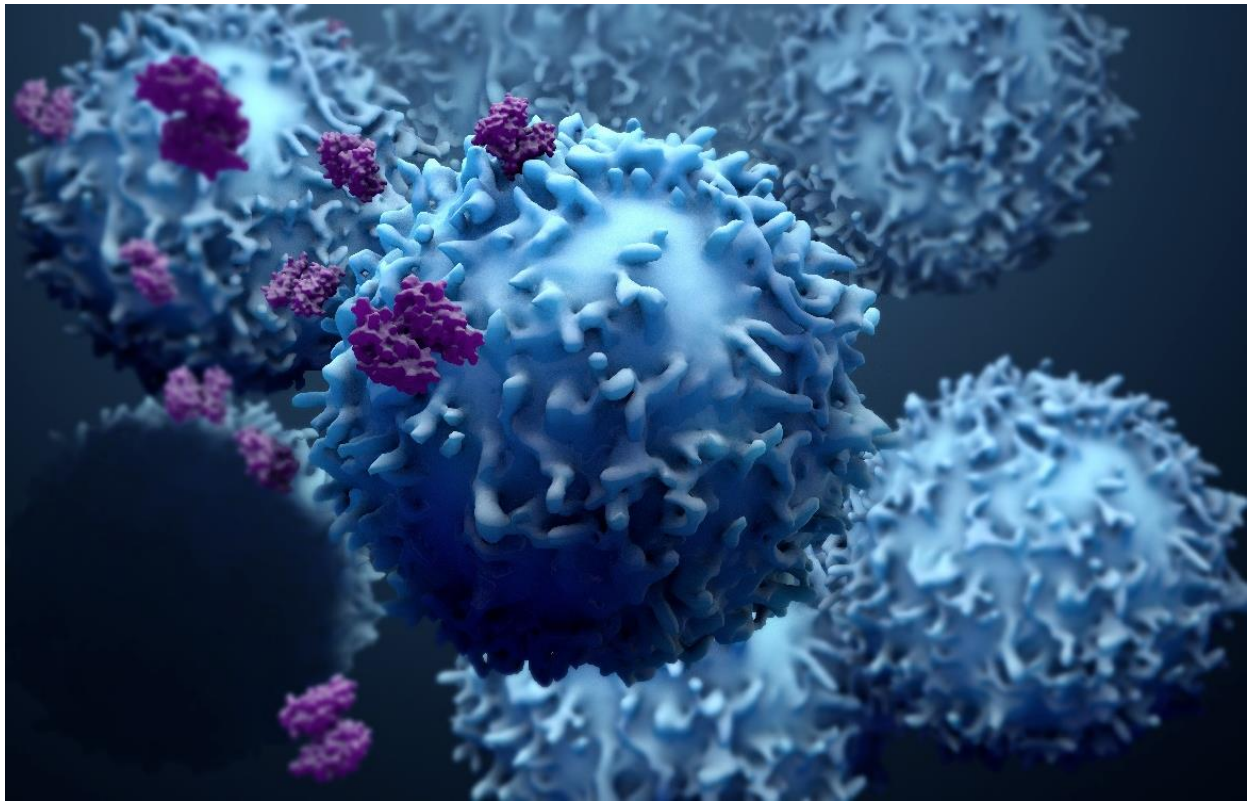
¿Qué hace diferente al GPRC5D de otras dianas terapéuticas frente al Mieloma Múltiple?

GPRC5D: miembro D del grupo 5 de la familia C del receptor acoplado a proteína G.

¿Qué hace diferente al GPRC5D?

- GPRC5D ha surgido como una **nueva diana terapéutica** para el tratamiento del MM[1]
- La expresión selectiva en las células de MM sugiere que GPRC5D es una **diana apropiada para la terapia mediada por células efectoras inmunitarias para tratar el MM**[1]

GPRC5D se expresa predominantemente en células plasmáticas y tiene una expresión de mínima a nula en linfocitos B normales, linfocitos T, células Natural Killer, monocitos, granulocitos y progenitores de médula ósea[1]

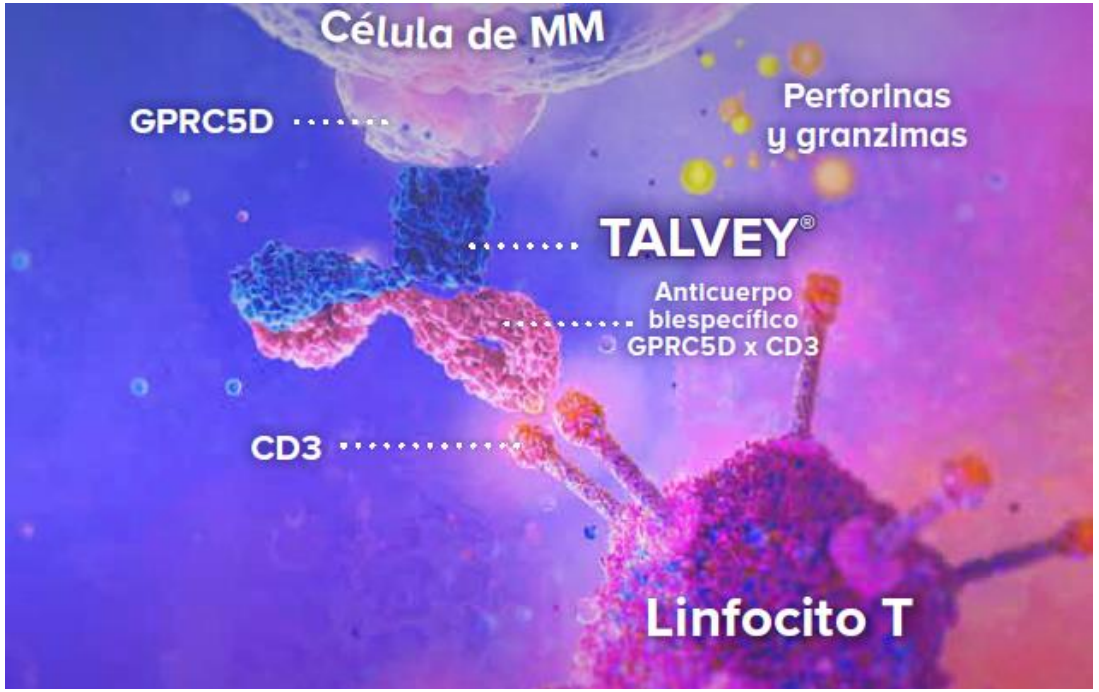


GPRC5D: miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; MM: mieloma múltiple.

1. Rodriguez-Otero P, *et al.* Correction: GPRC5D as a novel target for the treatment of multiple myeloma: a narrative review. Blood Cancer Journal.2024;14:24

TALVEY®: un anticuerpo biespecífico que se dirige contra CD3 y GPRC5D, redirige las células T1

TALVEY® se une simultáneamente a GPRC5D y a CD3 induciendo la muerte de las células de MM mediante el reclutamiento y activación de linfocitos T[2]

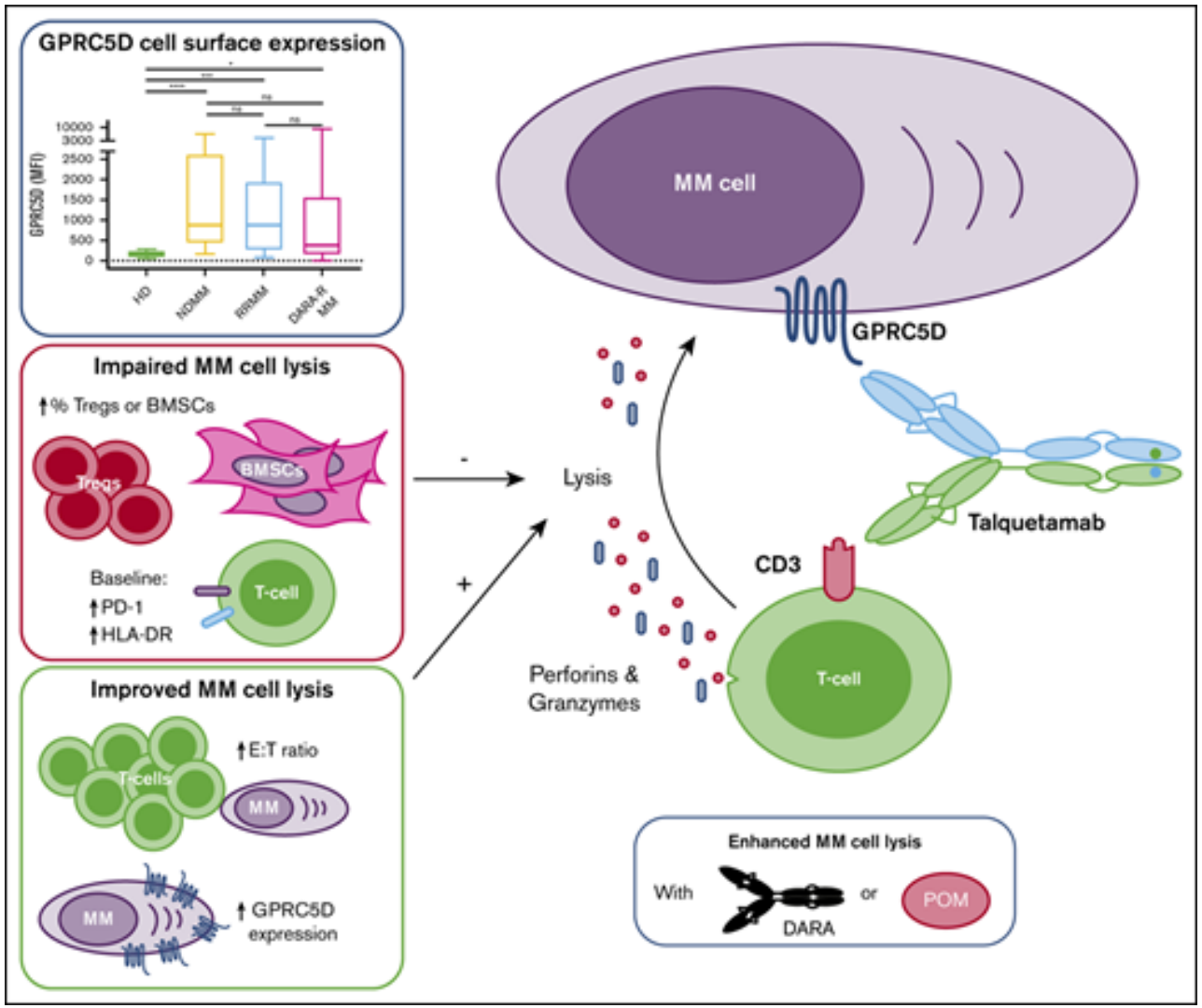


Adaptado del abstract gráfico de Verkleij CPM, *et al.* Blood Adv. 2021.[3] Figura original disponible AQUÍ

CD: *cluster of differentiation;* **GPRC5D:** miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; **MM:** mieloma múltiple.

1. Chari A, *et al.* Talquetamab, a T-Cell–Redirecting GPRC5D Bispecific Antibody for Multiple Myeloma. N Engl J Med. 2022;387(24):2232-2244; **2.** Shaver J, *et al.* Targeting GPRC5D With Talquetamab: A New Frontier in Bispecific Antibody Therapy for Relapsed/Refractory Multiple Myeloma. Ann Pharmacother. 2024 Aug 27:10600280241271192. doi: 10.1177/10600280241271192. Online ahead of print; **3.** Verkleij CP, *et al.* Preclinical activity and determinants of response of the GPRC5DxCD3 bispecific antibody talquetamab in multiple myeloma. Blood Adv 2021;5(8):2196-2215.

TALVEY®: un anticuerpo biespecífico que se dirige



Abstract gráfico de Verkleij CPM, *et al.* Blood Adv. 2021.

CD: *cluste*

1. Chari A, Bispecific Anti
mid determinants of response of the GPRC5DxCD3 bispecific antibody talquetamab in multiple myeloma. Blood Adv 2021;5(8):2196-2215.

Diseño del Ensayo Clínico MonumenTAL-1

Diseño del estudio Fase 1/2 MonumenTAL-1

Criterios de selección

Fase 1:

- Intolerancia o progresión con las terapias establecidas
- ECOG PS ≤1

Fase 2:

- ≥3 líneas de tratamiento previas (≥1 IP, ≥1 IMiD, y ≥1 anticuerpo anti-CD38)
- ECOG PS ≤2

TALVEY® 0,4 mg/kg SC
1 vez a la semana[a]
(TRL naïve) N = 143

TALVEY® 0,8 mg/kg SC
cada 2 semanas[a]
(TRL naïve) N = 154

TALVEY® 0,4 mg/kg SC
1 vez a la semana[a]
o
TALVEY® 0,8 mg/kg SC
cada 2 semanas[a]
(TRL previo) N = 78

Objetivos

Objetivo primario:

- TRG[b]

Objetivos secundarios:

- DR
- SLP
- SG
- Seguridad[c]
- Inmunogenicidad
- Farmacodinámicas

- MonumenTAL-1 incluyó pacientes con MMRR **naïve o previamente expuestos a TRL**[1]
- **Fase 1/2** abierto, multicéntrico, de un único brazo[1]

Figura 1 de Rasche L, *et al.* P915, EHA 2024.
[a]Con 2 o 3 aumentos de dosis.
[b]Evaluado por un Comité de Revisión Independiente utilizando los criterios del Grupo de Trabajo Internacional de Mieloma Múltiple.
[c]SLC e ICANS fueron clasificadas según los criterios de la Sociedad Americana de Trasplante y Terapia Celular; el resto de EAs fueron clasificados según los criterios terminológicos comunes para eventos adversos del Instituto Nacional del Cáncer de los Estados Unidos (CTCAE v4.03).

CD38: *cluster of differentiation* 38; **DR:** duración de la respuesta; **EAs:** eventos adversos; **ECOG PS:** Estado functional según el E*astern Cooperative Oncology Group;* **ICANS:** síndrome de neurotoxicidad asociada a células inmunoefectoras; **IMiD:** inmunomodulador; **IP:** inhibidor del proteasoma; **MMRR:** mieloma múltiple en recaída y refractario; **SC:** subcutáneo; **SG:** supervivencia global; **SLC:** síndrome de liberación de citoquinas; **SLP:** supervivencia libre de progresión; **TRG:** tasa de respuesta global; **TRL:** terapia redireccionadora de linfocitos T.
1. Rasche L, *et al.* Long-Term efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915. Presentado en European Association (EHA) 13-16 junio 2024; Madrid, España.

Características poblacionales MonumenTAL-1[1*]

Característica	TALVEY® 0,4 mg/kg sc 1 vez a la semana (n = 143)	TALVEY® 0,8 mg/kg sc cada 2 semanas (n = 145)	Tratamiento previo redireccionador de linfocitos T (n = 51)
Edad, mediana (rango), años	67,0 (46-86)	67,0 (38-84)	61,0 (38-78)
Hombres, n (%)	78 (54,5)	83 (57,2)	31 (60,8)
Células plasmáticas en médula ósea ≥60 %,[a] n (%)	17 (12,3)	32 (22,7)	8 (17,0)
Plasmacitomas extramedulares ≥1,[b] n (%)	33 (23,1)	37 (25,5)	16 (31,4)
Citogenética de alto riesgo,[c] n (%)	41 (31,1)	37 (28,9)	18 (40,9)
Estadio ISS,[d] n (%)			
I	62 (43,4)	64 (44,4)	24 (47,1)
II	53 (37,1)	45 (31,3)	18 (35,3)
III	28 (19,6)	35 (24,3)	9 (17,6)
Líneas de tratamiento previas, mediana (rango)	5 (2-13)	5 (2-17)	6 (3-15)
Tiempo desde el diagnóstico, mediana (rango), años	6,7 (1,4-20,8)	6,4 (0,8-25,4)	6,3 (1,7-19,6)
Exposición a tratamiento previos, n(%)			
Triple expuestos[e]	143 (100)	145 (100)	51 (100)
Penta expuestos[f]	105 (73,4)	101 (69,7)	40 (78,4)
BCMA previo, n (%)			
Belantamab	22 (15,4)	16 (11,0)	6 (11,8)
Anticuerpo biespecífico	NA	NA	16 (31,4)[g]
Terapia CAR-T	NA	NA	34 (66,7)[h]
Estado de refractariedad, n(%)			
IP[i]	114 (79,7)	120 (82,8)	46 (90,2)
IMiD[j]	133 (93,0)	130 (89,7)	49 (96,1)
Anticuerpo anti-CD38[k]	133 (93,0)	134 (92,4)	49 (96,1)
Belantamab	18 (12,6)	13 (9,0)	4 (7,8)
Triple refractarios[e]	106 (74,1)	100 (69,0)	43 (84,3)
Penta expuestos[f]	42 (29,4)	34 (23,4)	21 (41,2)
A la última línea de tratamiento	134 (93,7)	137 (94,5)	31 (60,8)

Adaptado de Touzeau C, *et al.* Oral Presentation, EHA 2023.[1] Tabla completa disponible AQUÍ
Fecha de corte de datos, 17 de enero de 2023.

Características de los pacientes tratados con TALVEY® cada dos semanas:[1‡]

Edad: 67 años
Mediana (rango), años (38-84)

Citogenética de alto riesgo[Ω]: 28,9%
(n/N) (37/128)

Líneas de tratamiento: 5
Mediana (rango) (2-17)

Triple expuestos[ϕ]: 100%
(n/N) (145/145)

*Las características basales de los grupos de dosis semanal, dosis quincenal y TCR previo en el corte de datos de 2024 fueron similares a las presentadas en 2023 con la excepción de un mayor número de pacientes afroamericanos en el actualizado (n = 32/375, 9%).[2]
[a]Se selecciona el valor máximo de la biopsia de medula ósea o del aspirado de medula ósea si ambos resultados están disponibles. Porcentajes calculados a partir de n = 138 para la cohorte de una vez a la semana, n = 141 para la cohorte de cada 2 semanas y n = 38 para la cohorte con tratamiento previo redireccionador de linfocitos T.
[b]Se incluyeron los plasmocitomas de tejidos blandos no asociados a plasmocitomas óseos.
[c]del (17p), t (4;14), y/o t (14;16). Porcentajes calculados a partir de n = 132 para la cohorte de 1 vez a la semana, n = 128 para la cohorte de cada 2 semanas y n = 44 para la cohorte con tratamiento previo redireccionador de linfocitos T.
[d]El estadio IIS se basa en β2-microglobuliuna sérica y albúmina. Porcentajes calculados a partir de n = 144 para la cohorte de cada 2 semanas.
[e]≥1 IP, ≥1 IMiD, y ≥1 anticuerpo anti-CD38.
[f]≥2 IP, ≥2 IMiD y ≥1 anticuerpo anti-CD38.
[g]Adicionalmente a los mostrados en la tabla, 2 pacientes recibieron un anticuerpo biespecífico no BCMA.
[h]Adicionalmente a los mostrados en la tabla, 2 pacientes recibieron terapia CAR-T no BCMA.
[i]Bortezomib, carfilzomib, y/o ixazomib.
[j]Talidomida, lenalidomida y/o pomalidomida.
[k]Darzalex®, isatuximab y/o un anticuerpo anti-CD38 en investigación. Nota: Ixazomib no está comercializado en España[3] y la licencia de belantamab está revocada a fecha de abril de 2025.[4] Para mayor información acerca de los medicamentos mencionados consultar sus respectivas fichas técnicas disponibles en CIMA.
‡Tras el escalado de dosis. Para mayor información acerca de la pauta posológica de TALVEY® autorizada, consultar sección 4.2 de la ficha técnica.
Ωdel(17p), t (4;14) y/o t (14;16). Porcentaje calculado a partir de n = 128 para la cohorte de cada 2 semanas.[1]
ϕ≥1 IP, ≥1 IMiD, y ≥1 anticuerpo anti-CD38 para la cohorte de cada 2 semanas.

BCMA: antígeno de maduración del linfocito B; **CAR-T:** linfocito T con receptores antigénicos quiméricos; **CD38:** *cluster of differentiation* 38; **CIMA:** Centro de Información de Medicamentos; **del:** deleción; **IMiD:** inmunomodulador; **IP:** inhibidor del proteasoma; **ISS:** *International Staging System;* **NA:** no alcanzada; **SC:** subcutáneo; **TRL:** terapia redireccionadora de linfocitos.

1. Touzeau C, *et al.* Pivotal Phase 2 MonumenTAL-1 Results of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, for Relapsed/Refractory Multiple Myeloma. Presentación oral presentada en European Hematology Association (EHA) 2023 Hybrid Congress. 8-11 junio 2023; Frankfurt, Alemania; **2.** Rasche L, *et al.* Long-Term efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915. Presentado en European Association (EHA) 13-16 junio 2014; Madrid, España; **3.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos - Nomenclátor de ABRIL - 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos.do?metodo=buscarMedicamentos Último acceso: abril 2025; **4.** EMA. Blenrep. Disponible en: https://www.ema.europa.eu/en/medicines/human/EPAR/blenrep Último acceso: abril 2025

Características poblacionales MonumenTAL-1

Característica	TALVEY® 0,4 mg/kg sc 1 vez a la semana (n = 143)	TALVEY® 0,8 mg/kg sc cada 2 semanas (n = 145)	Tratamiento previo redireccionador de linfocitos T (n = 51)
Edad, mediana (rango), años	67,0 (46-86)	67,0 (38-84)	61,0 (38-78)
Hombres, n (%)	78 (54,5)	83 (57,2)	31 (60,8)
Células plasmáticas en médula ósea ≥60 %,[a] n (%)	17 (12,3)	32 (22,7)	8 (17,0)
Plasmacitomas extramedulares ≥1,[b] n (%)	33 (23,1)	37 (25,5)	16 (31,4)
Citogenética de alto riesgo,[c] n (%)	41 (31,1)	37 (28,9)	18 (40,9)
Estadio ISS,[d] n (%)			
I	62 (43,4)	64 (44,4)	24 (47,1)
II	53 (37,1)	45 (31,3)	18 (35,3)
III	28 (19,6)	35 (24,3)	9 (17,6)
Líneas de tratamiento previas, mediana (rango)	5 (2-13)	5 (2-17)	6 (3-15)
Tiempo desde el diagnóstico, mediana (rango), años	6,7 (1,4-20,8)	6,4 (0,8-25,4)	6,3 (1,7-19,6)
Exposición a tratamiento previo, n (%)			
Triple expuestos[e]	143 (100)	145 (100)	51 (100)
Penta expuestos[f]	105 (73,4)	101 (69,7)	40 (78,4)
BCMA previo, n (%)			
Belantamab	22 (15,4)	16 (11,0)	6 (11,8)
Anticuerpo biespecífico	NA	NA	16 (31,4)[g]
Terapia CAR-T	NA	NA	34 (66,7)[h]
Estado de refractariedad, n(%)			
IP[i]	114 (79,7)	120 (82,8)	46 (90,2)
IMiD[j]	133 (93,0)	130 (89,7)	49 (96,1)
Anticuerpo anti-CD38[k]	133 (93,0)	134 (92,4)	49 (96,1)
Belantamab	18 (12,6)	13 (9,0)	4 (7,8)
Triple refractarios[e]	106 (74,1)	100 (69,0)	43 (84,3)
Penta expuestos[f]	42 (29,4)	34 (23,4)	21 (41,2)
A la última línea de tratamiento	134 (93,7)	137 (94,5)	31 (60,8)

Tabla de Touzeau C, *et al.* Oral Presentation, EHA 2023.[1]
Fecha de corte de datos, 17 de enero de 2023.
[a]Se selecciona el valor máximo de la biopsia de medula ósea o del aspirado de medula ósea si ambos resultados están disponibles. Porcentajes calculados a partir de n = 138 para la cohorte de una vez a la semana, n = 141 para la cohorte de cada 2 semanas y n = 38 para la cohorte con tratamiento previo redireccionador de linfocitos T.
[b]Se incluyeron los plasmocitomas de tejidos blandos no asociados a plasmocitomas óseos.
[c]del (17p), t (4;14), y/o t (14;16). Porcentajes calculados a partir de n = 132 para la cohorte de 1 vez a la semana, n = 128 para la cohorte de cada 2 semanas y n = 44 para la cohorte con tratamiento previo redireccionador de linfocitos T.
[d]El estadio IIS se basa en β2-microglobuliuna sérica y albúmina. Porcentajes calculados a partir de n = 144 para la cohorte de cada 2 semanas.
[e]≥1 IP, ≥1 IMiD, y ≥1 anticuerpo anti-CD38.
[f]≥2 IP, ≥2 IMiD y ≥1 anticuerpo anti-CD38.
[g]Adicionalmente a los mostrados en la tabla, 2 pacientes recibieron un anticuerpo biespecífico no BCMA.
[h]Adicionalmente a los mostrados en la tabla, 2 pacientes recibieron terapia CAR-T no BCMA.
[i]Bortezomib, carfilzomib, y/o ixazomib.
[j]Talidomida, lenalidomida y/o pomalidomida.
[k]Darzalex®, isatuximab y/o un anticuerpo anti-CD38 en investigación. Nota: Ixazomib no está comercializado en España[2] y la licencia de belantamab está revocada a fecha de abril de 2025.[3] Para mayor información acerca de los medicamentos mencionados consultar sus respectivas fichas técnicas disponibles en CIMA.
BCMA: antígeno de maduración del linfocito B; **CAR-T:** linfocito T con receptores antigénicos quiméricos; **CD38:** *cluster of differentiation* 38; **CIMA:** Centro de Información de Medicamentos; **del:** deleción; **IMiD:** inmunomodulador; **IP:** inhibidor del proteasoma; **ISS:** *International Staging System;* **NA:** no alcanzada; **SC:** subcutáneo; **TRL:** terapia redireccionadora de linfocitos.
1. Touzeau C, *et al.* Pivotal Phase 2 MonumenTAL-1 Results of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, for Relapsed/Refractory Multiple Myeloma. Presentación oral presentada en European Hematology Association (EHA) 2023 Hybrid Congress. 8-11 junio 2023; Frankfurt, Alemania; **2.** BIFIMED: Buscador de la Información sobre la situación de financiación de los medicamentos - Nomenclátor de ABRIL - 2025. Disponible en: https://www.sanidad.gob.es/profesionales/medicamentos.do?metodo=buscarMedicamentos Último acceso: abril 2025; **3.** EMA. Blenrep. Disponible en: https://www.ema.europa.eu/en/medicines/human/EPAR/blenrep Último acceso: abril 2025

BCMA: a
inhibidor de

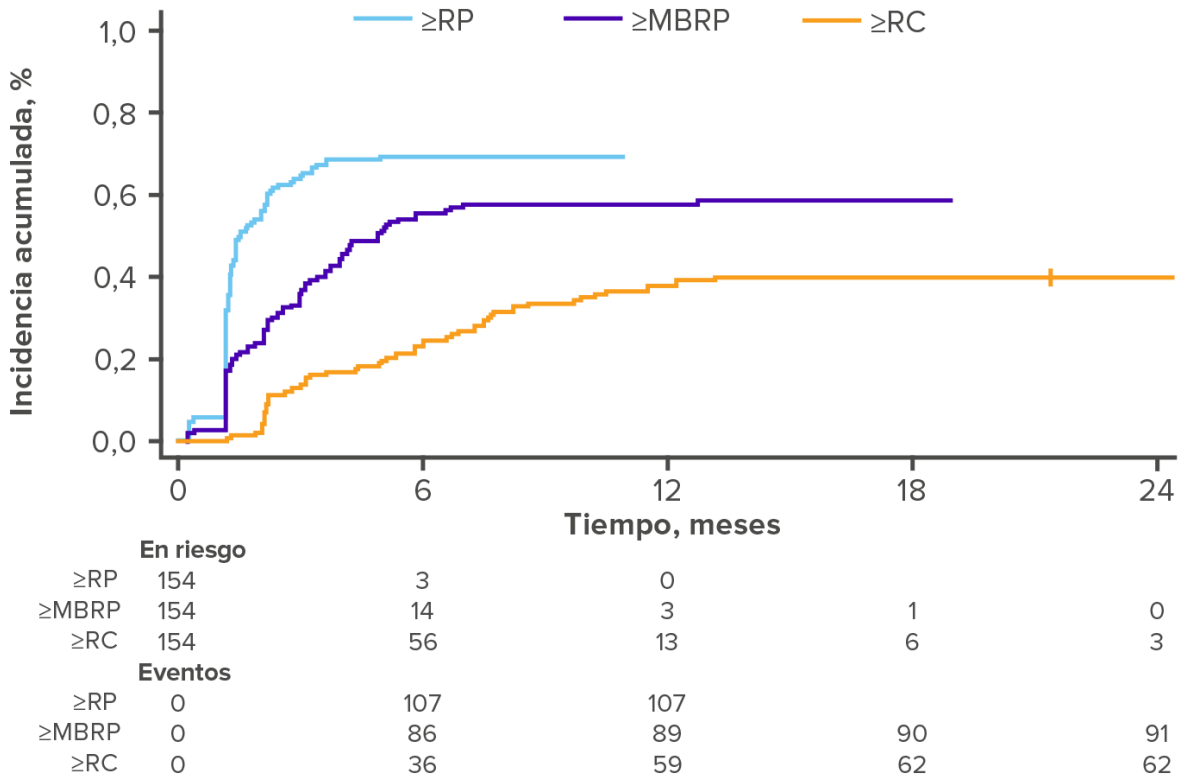
1. Touzeau C, *et al.* Pivotal Phase 2 MonumenTAL-1 Results of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, for Relapsed/Refractory Multiple Myeloma. Presentación oral presentada en European Hematology Association (EHA) 2023 Hybrid Congress. 8-11 junio 2023; Frankfurt, Alemania; **2.** Rasche L, *et al.* Long-Term efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915. Presentado en European Association (EHA) 13-16 junio 2014; Madrid, España.

Perfil de eficacia de talquetamab

Respuestas rápidas

Tiempo hasta la primera respuesta en la cohorte quincenal[1]

A



En riesgo					
≥RP	154	3	0		
≥MBRP	154	14	3	1	0
≥RC	154	56	13	6	3
Eventos					
≥RP	0	107	107		
≥MBRP	0	86	89	90	91
≥RC	0	36	59	62	62

Velocidad de la respuesta

La mediana de tiempo hasta la primera respuesta (intervalo) fue de:[1]

1,3 meses

(0,2-4,9) TALVEY® SC 0,8 mg/kg C2S

Gráfica A de la Figura 3 de Rasche L, *et al.* Póster P15. EHA 2024. Póster completo disponible AQUÍ
Mediana de seguimiento de la cohorte quincenal de TALVEY®: 23, 4 meses.[1]

MBRP: muy buena respuesta parcial; **RC:** respuesta completa; **RP:** respuesta parcial

1. Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.

P915

Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma

Leo Rasche[1], Carolina Schinke[2], Cyrille Touzeau[3], Monique C Minnema[4], Niels WCJ van de Donk[5], Paula Rodriguez-Otero[6], María-Victoria Mateos[7], Jing Christine Ye[8], Deeksha Vishwamitra[9], Indrajeet Singh[9], Xiang Qin[9], Michela Campagna[10], Tara Masterson[9], Brandi W Hilder[9], Jasziarne Tolbert[9], Thomas Renaud[10], Christoph Heuck[9], Colleen Kane[9], Ajai Chari[11]

[1]University Hospital of Würzburg, Würzburg, Germany; [2]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [3]Centre Hospitalier Universitaire de Nantes, Nantes, France; [4]University Medical Center Utrecht, Utrecht, Netherlands; [5]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [6]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [7]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [8]MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [9]Janssen Research & Development, Spring House, PA, USA; [10]Janssen Research & Development, Madrid, Spain; [11]Janssen Research & Development, Raritan, NJ, USA; [12]Mount Sinai School of Medicine, New York, NY, USA, at the time that the work was performed.

Key Takeaway

With long-term follow-up, tal continues to demonstrate deep and durable responses and no new safety signals in pts with RRMM

Conclusions

- High ORRs of ≥70% in the QW and Q2W TCR-naive cohorts and 67% in the prior TCR cohort were achieved with long-term follow-up at the approved tal doses
- Pts continued to demonstrate durable responses, with longer DORs observed in pts with deeper response
- The safety profile was consistent with previous reports; together with the efficacy data, these results highlight the overall clinical benefit of the approved tal doses and the flexibility to adjust dosing once response is achieved

Please scan QR code

Poster

Supplementary material

https://www.congresshub.com/Oncology/EHA2024/Talquetamab/Rasche

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Acknowledgments
This study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Rachael Smith, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

Disclosures
LR has received travel, accommodations, and expenses from BeiGene and Johnson & Johnson; has received honoraria from and reports a consulting/advisory role with Amgen, BeiGene, BMS, GSK, Pfizer, and Sanofi; and reports a leadership or fiduciary role within the International Myeloma Working Group and International Myeloma Society.

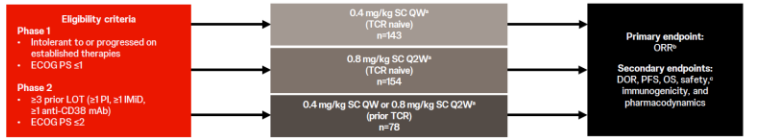
Introduction

- Talquetamab (tal) is the first approved bispecific antibody (BsAb) targeting the novel antigen G protein–coupled receptor class C group 5 member D (GPRC5D) for the treatment of patients (pts) with relapsed/refractory multiple myeloma (RRMM)[1,2]
- In previously reported results from MonumenTAL-1, tal showed overall response rates (ORRs) of >71% in pts naive to prior T-cell redirection therapy (TCR) and 65% in pts with prior TCR at the approved subcutaneous (SC) doses of 0.4 mg/kg weekly (QW) and 0.8 mg/kg every other week (Q2W)[3]
- Exposure–response (E–R) analyses showed increased ORRs with SC doses that plateaued at or above the approved doses (**Supplemental Figure 1**)[4,5]
  - An E–R relationship was observed for grade 1/2 dysgeusia; however, rates were similar at both approved doses (**Supplemental Figure 2**)[4,5]
- Early onset of GPRC5D-related adverse events (AEs), including dysgeusia, is associated with a higher likelihood of response; prior data support flexibility to adjust tal dosing in responders to mitigate AEs while maintaining efficacy[6]
- Here, we report the long-term follow-up results of pts receiving tal at the approved doses

Methods

- MonumenTAL-1 (NCT03399799/NCT04634552) enrolled pts with RRMM who were naive or exposed to prior TCR (**Figure 1**)

Figure 1: MonumenTAL-1 phase 1/2 study design



[a]With 2–3 step-up doses. [b]Assessed by IRC using International Myeloma Working Group criteria.[7,8] [c]CRS and ICANS were graded by ASTCT criteria[9]; all other AEs were graded by CTCAE v4.03. ASTCT, American Society of Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMID, immunomodulatory drug; IRC, independent review committee; LOT, line of therapy; mAb, monoclonal antibody; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor.

Results

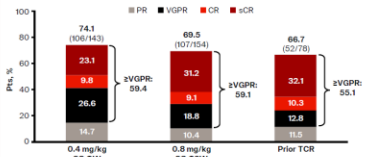
Baseline characteristics

- Baseline characteristics across the QW, Q2W, and prior TCR cohorts were similar to previous reports,[3] with the exception of more African American pts in the current analysis (n=32/375, 9%)

Efficacy

- As of January 29, 2024, ORR was 74%, 70%, and 67% for pts in the QW, Q2W, and prior TCR cohorts, respectively (**Figure 2**)
  - ORRs were consistent across high-risk subgroups, except for pts with extramedullary disease, who had lower ORRs (**Supplemental Table 1**)
  - In pts with prior TCR, ORR was 71% (n=40/56) with prior chimeric antigen receptor (CAR)-T cell therapy and 58% (n=15/26) with prior BsAb therapy
- Median time to first response (range) was 1.2 (0.2–10.9), 1.3 (0.2–4.9), and 1.2 (0.2–7.5) months, respectively
  - Median time to very good partial response (VGPR) as best response was 2.2 (0.8–6.2), 2.3 (0.3–18.9), and 1.8 (0.8–6.4) months and to complete response (CR) or better as best response was 3.0 (1.1–12.7), 5.8 (1.2–16.8), and 2.7 (1.2–18.7) months, respectively
- DOR, PFS, and OS are shown in **Table 1**
  - Better durability was observed in the Q2W vs QW cohort
  - In pts with prior TCR, the median PFS (mPFS) was 12.3 months with prior CAR-T cell therapy and 4.1 months with prior BsAb therapy
- In the Q2W cohort, 40% of pts achieved a ≥CR, most by ~12 months (**Figure 3A**); although a ≥CR may take longer to achieve, pts with deeper responses had a longer DOR (**Figure 3B**)

Figure 2: ORR[a]



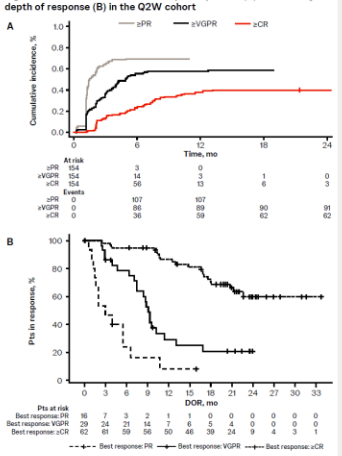
[a]Due to rounding, individual response rates may not sum to the ORR. PR, partial response; sCR, stringent complete response.

Table 1: Efficacy outcomes

Outcome	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
mFU, mo	29.8	23.4	20.5
mDOR (95% CI),[a] mo	9.5 (6.7–13.4)	17.5 (12.5–NE)	N/A[b]
mDOR in pts with ≥CR (95% CI), mo	28.6 (19.4–NE)	NR (21.2–NE)	N/A[b]
mPFS (95% CI), mo	7.5 (5.7–9.4)	11.2 (8.4–14.6)	7.7 (4.1–14.5)
24-mo OS rate (95% CI), %	60.6 (51.7–68.4)	67.1 (58.3–74.4)	57.3 (43.5–68.9)

[a]n=106 (QW), n=107 (Q2W), and n=52 (prior TCR). [b]NR due to heavy censoring from 12 to 20 mo; the estimate may not be reliable at this time point. See **Supplemental Table 2** for efficacy outcomes in the USPI population (≥4 prior LOT). mDOR, median duration of response; mFU, median follow-up; N/A, not available; NE, not estimable; NR, not reported; USPI, United States prescribing information.

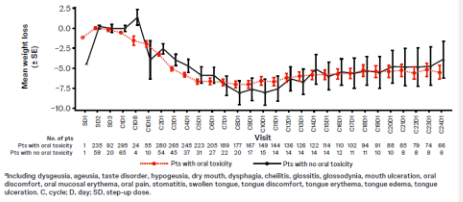
Figure 3: Time to first confirmed response per IRC (A) and DOR by depth of response (B) in the Q2W cohort



Safety

- The safety profile across cohorts was consistent with previous results[3]; no new safety signals were reported
- Weight loss, as assessed by vital signs, occurred in 39%, 34%, and 39% of pts in the QW, Q2W, and prior TCR cohorts, respectively
  - Weight loss was evident early, then stabilized and improved over time, including in pts with oral toxicities (**Figure 4**)
- Infection rates remained lower than in studies of B-cell maturation antigen–targeted BsAbs,[10,11] consistent with previous reports[3]; no increase in grade 3/4 infections was observed with longer follow-up (shown for the Q2W cohort; **Figure 5**)
- Modest intravenous immunoglobulin was required (16%, 14%, and 24% of pts, respectively)
- GPRC5D-associated AEs led to few dose reductions and discontinuations (**Table 2**); only 1 additional pt discontinued treatment since previous report[3]
- Similarly, overall rates of dose reductions and discontinuations due to AEs remained low at 15%, 10%, and 12% and 5%, 10%, and 5%, respectively
- There were no treatment-related deaths

Figure 4: Weight loss in pts with oral toxicity[a] in the QW and Q2W cohorts



[a]Including dysgeusia, ageusia, taste disorder, hypogeusia, dry mouth, dysphagia, cheilitis, glossitis, glossodynia, mouth ulceration, oral discomfort, oral mucosal erythema, oral pain, stomatitis, swollen tongue, tongue discomfort, tongue erythema, tongue edema, tongue ulceration. C, cycle; D, day; SD, step-up dose.

Figure 5: New-onset grade ≥3 infections over time in the Q2W cohort

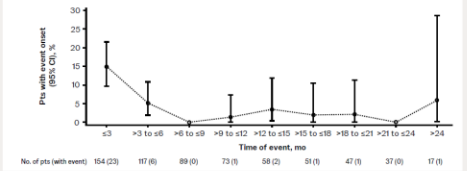


Table 2: GPRC5D-associated AEs

Any-grade AE, n (%)	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Taste-related[a]			
Total	103 (72.0)	110 (71.4)	59 (75.6)
Leading to dose reduction	10 (7.0)	6 (3.9)	4 (5.1)
Leading to discontinuation	0	3 (1.9)	0
Skin-related[b]			
Total	81 (56.6)	113 (73.4)[e]	50 (64.1)
Leading to dose reduction	5 (3.5)	1 (0.6)	2 (2.6)
Leading to discontinuation	2 (1.4)	1 (0.6)	0
Nail-related[c]			
Total	79 (55.2)	82 (53.2)	46 (59.0)
Leading to dose reduction	1 (0.7)	1 (0.6)	1 (1.3)
Leading to discontinuation	0	0	0
Rash-related[d]			
Total	57 (39.9)[f]	46 (29.9)[g]	25 (32.1)[h]
Leading to dose reduction	1 (0.7)	1 (0.6)	0
Leading to discontinuation	0	0	0

[a]Including ageusia, dysgeusia, hypogeusia, and taste disorder. [b]Including skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Including nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [d]Including rash, maculopapular rash, erythematous rash, and erythema. [e]Including 1 (0.6%) grade 3/4 event. [f]Including 2 (1.4%) grade 3/4 events. [g]Including 8 (5.2%) grade 3/4 events. [h]Including 2 (2.6%) grade 3/4 events.

References
1. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 2. Chari A, et al. Presented at ASH; December 10–13, 2022; New Orleans, LA, USA. #157. 3. Schinke C, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8036. 4. Ma X, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8041. 5. Zhou J, et al. Presented at ACOP; November 5–8, 2023; Oxon Hill, MD, USA. #T-015. 6. Chari A, et al. Presented at ASH; December 9–12, 2023; San Diego, CA, USA. #1010. 7. Rajkumar SV, et al. *Blood* 2011;117:4691-5. 8. Kumar S, et al. *Lancet Oncol* 2016;17:328-46. 9. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25:625-38. 10. van de Donk NWCJ, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8011. 11. Tomasson M, et al. *Blood* 2023;142 (Supplement 1): 3385.

Multiple Myeloma

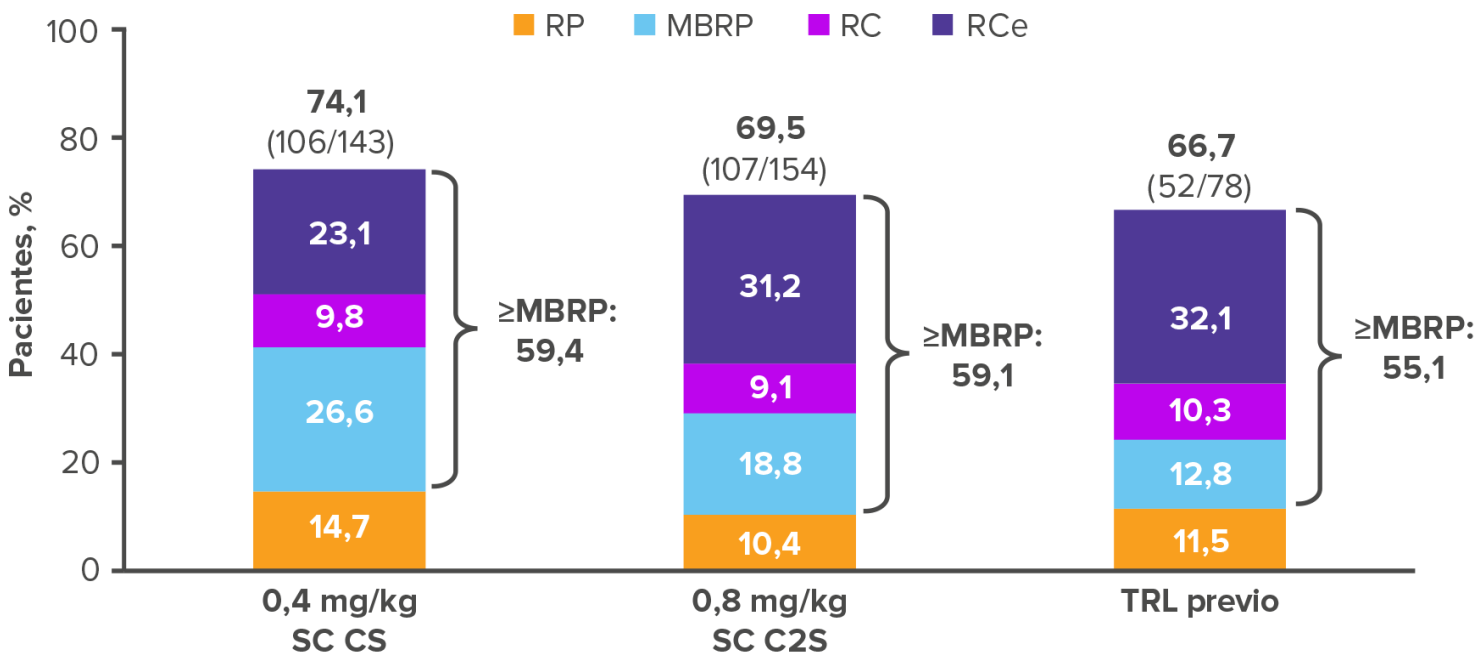
Presented by L Rasche at the European Hematology Association (EHA) 2024 Hybrid Congress; June 13–16, 2024; Madrid, Spain

MBRP: muy buena respuesta parcial; RC: respuesta completa; RP: respuesta parcial

1. Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.

Respuestas profundas

Tasa de Respuesta Global[a]



[a]Debido al redondeo las tasas de respuesta individual pueden no sumar la TRG.
Figura 2 de Rasche L, *et al.* Póster P915, EHA 2024. Póster completo disponible AQUÍ
Mediana de seguimiento de la cohorte semanal de TALVEY®: 29,8 meses.[1]
Mediana de seguimiento de la cohorte quincenal de TALVEY®: 23, 4 meses.[1]
Mediana de seguimiento de la cohorte que había recibido un TCR previo: 20,5 meses.[1]

En la cohorte quincenal, el **40,3 % de los pacientes** alcanzaron una **≥RC**[1]

Se alcanzaron elevadas **TRG de ≈70% en la cohorte C2S**[1]

CS: cada semana; C2S: cada dos semanas; MBRP: muy buena respuesta parcial; RC: respuesta completa; RCe: respuesta completa estricta; RP: respuesta parcial; SC: subcutáneo; TRG: tasa de respuesta global; TRL: tratamiento redireccionador de linfocitos T.

1. Jing C, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P-098 presentado en 21st International Myeloma Society (IMS) Annual Meeting; 25-28 septiembre 2024; Río de Janeiro, Brasil.

P915

Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma

Leo Rasche[1], Carolina Schinke[2], Cyrille Touzeau[3], Monique C Minnema[4], Niels WCJ van de Donk[5], Paula Rodriguez-Otero[6], María-Victoria Mateos[7], Jing Christine Ye[8], Deeksha Vishwamitra[9], Indrajeet Singh[9], Xiang Qin[9], Michela Campagna[10], Tara Masterson[9], Brandi W Hilder[9], Jasziarne Tolbert[9], Thomas Renaud[10], Christoph Heuck[9], Colleen Kane[9], Ajai Chari[11]

[1]University Hospital of Würzburg, Würzburg, Germany; [2]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [3]Centre Hospitalier Universitaire de Nantes, Nantes, France; [4]University Medical Center Utrecht, Utrecht, Netherlands; [5]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [6]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [7]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [8]MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [9]Janssen Research & Development, Spring House, PA, USA; [10]Janssen Research & Development, Madrid, Spain; [11]Janssen Research & Development, Raritan, NJ, USA; [12]Mount Sinai School of Medicine, New York, NY, USA, at the time that the work was performed.

Key Takeaway

With long-term follow-up, tal continues to demonstrate deep and durable responses and no new safety signals in pts with RRMM

Conclusions

- High ORRs of ≥70% in the QW and Q2W TCR-naive cohorts and 67% in the prior TCR cohort were achieved with long-term follow-up at the approved tal doses
- Pts continued to demonstrate durable responses, with longer DORs observed in pts with deeper response
- The safety profile was consistent with previous reports; together with the efficacy data, these results highlight the overall clinical benefit of the approved tal doses and the flexibility to adjust dosing once response is achieved

Please scan QR code

Poster

Supplementary material

https://www.congresshub.com/Oncology/EHA2024/Talquetamab/Rasche

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Acknowledgments

This study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Rachael Smith, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

Disclosures

LR has received travel, accommodations, and expenses from BeiGene and Johnson & Johnson; has received honoraria from and reports a consulting/advisory role with Amgen, BeiGene, BMS, GSK, Pfizer, and Sanofi; and reports a leadership or fiduciary role within the International Myeloma Working Group and International Myeloma Society.

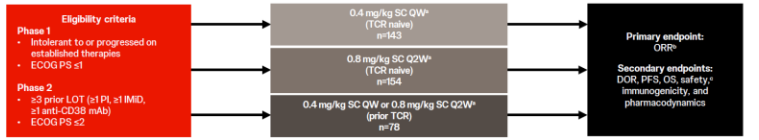
Introduction

- Talquetamab (tal) is the first approved bispecific antibody (BsAb) targeting the novel antigen G protein–coupled receptor class C group 5 member D (GPRC5D) for the treatment of patients (pts) with relapsed/refractory multiple myeloma (RRMM)[1,2]
- In previously reported results from MonumenTAL-1, tal showed overall response rates (ORRs) of >71% in pts naive to prior T-cell redirection therapy (TCR) and 65% in pts with prior TCR at the approved subcutaneous (SC) doses of 0.4 mg/kg weekly (QW) and 0.8 mg/kg every other week (Q2W)[3]
- Exposure–response (E–R) analyses showed increased ORRs with SC doses that plateaued at or above the approved doses (**Supplemental Figure 1**)[4,5]
  - An E–R relationship was observed for grade 1/2 dysgeusia; however, rates were similar at both approved doses (**Supplemental Figure 2**)[4,5]
- Early onset of GPRC5D-related adverse events (AEs), including dysgeusia, is associated with a higher likelihood of response; prior data support flexibility to adjust tal dosing in responders to mitigate AEs while maintaining efficacy[6]
- Here, we report the long-term follow-up results of pts receiving tal at the approved doses

Methods

- MonumenTAL-1 (NCT03399799/NCT04634552) enrolled pts with RRMM who were naive or exposed to prior TCR (**Figure 1**)

Figure 1: MonumenTAL-1 phase 1/2 study design



[a]With 2–3 step-up doses. [b]Assessed by IRC using International Myeloma Working Group criteria.[7,8] [c]CRS and ICANS were graded by ASTCT criteria[9]; all other AEs were graded by CTCAE v4.03. ASTCT, American Society of Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMID, immunomodulatory drug; IRC, independent review committee; LOT, line of therapy; mAb, monoclonal antibody; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor.

Results

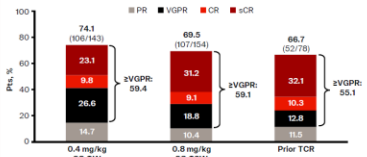
Baseline characteristics

- Baseline characteristics across the QW, Q2W, and prior TCR cohorts were similar to previous reports,[3] with the exception of more African American pts in the current analysis (n=32/375, 9%)

Efficacy

- As of January 29, 2024, ORR was 74%, 70%, and 67% for pts in the QW, Q2W, and prior TCR cohorts, respectively (**Figure 2**)
  - ORRs were consistent across high-risk subgroups, except for pts with extramedullary disease, who had lower ORRs (**Supplemental Table 1**)
  - In pts with prior TCR, ORR was 71% (n=40/56) with prior chimeric antigen receptor (CAR)-T cell therapy and 58% (n=15/26) with prior BsAb therapy
- Median time to first response (range) was 1.2 (0.2–10.9), 1.3 (0.2–4.9), and 1.2 (0.2–7.5) months, respectively
  - Median time to very good partial response (VGPR) as best response was 2.2 (0.8–6.2), 2.3 (0.3–18.9), and 1.8 (0.8–6.4) months and to complete response (CR) or better as best response was 3.0 (1.1–12.7), 5.8 (1.2–16.8), and 2.7 (1.2–18.7) months, respectively
- DOR, PFS, and OS are shown in **Table 1**
  - Better durability was observed in the Q2W vs QW cohort
  - In pts with prior TCR, the median PFS (mPFS) was 12.3 months with prior CAR-T cell therapy and 4.1 months with prior BsAb therapy
- In the Q2W cohort, 40% of pts achieved a ≥CR, most by ~12 months (**Figure 3A**); although a ≥CR may take longer to achieve, pts with deeper responses had a longer DOR (**Figure 3B**)

Figure 2: ORR[a]



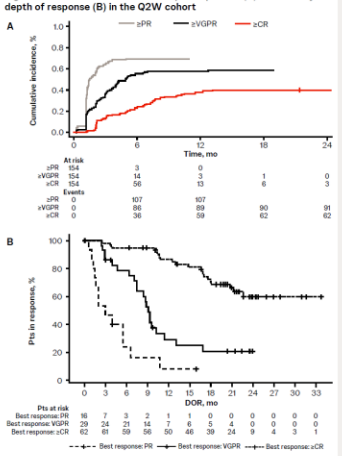
[a]Due to rounding, individual response rates may not sum to the ORR. PR, partial response; sCR, stringent complete response.

Table 1: Efficacy outcomes

Outcome	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
mFU, mo	29.8	23.4	20.6
mDOR (95% CI),[a] mo	9.5 (6.7–13.4)	17.5 (12.5–NE)	N/A[b]
mDOR in pts with ≥CR (95% CI), mo	28.6 (19.4–NE)	NR (21.2–NE)	N/A[b]
mPFS (95% CI), mo	7.5 (5.7–9.4)	11.2 (8.4–14.6)	7.7 (4.1–14.5)
24-mo OS rate (95% CI), %	60.6 (51.7–68.4)	67.1 (58.3–74.4)	57.3 (43.5–68.9)

[a]n=106 (QW), n=107 (Q2W), and n=52 (prior TCR). [b]NR due to heavy censoring from 12 to 20 mo; the estimate may not be reliable at this time point. See **Supplemental Table 2** for efficacy outcomes in the USPI population (≥4 prior LOT). mDOR, median duration of response; mFU, median follow-up; N/A, not available; NE, not estimable; NR, not reported; USPI, United States prescribing information.

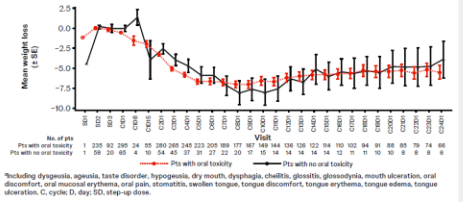
Figure 3: Time to first confirmed response per IRC (A) and DOR by depth of response (B) in the Q2W cohort



Safety

- The safety profile across cohorts was consistent with previous results[3]; no new safety signals were reported
- Weight loss, as assessed by vital signs, occurred in 39%, 34%, and 39% of pts in the QW, Q2W, and prior TCR cohorts, respectively
  - Weight loss was evident early, then stabilized and improved over time, including in pts with oral toxicities (**Figure 4**)
- Infection rates remained lower than in studies of B-cell maturation antigen–targeted BsAbs,[10,11] consistent with previous reports[3]; no increase in grade 3/4 infections was observed with longer follow-up (shown for the Q2W cohort; **Figure 5**)
- Modest intravenous immunoglobulin was required (16%, 14%, and 24% of pts, respectively)
- GPRC5D-associated AEs led to few dose reductions and discontinuations (**Table 2**); only 1 additional pt discontinued treatment since previous report[3]
- Similarly, overall rates of dose reductions and discontinuations due to AEs remained low at 15%, 10%, and 12% and 5%, 10%, and 5%, respectively
- There were no treatment-related deaths

Figure 4: Weight loss in pts with oral toxicity[a] in the QW and Q2W cohorts



[a]Including dysgeusia, ageusia, taste disorder, hypogeusia, dry mouth, dysphagia, cheilitis, glossitis, glossodynia, mouth ulceration, oral discomfort, oral mucosal erythema, oral pain, stomatitis, swollen tongue, tongue discomfort, tongue erythema, tongue edema, tongue ulceration. C, cycle; D, day; SD, step-up dose.

Figure 5: New-onset grade ≥3 infections over time in the Q2W cohort

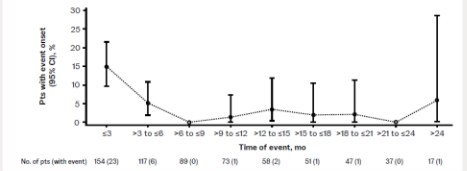


Table 2: GPRC5D-associated AEs

Any-grade AE, n (%)	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Taste-related[a]			
Total	103 (72.0)	110 (71.4)	59 (75.6)
Leading to dose reduction	10 (7.0)	6 (3.9)	4 (5.1)
Leading to discontinuation	0	3 (1.9)	0
Skin-related[b]			
Total	81 (56.6)	113 (73.4)[e]	50 (64.1)
Leading to dose reduction	5 (3.5)	1 (0.6)	2 (2.6)
Leading to discontinuation	2 (1.4)	1 (0.6)	0
Nail-related[c]			
Total	79 (55.2)	82 (53.2)	46 (59.0)
Leading to dose reduction	1 (0.7)	1 (0.6)	1 (1.3)
Leading to discontinuation	0	0	0
Rash-related[d]			
Total	57 (39.9)[f]	46 (29.9)[g]	25 (32.1)[h]
Leading to dose reduction	1 (0.7)	1 (0.6)	0
Leading to discontinuation	0	0	0

[a]Including ageusia, dysgeusia, hypogeusia, and taste disorder. [b]Including skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Including nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [d]Including rash, maculopapular rash, erythematous rash, and erythema. [e]Including 1 (0.6%) grade 3/4 event. [f]Including 2 (1.4%) grade 3/4 events. [g]Including 8 (5.2%) grade 3/4 events. [h]Including 2 (2.6%) grade 3/4 events.

References

1. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 2. Chari A, et al. Presented at ASH; December 10–13, 2022; New Orleans, LA, USA. #157. 3. Schinke C, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8036. 4. Ma X, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8041. 5. Zhou J, et al. Presented at ACOP; November 5–8, 2023; Oxon Hill, MD, USA. #T-015. 6. Chari A, et al. Presented at ASH; December 9–12, 2023; San Diego, CA, USA. #1010. 7. Rajkumar SV, et al. *Blood* 2011;117:4691-5. 8. Kumar S, et al. *Lancet Oncol* 2016;17:328-46. 9. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25:625-38. 10. van de Donk NWCJ, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8011. 11. Tomasson M, et al. *Blood* 2023;142 (Supplement 1): 3385.

Multiple Myeloma

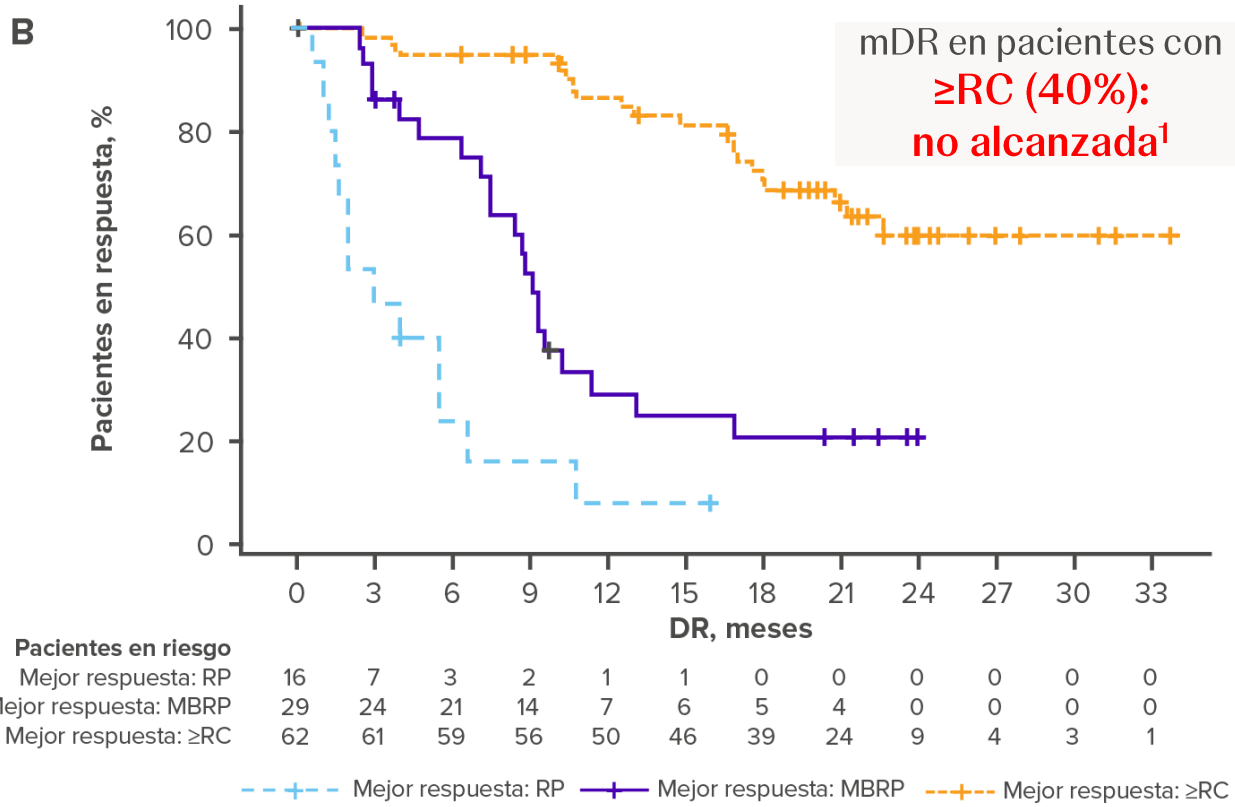
Presented by L Rasche at the European Hematology Association (EHA) 2024 Hybrid Congress; June 13–16, 2024; Madrid, Spain

CS: cada semana; C2S: cada dos semanas; MBRP: muy buena respuesta parcial; RC: respuesta completa; RCE: respuesta completa estricta; RP: respuesta parcial; SC: subcutáneo; TRG: tasa de respuesta global; TRT: tratamiento redireccionador de linfocitos T.

1. Jing C, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P-098 presentado en 21st International Myeloma Society (IMS) Annual Meeting; 25-28 septiembre 2024; Río de Janeiro, Brasil.

Los pacientes con respuestas más profundas alcanzaron DR más prolongadas[1]

Duración de la respuesta en función de la profundidad en la cohorte quincenal[1]



Gráfica B de la Figura 3 de Rasche L, *et al.* Póster P915. EHA 2024. Póster completo disponible AQUÍ

Mediana de DR para la cohorte tratada con la pauta **quincenal** de TALVEY®:

17,5 meses
(IC 95 %: 12,5-NE)*[1]

La mediana de seguimiento para la dosis quincenal fue de 23,4 meses.[1]
*Dato extraído de la Tabla 1 del póster P915 de Rasche L, *et al.* Póster presentado en EHA 2024. Póster completo disponible AQUÍ
DR: duración de la respuesta; **mDR:** mediana de duración de la respuesta; **IC:** intervalo de confianza; **MBRP:** muy buena respuesta parcial; **NE:** no estimable, RC: respuesta completa; **RP:** respuesta parcial.
1. Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.

Los pacientes con respuestas más profundas

P915

Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma

Leo Rasche[1], Carolina Schinke[2], Cyrille Touzeau[3], Monique C Minnema[4], Niels WCJ van de Donk[5], Paula Rodriguez-Otero[6], María-Victoria Mateos[7], Jing Christine Ye[8], Deeksha Vishwamitra[9], Indrajeet Singh[9], Xiang Qin[9], Michela Campagna[10], Tara Masterson[9], Brandi W Hilder[9], Jaszianne Tolbert[9], Thomas Renaud[10], Christoph Heuck[9], Colleen Kane[9], Ajai Chari[11]

[1]University Hospital of Würzburg, Würzburg, Germany; [2]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [3]Centre Hospitalier Universitaire de Nantes, Nantes, France; [4]University Medical Center Utrecht, Utrecht, Netherlands; [5]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [6]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [7]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [8]MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [9]Janssen Research & Development, Spring House, PA, USA; [10]Janssen Research & Development, Madrid, Spain; [11]Janssen Research & Development, Raritan, NJ, USA; [12]Mount Sinai School of Medicine, New York, NY, USA, at the time that the work was performed.

Key Takeaway

With long-term follow-up, tal continues to demonstrate deep and durable responses and no new safety signals in pts with RRMM

Conclusions

- High ORRs of ≥70% in the QW and Q2W TCR-naive cohorts and 67% in the prior TCR cohort were achieved with long-term follow-up at the approved tal doses
- Pts continued to demonstrate durable responses, with longer DORs observed in pts with deeper response
- The safety profile was consistent with previous reports; together with the efficacy data, these results highlight the overall clinical benefit of the approved tal doses and the flexibility to adjust dosing once response is achieved

Please scan QR code

Poster

Supplementary material

https://www.congresshub.com/Oncology/EHA2024/Talquetamab/Rasche

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Acknowledgments

This study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Rachael Smith, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

Disclosures

LR has received travel, accommodations, and expenses from BeiGene and Johnson & Johnson; has received honoraria from and reports a consulting/advisory role with Amgen, BeiGene, BMS, GSK, Pfizer, and Sanofi; and reports a leadership or fiduciary role within the International Myeloma Working Group and International Myeloma Society.

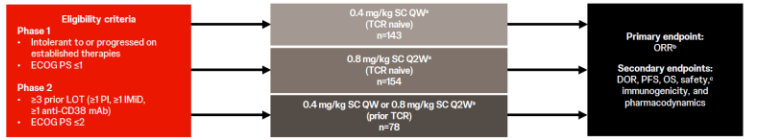
Introduction

- Talquetamab (tal) is the first approved bispecific antibody (BsAb) targeting the novel antigen G protein–coupled receptor class C group 5 member D (GPRC5D) for the treatment of patients (pts) with relapsed/refractory multiple myeloma (RRMM)[1,2]
- In previously reported results from MonumenTAL-1, tal showed overall response rates (ORRs) of >71% in pts naive to prior T-cell redirection therapy (TCR) and 65% in pts with prior TCR at the approved subcutaneous (SC) doses of 0.4 mg/kg weekly (QW) and 0.8 mg/kg every other week (Q2W)[3]
- Exposure–response (E–R) analyses showed increased ORRs with SC doses that plateaued at or above the approved doses (**Supplemental Figure 1**)[4,5]
  - An E–R relationship was observed for grade 1/2 dysgeusia; however, rates were similar at both approved doses (**Supplemental Figure 2**)[4,5]
- Early onset of GPRC5D-related adverse events (AEs), including dysgeusia, is associated with a higher likelihood of response; prior data support flexibility to adjust tal dosing in responders to mitigate AEs while maintaining efficacy[6]
- Here, we report the long-term follow-up results of pts receiving tal at the approved doses

Methods

- MonumenTAL-1 (NCT03399799/NCT04634552) enrolled pts with RRMM who were naive or exposed to prior TCR (**Figure 1**)

Figure 1: MonumenTAL-1 phase 1/2 study design



[a]With 2–3 step-up doses. [b]Assessed by IRC using International Myeloma Working Group criteria.[7,8] [c]CRS and ICANS were graded by ASTCT criteria[9]; all other AEs were graded by CTCAE v4.03. ASTCT, American Society of Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMID, immunomodulatory drug; IRC, independent review committee; LOT, line of therapy; mAb, monoclonal antibody; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor.

Results

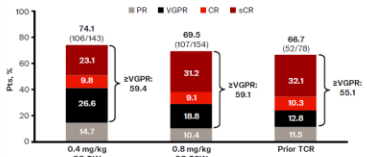
Baseline characteristics

- Baseline characteristics across the QW, Q2W, and prior TCR cohorts were similar to previous reports,[3] with the exception of more African American pts in the current analysis (n=32/375, 9%)

Efficacy

- As of January 29, 2024, ORR was 74%, 70%, and 67% for pts in the QW, Q2W, and prior TCR cohorts, respectively (**Figure 2**)
  - ORRs were consistent across high-risk subgroups, except for pts with extramedullary disease, who had lower ORRs (**Supplemental Table 1**)
  - In pts with prior TCR, ORR was 71% (n=40/56) with prior chimeric antigen receptor (CAR)-T cell therapy and 58% (n=15/26) with prior BsAb therapy
- Median time to first response (range) was 1.2 (0.2–10.9), 1.3 (0.2–4.9), and 1.2 (0.2–7.5) months, respectively
  - Median time to very good partial response (VGPR) as best response was 2.2 (0.8–6.2), 2.3 (0.3–18.9), and 1.8 (0.8–6.4) months and to complete response (CR) or better as best response was 3.0 (1.1–12.7), 5.8 (1.2–16.8), and 2.7 (1.2–18.7) months, respectively
- DOR, PFS, and OS are shown in **Table 1**
  - Better durability was observed in the Q2W vs QW cohort
  - In pts with prior TCR, the median PFS (mPFS) was 12.3 months with prior CAR-T cell therapy and 4.1 months with prior BsAb therapy
- In the Q2W cohort, 40% of pts achieved a ≥CR, most by ~12 months (**Figure 3A**); although a ≥CR may take longer to achieve, pts with deeper responses had a longer DOR (**Figure 3B**)

Figure 2: ORR[a]



[a]Due to rounding, individual response rates may not sum to the ORR. PR, partial response; sCR, stringent complete response.

Table 1: Efficacy outcomes

Outcome	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
mFU, mo	29.8	23.4	20.6
mDOR (95% CI),[a] mo	9.5 (6.7–13.4)	17.5 (12.5–NE)	N/A[b]
mDOR in pts with ≥CR (95% CI), mo	28.6 (19.4–NE)	NR (21.2–NE)	N/A[b]
mPFS (95% CI), mo	7.5 (5.7–9.4)	11.2 (8.4–14.6)	7.7 (4.1–14.5)
24-mo OS rate (95% CI), %	60.6 (51.7–68.4)	67.1 (58.3–74.4)	57.3 (43.5–68.9)

[a]n=106 (QW), n=107 (Q2W), and n=52 (prior TCR). [b]NR due to heavy censoring from 12 to 20 mo; the estimate may not be reliable at this time point. See **Supplemental Table 2** for efficacy outcomes in the USPI population (≥4 prior LOT). mDOR, median duration of response; mFU, median follow-up; N/A, not available; NE, not estimable; NR, not reported; USPI, United States prescribing information.

Figure 3: Time to first confirmed response per IRC (A) and DOR by depth of response (B) in the Q2W cohort

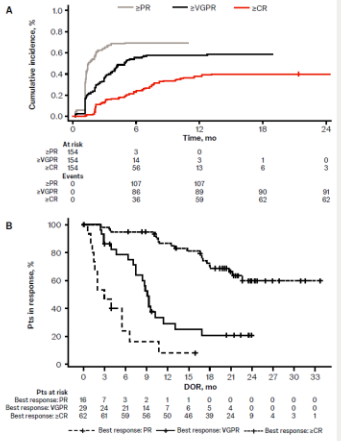
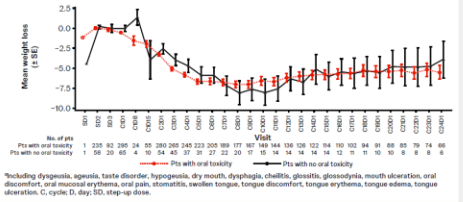


Figure 4: Weight loss in pts with oral toxicity[a] in the QW and Q2W cohorts



[a]Including dysgeusia, ageusia, taste disorder, hypogeusia, dry mouth, dysphagia, cheilitis, glossitis, glossodynia, mouth ulceration, oral discomfort, oral mucosal erythema, oral pain, stomatitis, swollen tongue, tongue discomfort, tongue erythema, tongue edema, tongue ulceration. C, cycle; D, day; SD, step-up dose.

Figure 5: New-onset grade ≥3 infections over time in the Q2W cohort

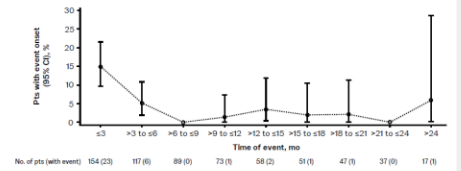


Table 2: GPRC5D-associated AEs

Any-grade AE, n (%)	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Taste-related[a]			
Total	103 (72.0)	110 (71.4)	59 (75.6)
Leading to dose reduction	10 (7.0)	6 (3.9)	4 (5.1)
Leading to discontinuation	0	3 (1.9)	0
Skin-related[b]			
Total	81 (56.6)	113 (73.4)[e]	50 (64.1)
Leading to dose reduction	5 (3.5)	1 (0.6)	2 (2.6)
Leading to discontinuation	2 (1.4)	1 (0.6)	0
Nail-related[c]			
Total	79 (55.2)	82 (53.2)	46 (59.0)
Leading to dose reduction	1 (0.7)	1 (0.6)	1 (1.3)
Leading to discontinuation	0	0	0
Rash-related[d]			
Total	57 (39.9)[f]	46 (29.9)[g]	25 (32.1)[h]
Leading to dose reduction	1 (0.7)	1 (0.6)	0
Leading to discontinuation	0	0	0

[a]Including ageusia, dysgeusia, hypogeusia, and taste disorder. [b]Including skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Including nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [d]Including rash, maculopapular rash, erythematous rash, and erythema. [e]Including 1 (0.6%) grade 3/4 event. [f]Including 2 (1.4%) grade 3/4 events. [g]Including 8 (5.2%) grade 3/4 events. [h]Including 2 (2.6%) grade 3/4 events.

Safety

- The safety profile across cohorts was consistent with previous results[3]; no new safety signals were reported
- Weight loss, as assessed by vital signs, occurred in 39%, 34%, and 39% of pts in the QW, Q2W, and prior TCR cohorts, respectively
  - Weight loss was evident early, then stabilized and improved over time, including in pts with oral toxicities (**Figure 4**)
- Infection rates remained lower than in studies of B-cell maturation antigen–targeted BsAbs,[10,11] consistent with previous reports[3]; no increase in grade 3/4 infections was observed with longer follow-up (shown for the Q2W cohort; **Figure 5**)
- Modest intravenous immunoglobulin was required (16%, 14%, and 24% of pts, respectively)
- GPRC5D-associated AEs led to few dose reductions and discontinuations (**Table 2**); only 1 additional pt discontinued treatment since previous report[3]
- Similarly, overall rates of dose reductions and discontinuations due to AEs remained low at 15%, 10%, and 12% and 5%, 10%, and 5%, respectively
- There were no treatment-related deaths

References

1. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 2. Chari A, et al. Presented at ASH; December 10–13, 2022; New Orleans, LA, USA. #157. 3. Schinke C, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8036. 4. Ma X, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8041. 5. Zhou J, et al. Presented at ACOP; November 5–8, 2023; Oxon Hill, MD, USA. #T-015. 6. Chari A, et al. Presented at ASH; December 9–12, 2023; San Diego, CA, USA. #1010. 7. Rajkumar SV, et al. *Blood* 2011;117:4691-5. 8. Kumar S, et al. *Lancet Oncol* 2016;17:328-46. 9. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25:625-38. 10. van de Donk NWCJ, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8011. 11. Tomasson M, et al. *Blood* 2023;142 (Supplement 1): 3385.

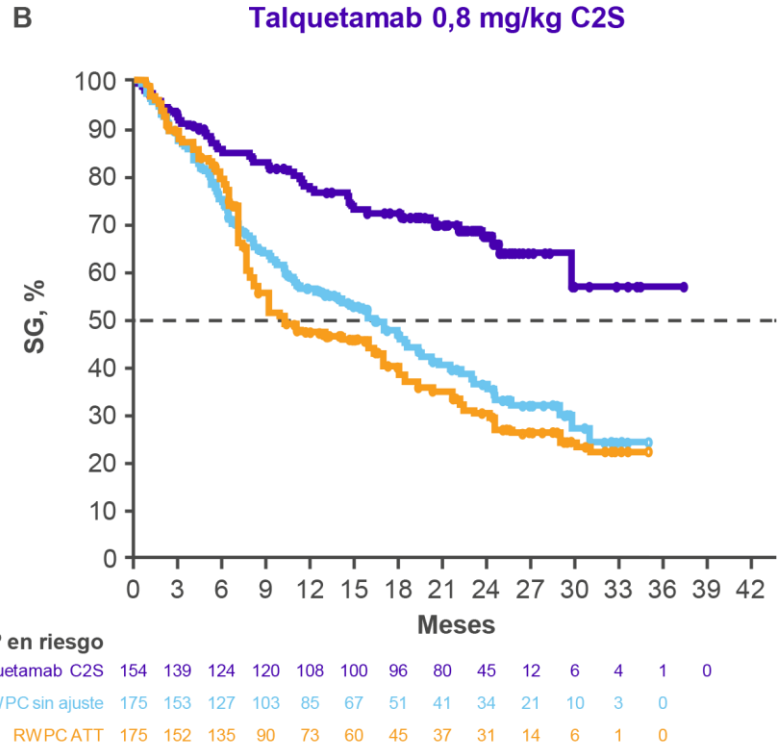
Multiple Myeloma

Presented by L Rasche at the European Hematology Association (EHA) 2024 Hybrid Congress; June 13–16, 2024; Madrid, Spain

La median
*Dato extra
mDR) media

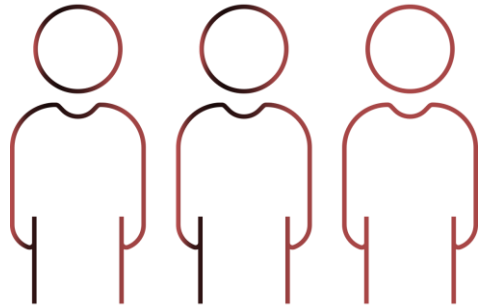
1. Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.

Los pacientes tratados con TALVEY® mostraron una mejora significativa de la SLP* y la SG frente a la elección de tratamiento del especialista en vida real[1]



Gráfica B de la Figura 4 de Einsele H, *et al.* IMS 2024. Póster completo disponible AQUÍ
La mediana de seguimiento para TALVEY® 0,8 mg/kg SC cada 2 semanas fue de 23,4 meses. Para el grupo RWPC, la mediana de seguimiento del estudio LocoMMotion fue de 26,4 meses y del estudio MoMMent de 13,9 meses.[1]

≈2 de cada 3 pacientes seguían vivos a los 2 años^

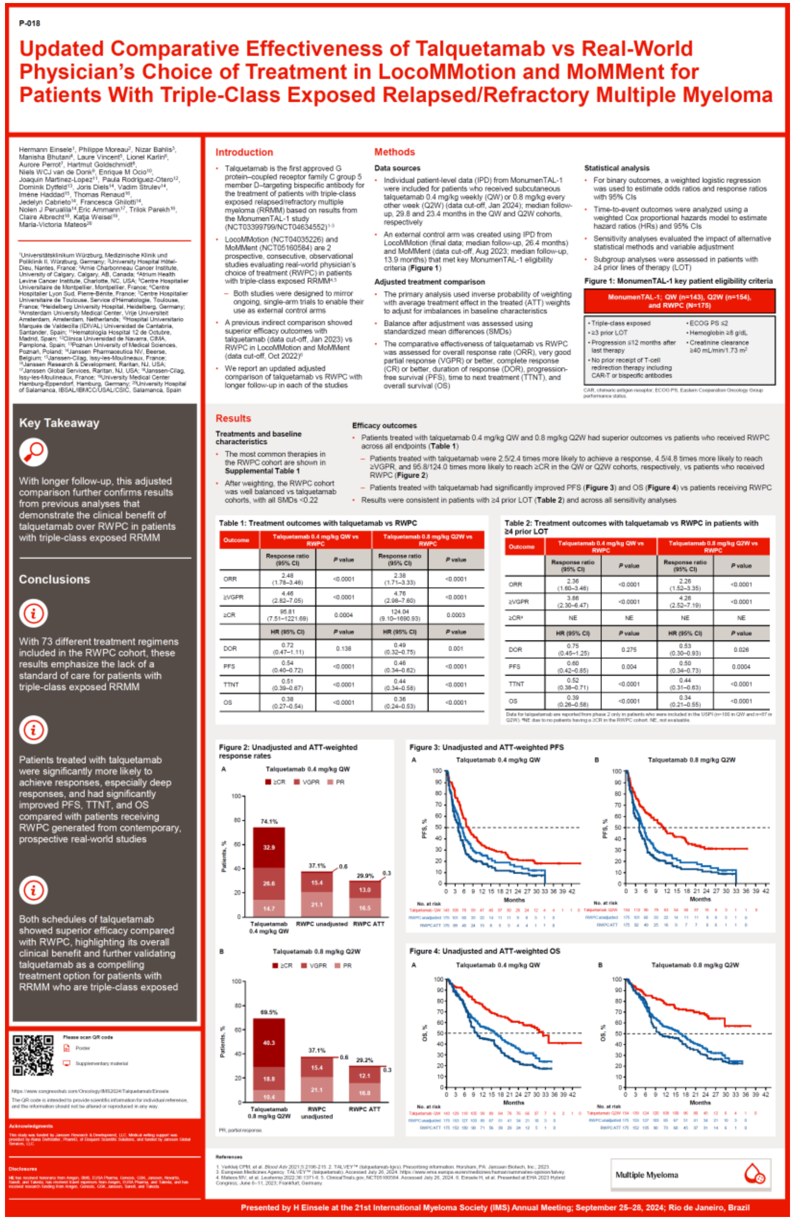


Tasa de SG a los 24 meses:[2]

67,1 %

(IC 95 %: 58,3-74,4)#

*SLP TALVEY® 0,8 mg/kg C2S vs. RWPC, HR (IC95%): 0,46 (0,34-0,62), p<0,0001. Datos extraídos de la Tabla 1 del Einsele H, *et al.* IMS 2024. Póster completo disponible AQUÍ
^Dato calculado a partir del 67,1%. La mediana de seguimiento para TALVEY® 0,8 mg/kg SC cada 2 semanas fue de 23,4 meses.[3] Dato extraído de la tabla 1 de Rasche L, *et al.* EHA 2024. Póster completo disponible AQUÍ
#Dato extraído de la tabla 1 de Rasche L, *et al.* EHA 2024. Póster completo disponible AQUÍ
ATT: efecto medio del tratamiento en los pacientes; **C2S:** cada 2 semanas; **HR:** Hazard ratio; **IC:** intervalo de confianza; **MMRR:** mieloma múltiple en recaída y refractario; **RWPC:** tratamiento de elección del médico en vida real; **SG:** supervivencia global; **SLP:** supervivencia libre de progresión.
1. Einsele H, *et al.* Updated Comparative Effectiveness of Talquetamab vs. Real-World Physician´s Choice of Treatment in LocoMMotion and MonuMMent for Patient With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma. Póster P-018 presentado en 21st International Myeloma Socity (IMS) Annual Meeting; 25-28, 2024; Río de Janeiro, Brasil; **2.** Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.


P-018

Updated Comparative Effectiveness of Talquetamab vs Real-World Physician's Choice of Treatment in LocoMMotion and MoMMent for Patients With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma

Hermann Einsele[1], Philippe Moreau[2], Nizar Bahlis[3], Manisha Bhutani[4], Laure Vincent[5], Lionel Karlin[6], Aurore Perrot[7], Hartmut Goldschmidt[8], Niels WCJ van de Donk[9], Enrique M Ocio[10], Joaquín Martínez-Lopez[11], Paula Rodríguez-Otero[12], Dominik Dytfeld[13], Joris Diels[14], Vadim Strulev[14], Imène Haddad[15], Thomas Renaud[16], Jedelyn Cabrieto[14], Francesca Ghilotti[14], Nolen J Perualila[14], Eric Ammann[17], Trilok Parekh[16], Claire Albrecht[18], Katja Weisel[19], María-Victoria Mateos[20]

[1]Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany; [2]University Hospital Hôtel-Dieu, Nantes, France; [3]Arnie Charbonneau Cancer Institute, University of Calgary, Calgary, AB, Canada; [4]Atrium Health Levine Cancer Institute, Charlotte, NC, USA; [5]Centre Hospitalier Universitaire de Montpellier, Montpellier, France; [6]Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [7]Centre Hospitalier Universitaire de Toulouse, Service d'Hématologie, Toulouse, France; [8]Heidelberg University Hospital, Heidelberg, Germany; [9]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [10]Hospital Universitario Marqués de Valdecilla (IDIVAL) Universidad de Cantabria, Santander, Spain; [11]Hematología Hospital 12 de Octubre, Madrid, Spain; [12]Clínica Universidad de Navarra, CIMA, Pamplona, Spain; [13]Poznan University of Medical Sciences, Poznań, Poland; [14]Janssen Pharmaceutica NV, Beerse, Belgium; [15]Janssen-Cilag, Issy-les-Moulineaux, France; [16]Janssen Research & Development, Raritan, NJ, USA; [17]Janssen Global Services, Raritan, NJ, USA; [18]Janssen-Cilag, Issy-les-Moulineaux, France; [19]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [20]University Hospital of Salamanca, IBSAL/IBMCC/USAL/CSIC, Salamanca, Spain

Introduction

- Talquetamab is the first approved G protein–coupled receptor family C group 5 member D–targeting bispecific antibody for the treatment of patients with triple-class exposed relapsed/refractory multiple myeloma (RRMM) based on results from the MonumenTAL-1 study (NCT03399799/NCT04634552)[1-3]
- LocoMMotion (NCT04035226) and MoMMent (NCT05160584) are 2 prospective, consecutive, observational studies evaluating real-world physician's choice of treatment (RWPC) in patients with triple-class exposed RRMM[4,5]
  - Both studies were designed to mirror ongoing, single-arm trials to enable their use as external control arms
- A previous indirect comparison showed superior efficacy outcomes with talquetamab (data cut-off, Jan 2023) vs RWPC in LocoMMotion and MoMMent (data cut-off, Oct 2022)[6]
- We report an updated adjusted comparison of talquetamab vs RWPC with longer follow-up in each of the studies

Methods

Data sources

- Individual patient-level data (IPD) from MonumenTAL-1 were included for patients who received subcutaneous talquetamab 0.4 mg/kg weekly (QW) or 0.8 mg/kg every other week (Q2W) (data cut-off, Jan 2024); median follow-up, 29.8 and 23.4 months in the QW and Q2W cohorts, respectively
- An external control arm was created using IPD from LocoMMotion (final data; median follow-up, 26.4 months) and MoMMent (data cut-off, Aug 2023; median follow-up, 13.9 months) that met key MonumenTAL-1 eligibility criteria (**Figure 1**)

Adjusted treatment comparison

- The primary analysis used inverse probability of weighting with average treatment effect in the treated (ATT) weights to adjust for imbalances in baseline characteristics
- Balance after adjustment was assessed using standardized mean differences (SMDs)
- The comparative effectiveness of talquetamab vs RWPC was assessed for overall response rate (ORR), very good partial response (VGPR) or better, complete response (CR) or better, duration of response (DOR), progression-free survival (PFS), time to next treatment (TTNT), and overall survival (OS)

Statistical analysis

- For binary outcomes, a weighted logistic regression was used to estimate odds ratios and response ratios with 95% CIs
- Time-to-event outcomes were analyzed using a weighted Cox proportional hazards model to estimate hazard ratios (HRs) and 95% CIs
- Sensitivity analyses evaluated the impact of alternative statistical methods and variable adjustment
- Subgroup analyses were assessed in patients with ≥4 prior lines of therapy (LOT)

Figure 1: MonumenTAL-1 key patient eligibility criteria

MonumenTAL-1; QW (n=143), Q2W (n=154), and RWPC (N=175)

- Triple-class exposed
- ≥3 prior LOT
- Progression ≤12 months after last therapy
- No prior receipt of T-cell redirection therapy including CAR-T or bispecific antibodies
- ECOG PS ≤2
- Hemoglobin ≥8 g/dL
- Creatinine clearance ≥40 mL/min/1.73 m^2

CAR, chimeric antigen receptor; ECOG PS, Eastern Cooperative Oncology Group performance status.

Key Takeaway

With longer follow-up, this adjusted comparison further confirms results from previous analyses that demonstrate the clinical benefit of talquetamab over RWPC in patients with triple-class exposed RRMM

Conclusions

With 73 different treatment regimens included in the RWPC cohort, these results emphasize the lack of a standard of care for patients with triple-class exposed RRMM

Patients treated with talquetamab were significantly more likely to achieve responses, especially deep responses, and had significantly improved PFS, TTNT, and OS compared with patients receiving RWPC generated from contemporary, prospective real-world studies

Both schedules of talquetamab showed superior efficacy compared with RWPC, highlighting its overall clinical benefit and further validating talquetamab as a compelling treatment option for patients with RRMM who are triple-class exposed

Results

Treatments and baseline characteristics

- The most common therapies in the RWPC cohort are shown in **Supplemental Table 1**
- After weighting, the RWPC cohort was well balanced vs talquetamab cohorts, with all SMDs <0.22

Efficacy outcomes

- Patients treated with talquetamab 0.4 mg/kg QW and 0.8 mg/kg Q2W had superior outcomes vs patients who received RWPC across all endpoints (**Table 1**)
  - Patients treated with talquetamab were 2.5/2.4 times more likely to achieve a response, 4.5/4.8 times more likely to reach ≥VGPR, and 95.8/124.0 times more likely to reach ≥CR in the QW or Q2W cohorts, respectively, vs patients who received RWPC (**Figure 2**)
  - Patients treated with talquetamab had significantly improved PFS (**Figure 3**) and OS (**Figure 4**) vs patients receiving RWPC
- Results were consistent in patients with ≥4 prior LOT (**Table 2**) and across all sensitivity analyses

Table 1: Treatment outcomes with talquetamab vs RWPC

Outcome	Talquetamab 0.4 mg/kg QW vs RWPC		Talquetamab 0.8 mg/kg Q2W vs RWPC	
	Response ratio (95% CI)	P value	Response ratio (95% CI)	P value
ORR	2.48 (1.78–3.46)	<0.0001	2.38 (1.71–3.33)	<0.0001
≥VGPR	4.46 (2.82–7.05)	<0.0001	4.76 (2.98–7.60)	<0.0001
≥CR	95.81 (7.51–1221.69)	0.0004	124.04 (9.10–1690.93)	0.0003
	HR (95% CI)	P value	HR (95% CI)	P value
DOR	0.72 (0.47–1.11)	0.138	0.49 (0.32–0.75)	0.001
PFS	0.54 (0.40–0.72)	<0.0001	0.46 (0.34–0.62)	<0.0001
TTNT	0.51 (0.39–0.67)	<0.0001	0.44 (0.34–0.58)	<0.0001
OS	0.38 (0.27–0.54)	<0.0001	0.36 (0.24–0.53)	<0.0001

Table 2: Treatment outcomes with talquetamab vs RWPC in patients with ≥4 prior LOT

Outcome	Talquetamab 0.4 mg/kg QW vs RWPC		Talquetamab 0.8 mg/kg Q2W vs RWPC	
	Response ratio (95% CI)	P value	Response ratio (95% CI)	P value
ORR	2.36 (1.60–3.46)	<0.0001	2.26 (1.52–3.35)	<0.0001
≥VGPR	3.86 (2.30–6.47)	<0.0001	4.26 (2.52–7.19)	<0.0001
≥CR[a]	NE	NE	NE	NE
	HR (95% CI)	P value	HR (95% CI)	P value
DOR	0.75 (0.45–1.25)	0.275	0.53 (0.30–0.93)	0.026
PFS	0.60 (0.42–0.85)	0.004	0.50 (0.34–0.73)	0.0004
TTNT	0.52 (0.38–0.71)	<0.0001	0.44 (0.31–0.63)	<0.0001
OS	0.39 (0.28–0.58)	<0.0001	0.34 (0.21–0.55)	<0.0001

Data for talquetamab are reported from phase 2 only in patients who were included in the USPI (n=100 in QW and n=87 in Q2W). [a]NE due to no patients having a ≥CR in the RWPC cohort. NE, not evaluable.

Figure 2: Unadjusted and ATT-weighted response rates

PR, partial response.

Figure 3: Unadjusted and ATT-weighted PFS

Figure 4: Unadjusted and ATT-weighted OS

Please scan QR code
Poster
Supplementary material

https://www.congresshub.com/Oncology/IMS2024/Talquetamab/Einsele

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Acknowledgments

This study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Alana Dorfstatter, PharmD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

Disclosures

HE has received honoraria from Amgen, BMS, EUSA Pharma, Genesis, GSK, Janssen, Novartis, Sanofi, and Takeda; has received travel expenses from Amgen, EUSA Pharma, and Takeda; and has received research funding from Amgen, Genesis, GSK, Janssen, Sanofi, and Takeda.

References

1. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 2. TALVEY™ (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2023. 3. European Medicines Agency. TALVEY™ (talquetamab). Accessed July 26, 2024. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/talvey. 4. Mateos MV, et al. *Leukemia* 2022;36:1371-6. 5. ClinicalTrials.gov. NCT05160584. Accessed July 26, 2024. 6. Einsele H, et al. Presented at EHA 2023 Hybrid Congress; June 8–11, 2023; Frankfurt, Germany.

Multiple Myeloma

Presented by H Einsele at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

P915

Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma

Leo Rasche[1], Carolina Schinke[2], Cyrille Touzeau[3], Monique C Minnema[4], Niels WCJ van de Donk[5], Paula Rodríguez-Otero[6], María-Victoria Mateos[7], Jing Christine Ye[8], Deeksha Vishwamitra[9], Indrajeet Singh[9], Xiang Qin[9], Michela Campagna[10], Tara Masterson[9], Brandi W Hilder[9], Jaszianne Tolbert[9], Thomas Renaud[11], Christoph Heuck[9], Colleen Kane[9], Ajai Chari[12]

[1]University Hospital of Würzburg, Würzburg, Germany; [2]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [3]Centre Hospitalier Universitaire de Nantes, Nantes, France; [4]University Medical Center Utrecht, Utrecht, Netherlands; [5]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [6]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [7]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [8]MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [9]Janssen Research & Development, Spring House, PA, USA; [10]Janssen Research & Development, Madrid, Spain; [11]Janssen Research & Development, Raritan, NJ, USA; [12]Mount Sinai School of Medicine, New York, NY, USA, at the time that the work was performed.

Key Takeaway

With long-term follow-up, tal continues to demonstrate deep and durable responses and no new safety signals in pts with RRMM

Conclusions

- High ORRs of ≥70% in the QW and Q2W TCR-naive cohorts and 67% in the prior TCR cohort were achieved with long-term follow-up at the approved tal doses
- Pts continued to demonstrate durable responses, with longer DORs observed in pts with deeper response
- The safety profile was consistent with previous reports; together with the efficacy data, these results highlight the overall clinical benefit of the approved tal doses and the flexibility to adjust dosing once response is achieved

Please scan QR code

Poster

Supplementary material

https://www.congresshub.com/Oncology/EHA2024/Talquetamab/Rasche

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Acknowledgments

This study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Rachael Smith, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

Disclosures

LR has received travel, accommodations, and expenses from BeiGene and Johnson & Johnson; has received honoraria from and reports a consulting/advisory role with Amgen, BeiGene, BMS, GSK, Pfizer, and Sanofi; and reports a leadership or fiduciary role within the International Myeloma Working Group and International Myeloma Society.

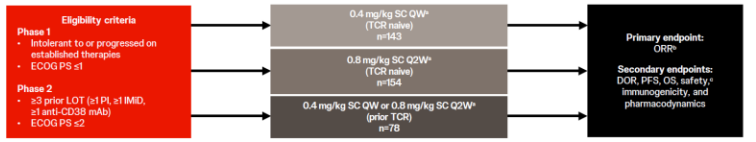
Introduction

- Talquetamab (tal) is the first approved bispecific antibody (BsAb) targeting the novel antigen G protein–coupled receptor class C group 5 member D (GPRC5D) for the treatment of patients (pts) with relapsed/refractory multiple myeloma (RRMM)[1,2]
- In previously reported results from MonumenTAL-1, tal showed overall response rates (ORRs) of >71% in pts naive to prior T-cell redirection therapy (TCR) and 65% in pts with prior TCR at the approved subcutaneous (SC) doses of 0.4 mg/kg weekly (QW) and 0.8 mg/kg every other week (Q2W)[3]
- Exposure–response (E–R) analyses showed increased ORRs with SC doses that plateaued at or above the approved doses (**Supplemental Figure 1**)[4,5]
  - An E–R relationship was observed for grade 1/2 dysgeusia; however, rates were similar at both approved doses (**Supplemental Figure 2**)[4,5]
- Early onset of GPRC5D-related adverse events (AEs), including dysgeusia, is associated with a higher likelihood of response; prior data support flexibility to adjust tal dosing in responders to mitigate AEs while maintaining efficacy[6]
- Here, we report the long-term follow-up results of pts receiving tal at the approved doses

Methods

- MonumenTAL-1 (NCT03399798/NCT04634552) enrolled pts with RRMM who were naive or exposed to prior TCR (**Figure 1**)

Figure 1: MonumenTAL-1 phase 1/2 study design



[a]With 2–3 step-up doses. [b]Assessed by IRC using International Myeloma Working Group criteria.[7,8] [c]CRS and ICANS were graded by ASTCT criteria[9]; all other AEs were graded by CTCAE v4.03. ASTCT, American Society of Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMiD, immunomodulatory drug; IRC, independent review committee; LOT, line of therapy; mAb, monoclonal antibody; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor.

Results

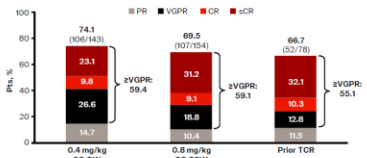
Baseline characteristics

- Baseline characteristics across the QW, Q2W, and prior TCR cohorts were similar to previous reports,[3] with the exception of more African American pts in the current analysis (n=32/375, 9%)

Efficacy

- As of January 29, 2024, ORR was 74%, 70%, and 67% for pts in the QW, Q2W, and prior TCR cohorts, respectively (**Figure 2**)
  - ORRs were consistent across high-risk subgroups, except for pts with extramedullary disease, who had lower ORRs (**Supplemental Table 1**)
  - In pts with prior TCR, ORR was 71% (n=40/56) with prior chimeric antigen receptor (CAR)-T cell therapy and 58% (n=15/26) with prior BsAb therapy
- Median time to first response (range) was 1.2 (0.2–10.9), 1.3 (0.2–4.9), and 1.2 (0.2–7.5) months, respectively
  - Median time to very good partial response (VGPR) as best response was 2.2 (0.6–6.2), 2.3 (0.3–16.9), and 1.8 (0.8–6.4) months and to complete response (CR) or better as best response was 3.0 (1.1–12.7), 5.8 (1.2–16.8), and 2.7 (1.2–18.7) months, respectively
- DOR, PFS, and OS are shown in **Table 1**
  - Better durability was observed in the Q2W vs QW cohort
  - In pts with prior TCR, the median PFS (mPFS) was 12.3 months with prior CAR-T cell therapy and 4.1 months with prior BsAb therapy
- In the Q2W cohort, 40% of pts achieved a ≥CR, most by ~12 months (**Figure 3A**); although a ≥CR may take longer to achieve, pts with deeper responses had a longer DOR (**Figure 3B**)

Figure 2: ORR[a]



[a]Due to rounding, individual response rates may not sum to the ORR. PR, partial response; ≥CR, stringent complete response.

Table 1: Efficacy outcomes

Outcome	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
mFU, mo	29.8	23.4	20.5
mDOR (95% CI),[a] mo	9.5 (6.7–13.4)	17.5 (12.5–NE)	N/A[b]
mDOR in pts with ≥CR (95% CI), mo	28.6 (19.4–NE)	NR (21.2–NE)	N/A[b]
mPFS (95% CI), mo	7.5 (5.7–9.4)	11.2 (8.4–14.6)	7.7 (4.1–14.5)
24-mo OS rate (95% CI), %	60.6 (51.7–68.4)	67.1 (58.3–74.4)	57.3 (43.5–68.9)

[a]n=106 (QW), n=107 (Q2W), and n=52 (prior TCR). [b]NR due to heavy censoring from 12 to 20 mo; the estimate may not be reliable at this time point. See **Supplemental Table 2** for efficacy outcomes in the USPI population (≥4 prior LOT). mDOR, median duration of response; mFU, median follow-up; N/A, not available; NE, not estimable; NR, not reported; USPI, United States prescribing information.

Figure 3: Time to first confirmed response per IRC (A) and DOR by depth of response (B) in the Q2W cohort

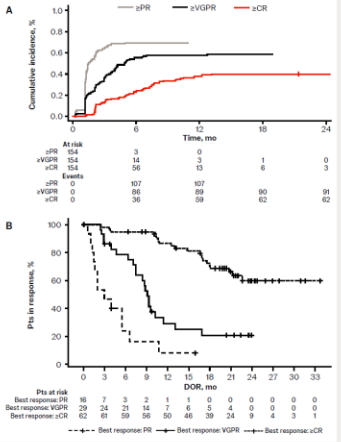
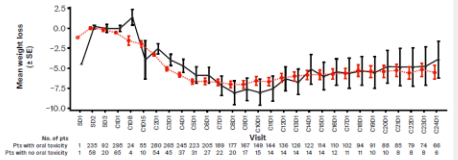
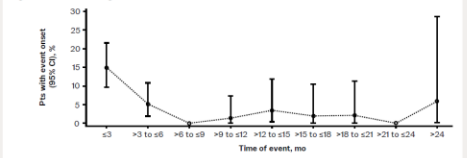


Figure 4: Weight loss in pts with oral toxicity[a] in the QW and Q2W cohorts



[a]Including dysgeusia, ageusia, taste disorder, hypogeusia, dry mouth, dysphagia, cheilitis, glossitis, glossodynia, mouth ulceration, oral discomfort, oral mucosal erythema, oral pain, stomatitis, swollen tongue, tongue discomfort, tongue erythema, tongue edema, tongue ulceration. C, cycle; D, day; SD, step-up dose.

Figure 5: New-onset grade ≥3 infections over time in the Q2W cohort



Safety

- The safety profile across cohorts was consistent with previous results[3]; no new safety signals were reported
- Weight loss, as assessed by vital signs, occurred in 39%, 34%, and 39% of pts in the QW, Q2W, and prior TCR cohorts, respectively
  - Weight loss was evident early, then stabilized and improved over time, including in pts with oral toxicities (**Figure 4**)
- Infection rates remained lower than in studies of B-cell maturation antigen–targeted BsAbs,[10,11] consistent with previous reports[3]; no increase in grade 3/4 infections was observed with longer follow-up (shown for the Q2W cohort; **Figure 5**)
- Modest intravenous immunoglobulin was required (16%, 14%, and 24% of pts, respectively)
- GPRC5D-associated AEs led to few dose reductions and discontinuations (**Table 2**); only 1 additional pt discontinued treatment since previous report[3]
- Similarly, overall rates of dose reductions and discontinuations due to AEs remained low at 15%, 10%, and 12% and 5%, 10%, and 5%, respectively
- There were no treatment-related deaths

Table 2: GPRC5D-associated AEs

Any-grade AE, n (%)	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Taste-related[a]			
Total	103 (72.0)	110 (71.4)	59 (75.6)
Leading to dose reduction	10 (7.0)	6 (3.9)	4 (5.1)
Leading to discontinuation	0	3 (1.9)	0
Skin-related[b]			
Total	81 (56.6)	113 (73.4)[e]	50 (64.1)
Leading to dose reduction	5 (3.5)	1 (0.6)	2 (2.6)
Leading to discontinuation	2 (1.4)	1 (0.6)	0
Nail-related[c]			
Total	79 (55.2)	82 (53.2)	46 (59.0)
Leading to dose reduction	1 (0.7)	1 (0.6)	1 (1.3)
Leading to discontinuation	0	0	0
Rash-related[d]			
Total	57 (39.9)[f]	46 (29.9)[g]	25 (32.1)[h]
Leading to dose reduction	1 (0.7)	1 (0.6)	0
Leading to discontinuation	0	0	0

[a]Including ageusia, dysgeusia, hypogeusia, and taste disorder. [b]Including skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Including nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [d]Including rash, maculopapular rash, erythematous rash, and erythema. [e]Including 1 (0.6%) grade 3/4 event. [f]Including 2 (1.4%) grade 3/4 events. [g]Including 8 (5.2%) grade 3/4 events. [h]Including 2 (2.6%) grade 3/4 events.

References

1. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 2. Chari A, et al. Presented at ASH; December 10–13, 2022; New Orleans, LA, USA. #157. 3. Schinke C, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8036. 4. Ma X, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8041. 5. Zhou J, et al. Presented at ACOP; November 5–8, 2023; Oxon Hill, MD, USA. #T-015. 6. Chari A, et al. Presented at ASH; December 9–12, 2023; San Diego, CA, USA. #1010. 7. Rajkumar SV, et al. *Blood* 2011;117:4691-5. 8. Kumar S, et al. *Lancet Oncol* 2016;17:328-46. 9. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25:625-38. 10. van de Donk NWCJ, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8011. 11. Tomasson M, et al. *Blood* 2023;142 (Supplement 1): 3385.

Multiple Myeloma

Presented by L Rasche at the European Hematology Association (EHA) 2024 Hybrid Congress; June 13–16, 2024; Madrid, Spain

Perfil de eficacia por subgrupos

Eficacia demostrada en pacientes de alto riesgo[1]

TRG en subgrupos, % (IC95%)	0,4 mg/kg SC CS (n=143)	0,8 mg/kg SC C2S (n=154)	TRL previo (n=78)
Edad ≥75 años	71,4 (47,8–88,7)	75,8 (57,7–88,9)	80,0 (28,4–99,5)
Características de alto riesgo citogenético[a]	70,7 (54,5–83,9)	75,0 (58,8–87,3)	52,0 (31,3–72,2)
Estadio ISS III	64,3 (44,1–81,4)	59,5 (42,1–75,2)	76,9 (46,2–95,0)
Función renal basal ≤60 ml/min/1,73m²	65,0 (48,3–79,4)	65,2 (49,8–78,6)	63,2 (38,4–83,7)
Estado refractario			
Triple clase[b]	72,9 (63,4–81,0)	67,3 (57,7–75,9)	65,2 (52,4–76,5)
5 fármacos[c]	71,1 (55,7–83,6)	69,2 (52,4–83,0)	58,8 (40,7–75,4)
≥ plasmocitoma extramedular[d]	48,5 (30,8–66,5)	41,5 (26,3–57,9)	44,0 (24,4–65,1)

[a]Definido por del(17p), t(4;14), y/o t(14;16).
[b]≥1 IP, ≥1 IMiD, y ≥1 mAb anti-CD38.
[c]≥2 IPs, ≥2 IMiDs, y ≥1 mAb anti-CD38
[d]Se incluyeron los plasmocitomas de tejido blando no asociado a hueso
Adaptado de la Tabla 1 del Suplemento de Rasche L, *et al.* Póster P915. EHA 2024. Tabla completa disponible AQUÍ

La mediana de seguimiento para las dosis semanales y quincenales fue de 29,8 y 23,4 meses, respectivamente. La mediana de seguimiento para el grupo de TCR previo fue de 20,5 meses.[1]
CD38: *cluster of differentiation* 38; **CS:** cada semana; **C2S:** cada 2 semanas; **del:** deleción; **IC:** intervalo de confianza; **IMID:** inmunomodulador; **IP:** inhibidor del proteasoma; **ISS:** *International Staging System;* **SC:** subcutáneo; **TRG:** tasa de respuesta global; **TRL:** tratamiento redireccionador de linfocitos T

1. Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.

TRG en subgrupos, % (IC95%)	0,4 mg/kg SC CS (n=143)	0,8 mg/kg SC C2S (n=154)	TRL previo (n=78)
Edad ≥75 años	71,4 (47,8–88,7)	75,8 (57,7–88,9)	80,0 (28,4–99,5)
Características de alto riesgo citogenético[a]	70,7 (54,5–83,9)	75,0 (58,8–87,3)	52,0 (31,3–72,2)
Estadio ISS III	64,3 (44,1–81,4)	59,5 (42,1–75,2)	76,9 (46,2–95,0)
Función renal basal ≤60 ml/min/1,73m²	65,0 (48,3–79,4)	65,2 (49,8–78,6)	63,2 (38,4–83,7)
Estado refractario			
Triple clase[b]	72,9 (63,4–81,0)	67,3 (57,7–75,9)	65,2 (52,4–76,5)
5 fármacos[c]	71,1 (55,7–83,6)	69,2 (52,4–83,0)	58,8 (40,7–75,4)
≥ plasmocitoma extramedular[d]	48,5 (30,8–66,5)	41,5 (26,3–57,9)	44,0 (24,4–65,1)

[a]Definido por del(17p), t(4;14), y/o t(14;16).
[b]≥1 IP, ≥1 IMiD, y ≥1 mAb anti-CD38.
[c]≥2 IPs, ≥2 IMiDs, y ≥1 mAb anti-CD38
[d]Se incluyeron los plasmocitomas de tejido blando no asociado a hueso
Tabla 1 del Suplemento de Rasche L, *et al.* Póster P915. EHA 2024.

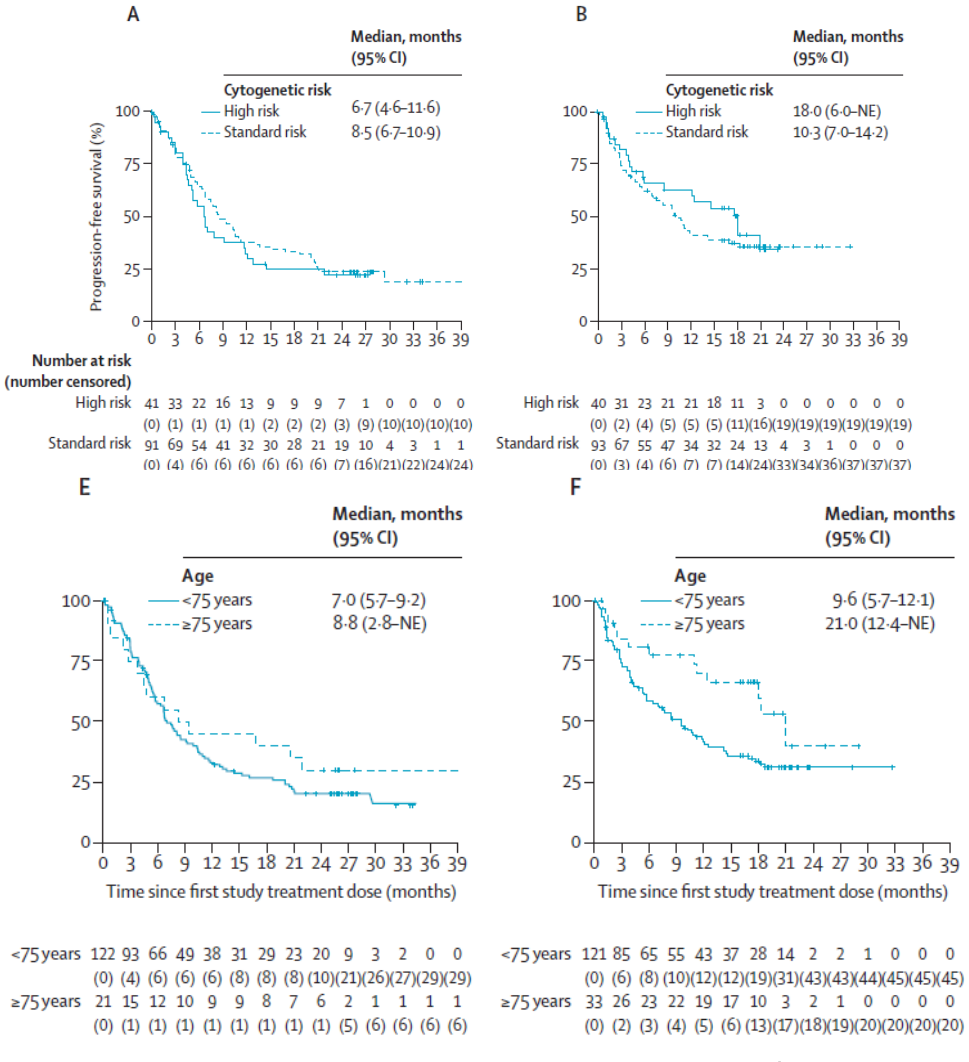
La mediana de seguimiento para las dosis semanales y quincenales fue de 29,8 y 23,4 meses, respectivamente. La mediana de seguimiento para el grupo de TCR previo fue de 20,5 meses.[1]
CD38: *cluster of differentiation* 38; **CS:** cada semana; **C2S:** cada 2 semanas; **del:** deleción; **IC:** intervalo de confianza; **IMID:** inmunomodulador; **IP:** inhibidor del proteasoma; **ISS:** *International Staging System;* **SC:** subcutáneo; **TRG:** tasa de respuesta global; **TRL:** tratamiento redireccionador de linfocitos T

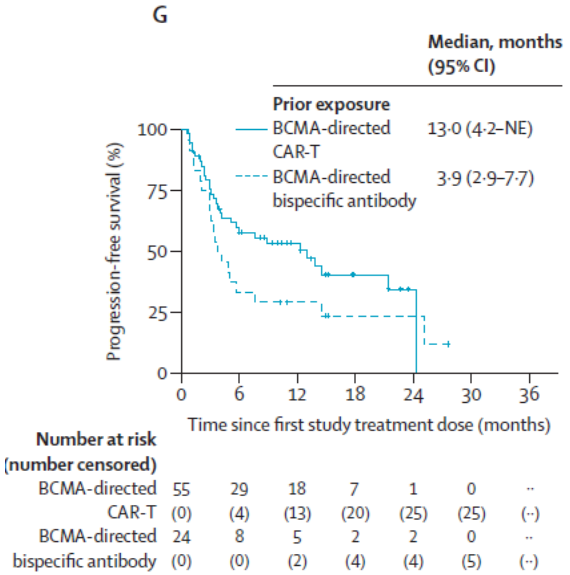
1. Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.

redireccionador de linfocitos T
1. Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.

Resultados de eficacia por subgrupos[1]

SLP en subgrupos seleccionado de alto riesgo (análisis post-hoc)[1]






NEW

Articles

Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study

Ajai Chari, Cyrille Touzeau, Carolina Schinke, Monique C Minnema, Jesus G Berdeja, Albert Oriol, Niels W C J van de Donk, Paula Rodriguez-Otero, Daniel Morillo, Carmen Martinez-Chamorro, Maria-Victoria Mateos, Luciano J Costa, Jo Caers, Leo Rasche, Annita Krishnan, Jing Christine Ye, Lionel Karlin, Brea L Lipe, Deepika Vishwamitra, Shari Skerget, Rakusi Verona, Xunwen Ma, Xiang Qin, Heinl Lullage, Michela Campagna, Tara Masterson, Brandi Hilder, Jazzianne Tolbert, Thomas Renaud, Jenna D Goldberg, Colleen Kane, Christoph Heuck, Jesus San-Miguel, Philippe Moreau

Summary

Background Talquetamab is the first GPRC5D × CD3 bispecific antibody approved for relapsed or refractory multiple myeloma. In phase 1 of the MonumenTAL-1 study, initial results of subcutaneous talquetamab 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks showed preliminary clinical activity. We describe safety and activity results in patients treated with talquetamab, including patients who had received previous T-cell redirection therapy (TCR). This post-hoc analysis was done with more mature median follow-up to evaluate duration of response in patients treated with talquetamab 0·8 mg/kg every 2 weeks.

Methods MonumenTAL-1 is a multicentre, open-label, phase 1–2 study of talquetamab, phase 1 of which has previously been published. The 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks recommended subcutaneous doses identified in phase 1 were evaluated in phase 2 in patients who were 18 years of age or older, had at least three previous lines of therapy, had an Eastern Cooperative Oncology Group performance status of 0 to 2, and were naive or exposed to previous TCR. The primary endpoint was overall response rate assessed by independent review committee in all patients who received at least one dose of talquetamab. Safety was assessed in all patients who received at least one dose of talquetamab. This study was registered with ClinicalTrials.gov, NCT03399799 (phase 1) and NCT04634552 (phase 2).

Findings Between Jan 3, 2018, and Feb 20, 2023, 735 patients were screened across all phase 1–2 cohorts. Of these, 537 patients screened for inclusion were treated across phase 1 and 2 cohorts, of whom 198 (27%) patients were excluded from the study, most commonly due to not meeting eligibility criteria or not having measurable disease. As of Oct 11, 2023, 375 patients had received recommended talquetamab doses across three groups: 143 (0·4 mg/kg once a week group) and 154 (0·8 mg/kg every 2 weeks group) TCR-naive patients and 78 with previous TCR who received either recommended dose (previous TCR group). 217 (58%) of 375 patients were male and 158 (42%) were female. 325 (87%) of 375 patients were White and 32 (9%) patients were Black. Median follow-up was 25·6 months (IQR 8·5–25·9) in the 0·4 mg/kg once a week group, 19·4 months (9·2–20·7) in the 0·8 mg/kg every 2 weeks group, and 16·8 months (7·6–18·7) in the previous TCR group. Overall response rate was 74% (106 of 143 patients, 95% CI 66–81) in the 0·4 mg/kg once a week group, 69% (107 of 154 patients, 62–77) in the 0·8 mg/kg every 2 weeks group, and 67% (52 of 78 patients, 55–77) in the previous TCR group. Most common adverse events in the 0·4 mg/kg once a week, 0·8 mg/kg every 2 weeks, and previous TCR groups were cytokine release syndrome (113 [79%] of 143 patients, 115 [75%] of 154 patients, and 57 [73%] of 78 patients), taste changes (103 [72%], 110 [71%], and 59 [76%]), and infections (85 [59%], 105 [68%], and 59 [76%]). Most common grade 3–4 adverse events were neutropenia (44 [31%], 33 [21%], and 37 [47%]), anaemia (45 [31%], 40 [26%], and 21 [27%]), and lymphopenia (37 [26%], 40 [26%], and 13 [17%]). Fatal adverse events occurred in five patients in the 0·4 mg/kg once a week group, seven patients in the 0·8 mg/kg every 2 weeks group, and no patients in the previous TCR group; none were related to treatment.

Interpretation Talquetamab continued to demonstrate high overall response rates in heavily pretreated patients with relapsed or refractory multiple myeloma with longer follow-up in this post-hoc analysis. Overall response rate was promising in patients with previous TCR, including therapies targeting BCMA. On-target, off-tumour adverse events were common but led to few treatment discontinuations.

Funding Janssen.

Copyright © 2025 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

Lancet Haematol 2025

Published Online March 13, 2025 https://doi.org/10.1016/S2352-3026(24)00385-5

See Online/Comment https://doi.org/10.1016/S2352-3026(25)00009-2

Mount Sinai School of Medicine, New York, NY, USA (Prof A Chari MD); Centre Hospitalier Universitaire de Nantes, Nantes, France (Prof C Touzeau MD); Prof P Moreau MD); Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA (C Schinke MD); University Medical Center Utrecht, Utrecht, Netherlands (Prof M C Minnema MD); Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN, USA (J G Berdeja MD); Institut Català d'Oncologia and Institut Josep Carreras, Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain (A Oriol MD); Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands (Prof N W C J van de Donk MD); Cancer Center Clínica Universidad de Navarra, CCUN; CIMA, CIBERONC, IDISNA, Pamplona, Spain (P Rodriguez-Otero MD, Prof J San-Miguel MD); University Hospital Fundación Jiménez Díaz, START Madrid-FJD early phase unit, Madrid, Spain (D Morillo MD); Hospital Universitario Quirónsalud Madrid and Universidad Europea de Madrid, Madrid, Spain (C Martinez-Chamorro MD); University Hospital of Salamanca/IBSAL/CSC/CIBERONC, Salamanca, Spain (M-V Mateos MD); The University of Alabama at Birmingham, Birmingham, AL, USA (Prof L J Costa MD); Centro

www.thelancet.com/haematology Published online March 13, 2025 https://doi.org/10.1016/S2352-3026(24)00385-5 1

Gráficas estraídas de la Figura 3 de Chari A, *et al* Lancet 2025. Figura completa disponible AQUÍ

Se describen los resultados actualizados de seguridad y actividad con un seguimiento más prolongado de MonumenTAL-1 en pacientes tratados con talquetamab subcutáneo 0-4 mg/kg una vez a la semana o 0-8 mg/kg cada 2 semanas (mediana de seguimiento 25-6 y 19-4 meses, respectivamente), incluyendo análisis en pacientes que habían recibido previamente terapia de redirección de células T [TCR; terapias de células T con receptores de antígenos quiméricos (CAR-T) o anticuerpos biespecíficos (mediana de seguimiento 16-8 meses)]. Crucialmente, este análisis post-hoc se realizó con una mediana de seguimiento más madura para evaluar la duración de la respuesta en pacientes tratados con talquetamab 0-8 mg/kg cada 2 semanas. Las limitaciones de este estudio incluyen que sólo 537 de los 735 pacientes seleccionados para su inclusión fueron tratados en las cohortes de fase 1-2 y la ausencia de tratamientos de comparación evaluados frente a talquetamab.[1]

BCMA: antígeno de maduración del linfocito B; **CAR-T:** linfocito T con receptores antigénicos quiméricos; **CI:** intervalo de confianza; **NE:** no estimable.

1. Chari A, *et al.* Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet Haematol. 2025 Mar 13.

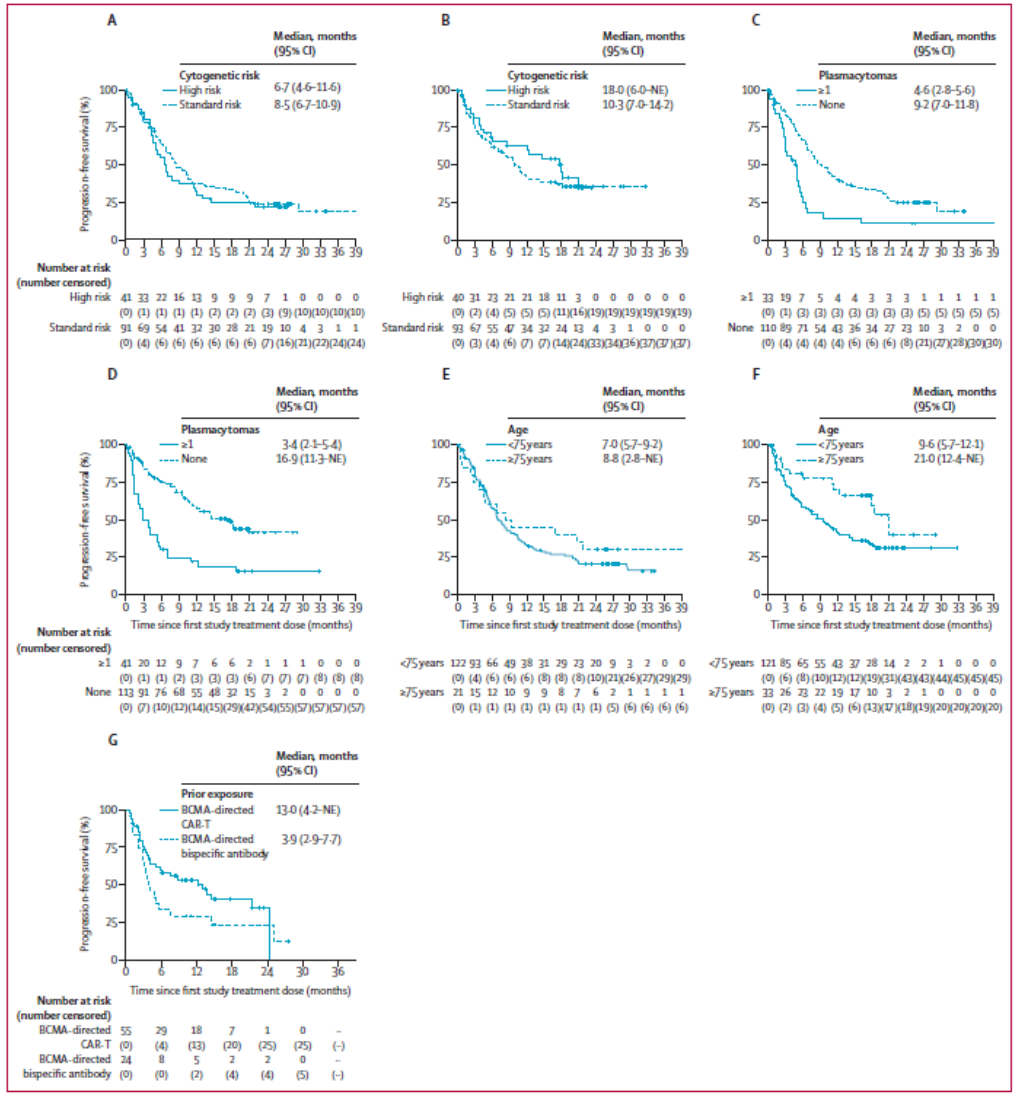


Figura 3 de Chari A, *et al* Lancet 2025.[1]

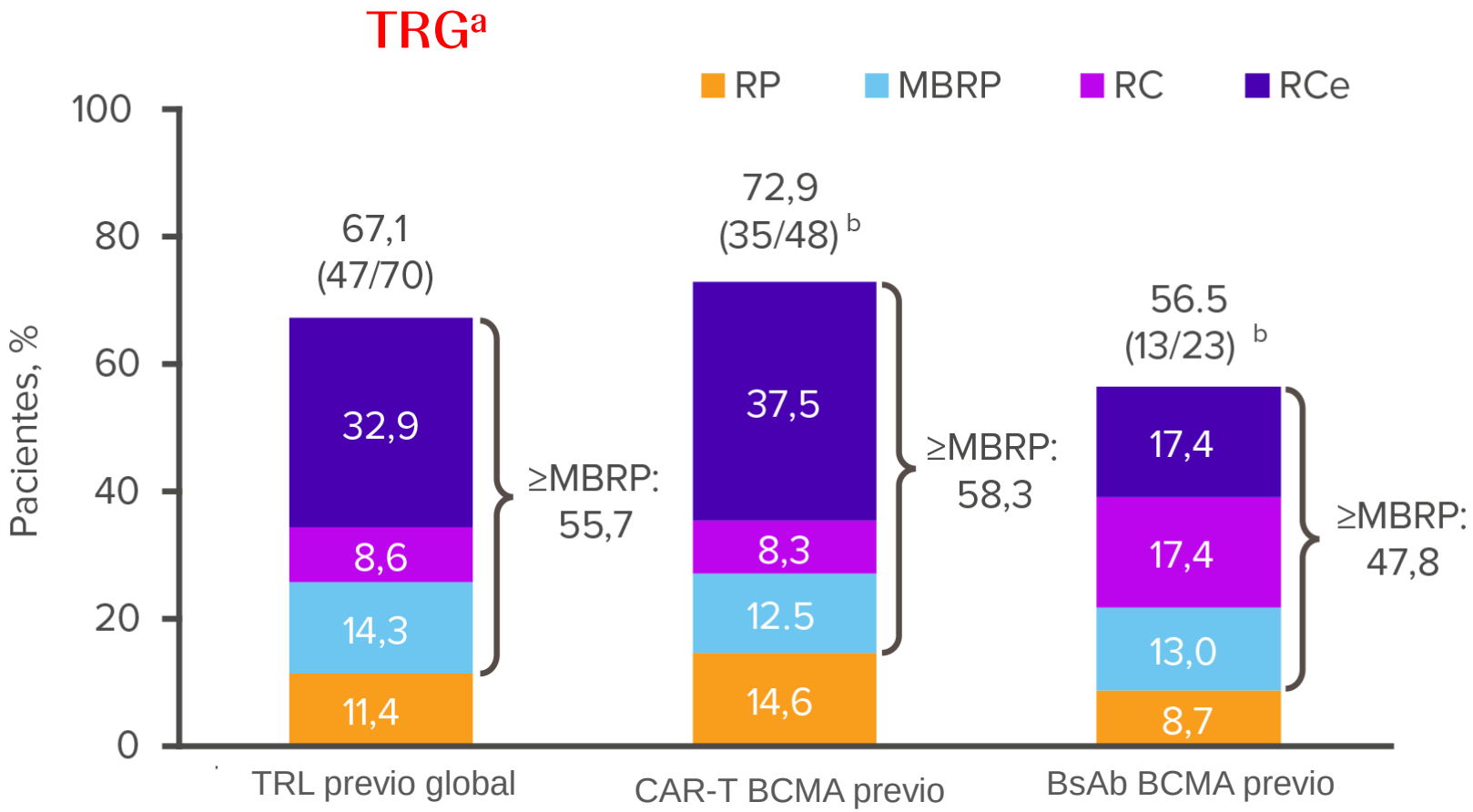
BCMA: antígeno de maduración del linfocito B; **CAR-T:** linfocito T con receptores antigénicos quiméricos; **CI:** intervalo de confianza; **NE:** no estimable.

1. Chari A, *et al.* Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet Haematol. 2025 Mar 13.

Resultados de eficacia en la población post TRL

TRL: tratamiento redireccionador de linfocitos T.

La TRG fue ligeramente superior en los pacientes con CAR-T BCMA previo frente a la población general con TCR previo; la TRG fue inferior en los pacientes con BsAb BCMA previo frente a ambas poblaciones.[1]



[a]Debido al redondeo, las tasas de respuesta individuales pueden no sumar la TRG.
[b]4 pacientes recibieron tanto CAR-T BCMA como BsAb BCMA.
Figura 2 de Jakubowiak A, *et al.* Póster 3377 ASH 2023

La mediana de seguimiento para los pacientes que habían recibido un TRL previo fue de 18,4 meses, así como para los que habían recibido un CAR-T y de 16,3 meses para los que habían recibido un BsAb BCMA[1]. Dato extraído de la Tabla 2 de Jakubowiak A, *et al.* Póster 3377 ASH 2023. Póster completo disponible AQUÍ

BCMA: antígeno de maduración de células B; **BsAb:** anticuerpo biespecífico; **CAR-T:** linfocito T con receptores antigénicos quiméricos; **IC:** intervalo de confianza; **MBRP:** muy buena respuesta parcial; **RC:** respuesta completa; **RCe:** respuesta completa estricta; **RP:** respuesta parcial; **TRG:** tasa de respuesta global; **TRL:** tratamiento redireccionador de linfocitos T.

1. Jakubowiak A, *et al.* Updated Results of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma With Prior Exposure to T-Cell Redirecting Therapies: Results of the Phase 1/2 MonumenTAL-1 Study. Póster 3377 presentado en 65th American Society of Hematology (ASH) Annual Meeting; 9-12 diciembre 2023; San Diego, CA, EEUU;

Updated Results of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma With Prior Exposure to T-Cell Redirecting Therapies: Results of the Phase 1/2 MonumenTAL-1 Study

Andrzej J Jakubowiak[1], Sébastien Anguille[2], Lionel Karlin[3], Ajai Chari[4], Carolina Schinke[5], Leo Rasche[6], Jesús San-Miguel[7], Michela Campagna[8], Brandi W Hilder[9], Tara J Masterson[9], Xiang Qin[9], Thomas Renaud[10], Jaszianne Tolbert[9], Deeksha Vishwamitra[9], Sheri Skerget[9], Philippe Moreau[11]

[1]University of Chicago, Chicago, IL, USA; [2]Vaccine and Infectious Disease Institute, University of Antwerp, Center for Cell Therapy and Regenerative Medicine, Antwerp University Hospital, Edegem, Belgium; [3]Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [4]Mount Sinai School of Medicine, New York, NY, USA, at the time that the work was performed; [5]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [6]University Hospital of Würzburg, Würzburg, Germany; [7]University of Navarra, Pamplona, Spain; [8]Janssen Research & Development, Madrid, Spain; [9]Janssen Research & Development, Spring House, PA, USA; [10]Janssen Research & Development, Raritan, NJ, USA; [11]Hematology Clinic, University Hospital Hôtel-Dieu, Nantes, France

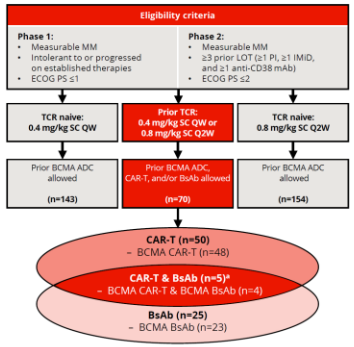
INTRODUCTION

- Novel T-cell redirection therapies (TCRs), including chimeric antigen receptor T-cell therapy (CAR-T) and bispecific antibodies (BsAbs), are important new treatment options for relapsed/refractory multiple myeloma (RRMM) but result in a new unmet need for patients who relapse following these therapies[1-3]
- Talquetamab is the first and only G protein–coupled receptor family C group 5 member D (GPRC5D) BsAb approved for RRMM[4-6]
- Previous results from the MonumenTAL-1 study demonstrated deep and durable responses with talquetamab in patients with RRMM, with an overall response rate (ORR) of >71% in 288 patients naive to TCR and 65% in 51 patients with prior TCR[7]
- Here, we present updated results in patients with prior TCR, including an additional 19 patients enrolled since the prior analysis

METHODS

- MonumenTAL-1 enrolled patients who were naive or exposed to prior TCR (**Figure 1**)
  - As of Oct 11, 2023, 70 patients with prior TCR were enrolled; of these, 8 patients also received prior B-cell maturation antigen (BCMA) antibody-drug conjugate (ADC)

FIGURE 1: MonumenTAL-1 phase 1/2 study design



MonumenTAL-1 ClinicalTrials.gov identifiers: NCT03399799/NCT04634552. [a]Among the overall prior TCR group (N=70), 5 patients treated with both prior CAR-T and BsAb were also counted in each of the respective overall CAR-T (n=50) and BsAb (n=25) groups. CD, cluster of differentiation; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; PI, proteasome inhibitor; QW, every other week; QW, weekly; SC, subcutaneous.

Multiple Myeloma

RESULTS

Baseline characteristics

- Majority of patients (67/70, 95.7%) were exposed to BCMA-targeting TCR (**Table 1**)

TABLE 1: Baseline characteristics

Characteristic, n (%)	0.4 mg/kg SC QW (n=62)	0.8 mg/kg SC Q2W (n=8)	Overall (N=70)
Age <65 years	38 (61.3)	6 (75.0)	44 (62.9)
Male	40 (64.5)	5 (62.5)	45 (64.3)
Bone marrow plasma cells ≥60%	10 (16.1)	0	10 (14.3)
Extramedullary plasmacytomas ≥1[a]	17 (27.4)	4 (50.0)	21 (30.0)
High-risk cytogenetics[b]	21 (33.9)	3 (37.5)	24 (34.3)
ISS stage[c]			
I	29 (46.8)	4 (50.0)	33 (47.1)
II	23 (37.1)	2 (25.0)	25 (35.7)
III	10 (16.1)	2 (25.0)	12 (17.1)
Exposure status			
CAR-T	46 (74.2)	4 (50.0)	50 (71.4)
BCMA CAR-T	44 (71.0)	4 (50.0)	48[d] (68.6)
BsAb	21 (33.9)	4 (50.0)	25 (35.7)
BCMA BsAb	19 (30.6)	4 (50.0)	23[d] (32.9)
ADC (belantamab)	8 (12.9)	0	8 (11.4)
≥4 prior LOT	58 (93.5)	7 (87.5)	65 (92.9)
Refractory status[e]			
Triple-class[f]	51 (82.3)	8 (100.0)	59 (84.3)
Penta-drug[g]	27 (43.5)	4 (50.0)	31 (44.3)
To last LOT	36 (58.1)	6 (75.0)	42 (60.0)

[a]Soft tissue plasmacytomas not associated with the bone were included. [b](14;16), (14;14), and/or del(17p). [c]ISS staging is derived based on serum β_2-microglobulin and albumin. [d]4 patients received both BCMA CAR-T and BCMA BsAb. [e]Patients were considered refractory to a LOT if the best response was SD or PD; or if they progressed ≤60 days after end of treatment. The end of treatment for CAR-T therapy was considered the final day of CAR-T cell infusion. [f]≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb. [g]≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb. ISS, International Staging System; PD, progressive disease; SD, stable disease.

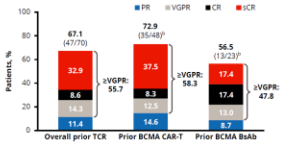
Safety

- Patients with prior TCR had a higher overall infection rate and slightly higher proportion of severe infections vs TCR-naive patients, consistent with previously reported results[7]
- Patients with prior CAR-T had similar rates of infections, cytopenias, cytokine release syndrome, and GPRC5D-related adverse events (AEs) (dysgeusia, skin-, nail-, and rash-related AEs) as patients with prior BsAb (**Supplemental Table 1**)

Efficacy outcomes by prior BCMA groups

- ORR was slightly higher in patients with prior BCMA CAR-T vs the overall prior TCR population; ORR was lower in patients with prior BCMA BsAb vs both populations (**Figure 2**)
- 12-month progression-free survival (PFS) and duration of response (DOR) rates were higher in patients with prior BCMA CAR-T vs BCMA BsAb (**Table 2**)

FIGURE 2: ORR[a]



[a]Due to rounding, individual response rates may not sum to the ORR. [b]4 patients received both BCMA CAR-T and BCMA BsAb. CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

TABLE 2: 12-mo PFS and DOR rates

Outcome	Overall prior TCR (N=70)	Prior BCMA CAR-T (n=48[a])	Prior BCMA BsAb (n=23[a])
mFU,[b] mo	18.4	18.4	16.3
12-mo PFS rate, % (95% CI)	44.1 (32.1–55.4)	50.0 (34.9–63.4)	30.4 (13.5–49.3)
12-mo DOR rate, % (95% CI)	55.2 (39.3–68.5)	54.7 (36.0–70.0)	43.3 (16.3–67.9)

[a]4 patients received both BCMA CAR-T and BCMA BsAb. [b]Based on Kaplan-Meier product limit estimate. mFU, median follow-up; mo, month.

TABLE 3: ORR and 12-mo DOR rate by interval

Time from last dose of prior BCMA TCR to first dose of talquetamab		ORR, % (n/N)	12-mo DOR rate, % (95% CI)
BCMA CAR-T	<9 mo	93.8 (15/16)	57.1 (27.5–78.5)
	≥9 mo	62.5 (20/32)	53.0 (28.6–72.4)
BCMA BsAb	<9 mo	50.0 (8/16)	50.0 (15.2–77.5)
	≥9 mo	71.4 (5/7)	26.7 (1.0–68.6)

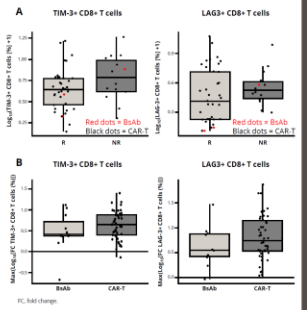
Efficacy outcomes by intervals

- Although numbers were small at each interval, ORR trended higher in patients with <9 mo between last dose of prior BCMA CAR-T and talquetamab; in contrast, ORR trended higher in patients with ≥9 mo between last dose of prior BCMA BsAb and talquetamab (**Table 3**)
- ORR was comparable in patients who received CAR-T prior to last therapy vs as last therapy before talquetamab (71.4% vs 75.9%); ORR trended higher in patients who received BsAb prior to last therapy vs as last therapy before talquetamab (66.7% vs 28.6%) (**Supplementary Table 2**)

Translational data

- At baseline, the pharmacodynamic profile in patients with prior TCR had a more exhausted immune phenotype vs TCR-naive patients (see **Poster 1933**)
- Among patients with prior TCR, nonresponders to talquetamab had a more exhausted immune phenotype vs responders, indicated by lower T-cell counts (see **Poster 1933**) and higher counts of TIM-3– and LAG-3–expressing CD8+ T cells at baseline (**Figure 4A**)
- Following talquetamab, patients with prior CAR-T had greater T-cell activation vs patients with prior BsAb, indicated by higher max fold induction of TIM-3– and LAG-3–expressing CD8+ T cells in the first cycle (**Figure 4B**)

FIGURE 4: CD8+ T-cell profile in (A) responders (R) vs nonresponders (NR) receiving prior TCR at baseline and (B) patients receiving prior CAR-T vs BsAb following talquetamab



FC, fold change.

REFERENCES:

1. Granger K, et al. *J Oncol Pharm Pract* 2023;29:722-6. 2. Zhang X, et al. *Front Immunol* 2023;14:1101495. 3. ELREXFIO™ (elranatamab-bcmm). Prescribing information. New York, NY: Pfizer Inc.; 2023. 4. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 5. TALVEY (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2023. 6. TALVEY. Summary of product characteristics. Leiden, Netherlands: Janssen Biologics B.V.; 2023. 7. Schinke CD, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. Poster 8036.

Presented at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

KEY TAKEAWAY

Assessment of talquetamab in patients with prior TCR, including a large population of patients with prior BCMA BsAb exposure (n=23), showed continued efficacy in this population; ORR was 57% in patients with prior BCMA BsAb and 73% in patients with prior BCMA CAR-T

CONCLUSIONS

- Our results showed trends for higher ORRs and improved PFS and DOR rates in patients with prior BCMA CAR-T vs BsAb; outcomes data in these patients may offer insight into strategies for optimizing sequencing of TCRs that target independent MM antigens
- Patients with prior CAR-T and BsAb had similar safety profiles
- Although prior TCR patients have a less favorable immune profile at baseline vs TCR-naive patients, high response rates are observed, particularly with prior CAR-T, which was associated with greater T-cell activation in the first cycle
- These results support talquetamab as a versatile treatment option that provides robust responses in patients with RRMM and prior exposure to TCR (predominantly targeting BCMA)

ACKNOWLEDGMENTS

This study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Michelle Yang, PharmD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

DISCLOSURES

AJ has received honoraria from and reports a consulting/advisory role for AbbVie, Amgen, BMS, GSK, Janssen, and Sanofi. **SA** and **CS** have no conflicts to disclose. **LK** has received honoraria from AbbVie, Amgen, Celgene, Janssen, Sanofi, and Takeda; and reports a consulting role for Amgen, Celgene, GSK, Janssen, and Takeda. **AC** has served in a consulting/advisory role for AbbVie, Amgen, Antengene, BMS, Genentech, GSK, Janssen, Karyopharm Therapeutics, Sanofi, Seagen, Secura Bio, Shattuck Labs, and Takeda; and has received research funding from Amgen, BMS, Janssen, Seagen, and Takeda. **LR** has received honoraria from BMS, GSK, Janssen, Pfizer, Roche, and Sanofi; has served in a consulting role for Amgen, BMS, GSK, Janssen, Pfizer, and Sanofi; and has received research funding from BMS and SkylineDx. **JS-M** has served in a consulting/advisory role for AbbVie, Amgen, BMS, Celgene, GSK, Haemalogix, Janssen, Karyopharm Therapeutics, MSD, Novartis, Regeneron, Roche, Sanofi, Secura Bio, and Takeda. **MC, BWH, TJM, TR, DV,** and **SS** are employees of Janssen/Johnson & Johnson and may own stock in Janssen/Johnson & Johnson. **XQ** and **JT** are employees of Janssen. **PM** has received honoraria from and has served in a consulting/advisory role for AbbVie, Amgen, BMS, Celgene, GSK, Janssen, Pfizer, Sanofi, and Takeda.

Scan the QR code

https://www.congresshub.com/Oncology/ASH2023/Talquetamab/Jakubowiak

¿Qué podemos esperar del perfil de seguridad*?

*Para mayor información acerca del perfil de seguridad de TALVEY® consultar sección 4.4 y 4.8 de la Ficha Técnica.

La expresión de GPRC5D es limitada en tejidos sanos[1]

Mapa de expresión de la proteína GPRC5D por inmunohistoquímica en tejidos con expresión génica positiva para GPRC5D[2]

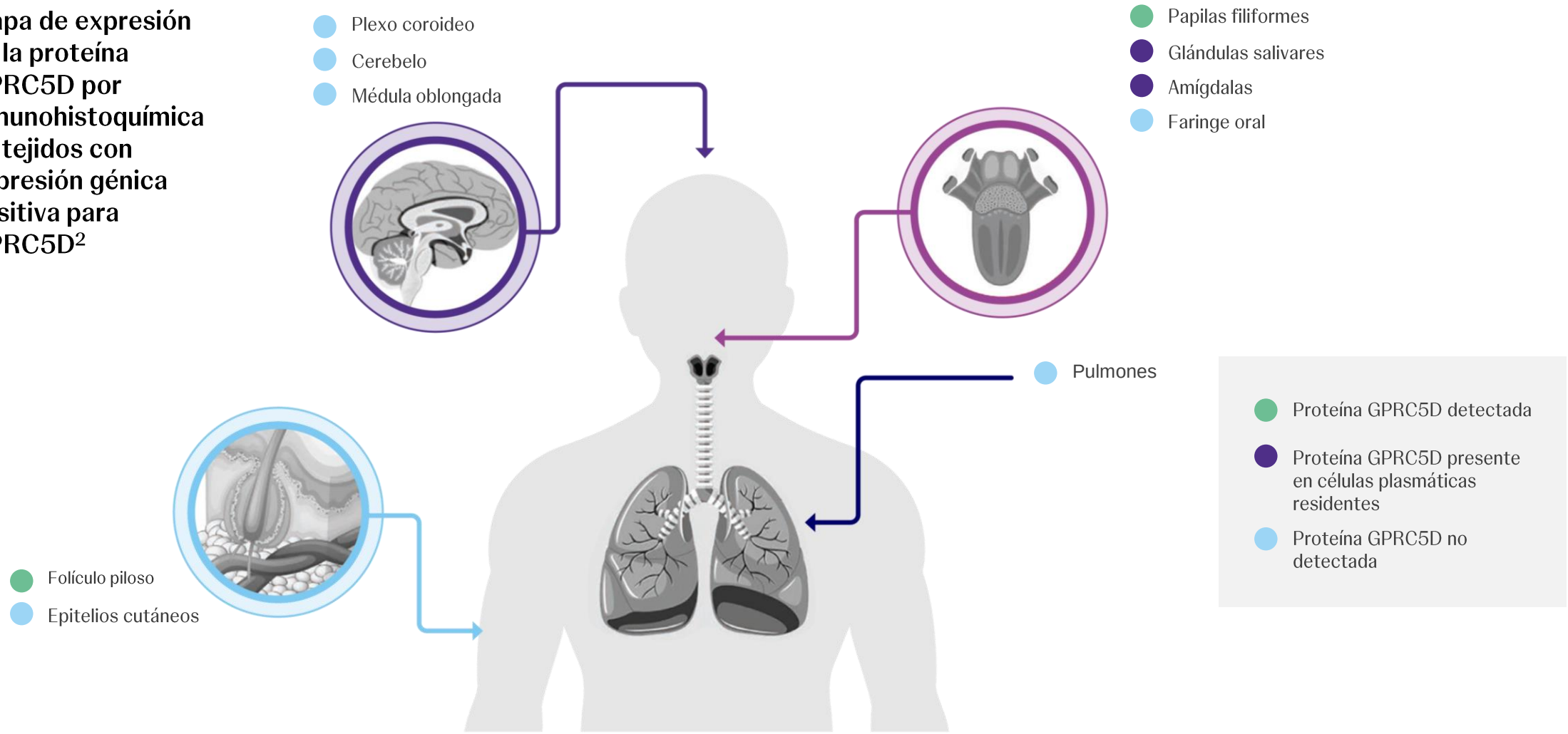


Figura 1 de Chari A, et al. Clin Lymphoma Myeloma Leuk 2024.
GPRC5D: miembro D del grupo 5 de la familia C del receptor acoplado a proteína G.
1. Atamaniuk J, *et al.* Overexpression of G protein-coupled receptor 5D in the bone marrow is associated with poor prognosis in patients with multiple myeloma. Eur J Clin invest 2012; 42(9):953–960; 2. Chari A, *et al.* Clinical Management of Patients With Relapsed/Refractory Multiple Myeloma Treated With Talquetamab. Clin Lymphoma Myeloma Leuk 2024;24(10):665-693.e14.

Perfil de seguridad de talquetamab*

EAs asociados al GPRC5D[1]	**Dermatológicos**				**Orales**		**Pérdida de Peso**
	Trastornos eruptivos	Trastornos cutáneos no eruptivos	Toxicidad ungueal	Boca seca / Xerostomía	Disgeusia	Disfagia	
Relacionados con el TCR[1]	**SLC**			**ICANS**			
Infecciones[1]	**Infecciones**						

Con un seguimiento de 23,4 meses, un **10 %** de los pacientes tratados con la **dosis quincenal** de TALVEY® **discontinuó el tratamiento** debido a eventos adversos.[2]

*Para mayor información acerca del perfil de seguridad, consultar secciones 4.4 y 4.8 de la Ficha Técnica

EAs: eventos adversos; **GPRC5D:** miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; **ICANS:** síndrome de neurotoxicidad asociado a células inmunoefectoras; **SLC:** síndrome de liberación de citoquinas; **TCR:** receptor de células T.

Para mayor información acerca del perfil de seguridad de talquetamab® consultar sección 4.4 y 4.8 de la Ficha Técnica.

1. Chari A, *et al.* Clinical Management of Patients With Relapsed/Refractory Multiple Myeloma Treated With Talquetamab. Clin Lymphoma Myeloma Leuk 2024;24(10):665-693.e14; **2.** Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.

EAs asociados al GPRC5D*

Table 2: GPRC5D-associated AEs

Any-grade AE, n (%)	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Taste-related[a]			
Total	103 (72.0)	110 (71.4)	59 (75.6)
Leading to dose reduction	10 (7.0)	6 (3.9)	4 (5.1)
Leading to discontinuation	0	3 (1.9)	0
Skin-related[b]			
Total	81 (56.6)	113 (73.4)[e]	50 (64.1)
Leading to dose reduction	5 (3.5)	1 (0.6)	2 (2.6)
Leading to discontinuation	2 (1.4)	1 (0.6)	0
Nail-related[c]			
Total	79 (55.2)	82 (53.2)	46 (59.0)
Leading to dose reduction	1 (0.7)	1 (0.6)	1 (1.3)
Leading to discontinuation	0	0	0
Rash-related[d]			
Total	57 (39.9)[f]	46 (29.9)[g]	25 (32.1)[h]
Leading to dose reduction	1 (0.7)	1 (0.6)	0
Leading to discontinuation	0	0	0

[a]Including ageusia, dysgeusia, hypogeusia, and taste disorder. [b]Including skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Including nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [d]Including rash, maculopapular rash, erythematous rash, and erythema. [e]Including 1 (0.6%) grade 3/4 event. [f]Including 2 (1.4%) grade 3/4 events. [g]Including 8 (5.2%) grade 3/4 events. [h]Including 2 (2.6%) grade 3/4 events.

Tabla 2 de Rasche L, EHA 2024.[1]

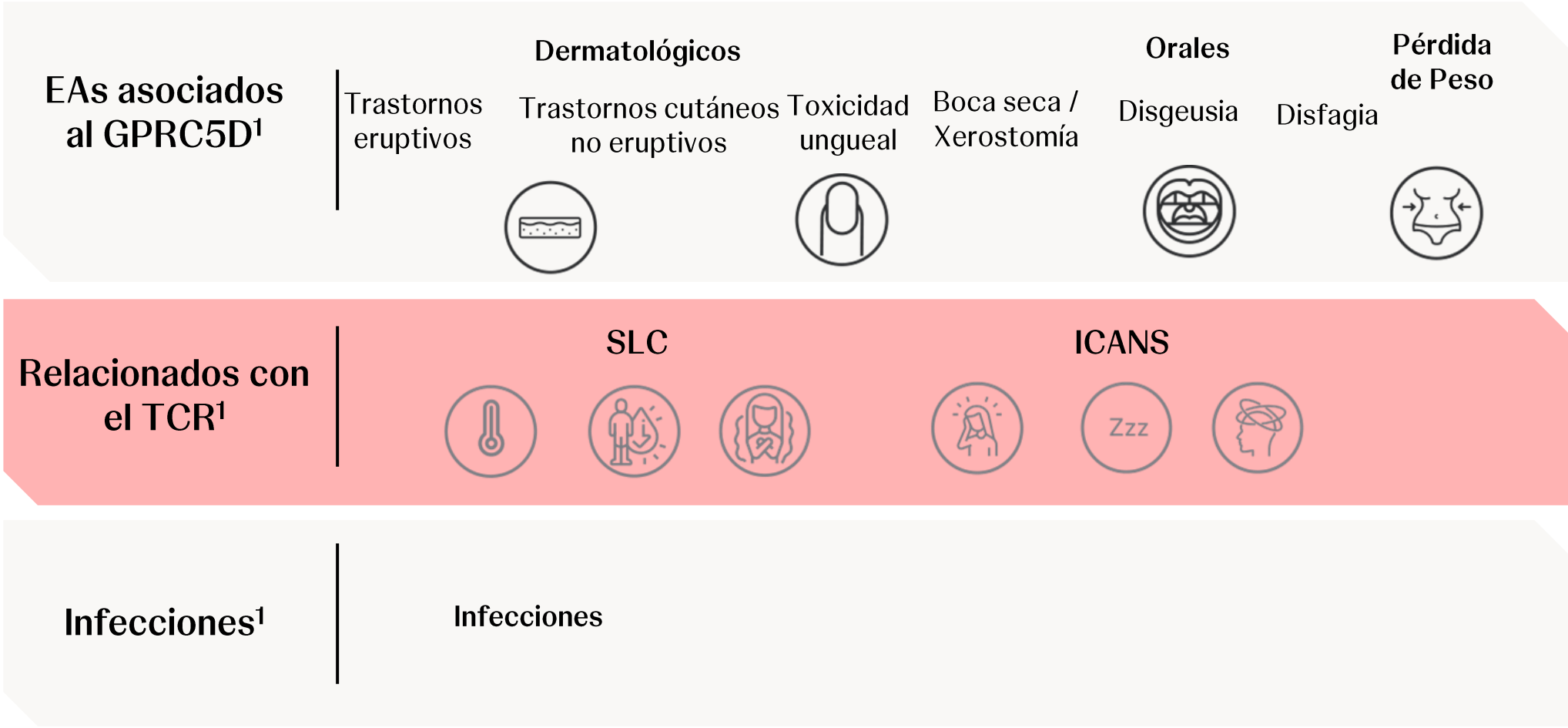
Los EAs asociados al GPRC5D dieron lugar a pocas reducciones de dosis e interrupciones.[1]

*Para mayor información acerca del perfil de seguridad de talquetamab consultar 4.4 y 4.8 de la Ficha Técnica.

EAs: eventos adversos; **GPRC5D:** miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; **TRL:** tratamiento redireccionador de linfocitos T

1. Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España.

Perfil de seguridad de talquetamab*



*Para mayor información acerca del perfil de seguridad de talquetamab®, consultar secciones 4.4 y 4.8 de la Ficha Técnica
EAs: eventos adversos; **GPRC5D**: miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; **ICANS:** síndrome de neurotoxicidad asociado a células inmunoefectoras; **TCR:** receptor de células T; **SLC:** síndrome de liberación de citoquinas.

1. Chari A, *et al.* Clinical Management of Patients With Relapsed/Refractory Multiple Myeloma Treated With Talquetamab. Clin Lymphoma Myeloma Leuk 2024;24(10):665-693.e14.

SLC e ICANS durante el tratamiento con TALVEY® en MonumenTAL-1

SLC

El 75 % (n = 115) de los pacientes tratados con la dosis quincenal de TALVEY® experimentó **SLC.**[1ϕ]

Mediana de tiempo hasta la aparición del evento:
27,8 horas[1*]

Mediana de duración de cada evento:
17,0 horas[1#]

SLC resueltos:
100 %[3†]

Las tasas de SLC fueron en general comparables con las observadas con otros anticuerpos biespecíficos redireccionadores de células T[3]

ICANS

El 10,0 % (n = 12) de los pacientes tratados con la dosis quincenal de TALVEY® experimentó **ICANS.**[1^]

Mediana de tiempo hasta la aparición del evento:
31,9 horas[1^]

Mediana de duración de cada evento:
7,8 horas[1Ω]

SLC resueltos:
80 %[3†]

La mayoría de los casos de ICANS se observaron simultáneamente con SLC: 66,7 %[3]

La mayoría de los eventos fueron de grado 1/2, ocurrieron durante el escalado de dosis o la primera dosis completa, y la mayoría se resolvieron[1]

Para mayor información acerca del perfil de seguridad de TALVEY® consultar sección 4.4 y 4.8 de la Ficha Técnica.
ϕDato extraído de la tabla suplementaria S5 de Chari A, *et al.* Lancet Hematol 2025 Suppl. Tabla completa disponible **AQUÍ.** Mediana de seguimiento: 19,4 meses[2]
*Relativo a la dosis más reciente.[1] Dato extraído de la tabla S5 de Chari A, *et al.* Lancet Hematol 2025 Suppl. Tabla completa disponible **AQUÍ.** Mediana de seguimiento: 19,4 meses[2]
#Incluye SLC con fechas de inicio y finalización disponibles.[1] Dato extraído de la tabla S5 de Chari A, *et al.* Lancet Hematol 2025 Suppl. Tabla completa disponible **AQUÍ.** Mediana de seguimiento: 19,4 meses[2]
^Relativo a la dosis más reciente.[1] Dato extraído de la tabla S7 de Chari A, *et al.* Lancet Hematol 2025 Suppl. Tabla completa disponible **AQUÍ.** Mediana de seguimiento: 19,4 meses.[2]
ΩDato extraído de la tabla S7 de Chari A, *et al.* Lancet Hematol 2025 Suppl. Tabla completa disponible **AQUÍ.** Mediana de seguimiento: 19,4 meses.[2]
†Los pacientes podían tener más de 1 evento. Los porcentajes se calculan con el número de eventos como denominador. Mediana de seguimiento: 12,7 meses.[3] Dato extraído de la Tabla 2 de Chari A, *et al.* Clinical Lymphoma, Myeloma and Leukemia 2024. Tabla completa disponible **AQUÍ.**
CS: cada semana; **C2S:** cada 2 semanas; **ICANS:** síndrome de neurotoxicidad asociado a células inmunoefectoras; **SLC:** síndrome de liberación de citoquinas.
1. Chari A, *et al.* Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet Haematol 2025; 12: e269–81; Supplement. **2.** Chari A, *et al.* Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet Haematol 2025; 12: e269–81 **3.** Chari A, *et al.* Clinical Management of Patients With Relapsed/Refractory Multiple Myeloma Treated With Talquetamab. Clin Lymphoma Myeloma Leuk 2024;24(10):665-693.e14.

SLC en los grupos CS, C2S y TRL previos[1]

	0·4 mg/kg SC QW* (N=143)	0·8 mg/kg SC Q2W* (N=154)	Patients with previous TCR* (N=78)
Patients with CRS, no. (%)	113 (79)	115 (75)	57 (73)
Grade 1	89 (62)	88 (57)	39 (50)
Grade 2	21 (15)	26 (17)	17 (22)
Grade 3	3 (2)	1 (1)	1 (1)
Symptoms of CRS (>10% any cohort), no. (%)			
Pyrexia	113 (79)	114 (74)	56 (72)
Hypotension	19 (13)	20 (13)	15 (19)
Chills	13 (9)	21 (14)	11 (14)
Hypoxia	11 (8)	9 (6)	8 (10)
Time to onset, hours, median (IQR)†	25·9 (17·8–31·9)	27·8 (21·0–34·6)	27·4 (21·2–34·5)
Duration, hours, median (IQR)‡	14·5 (4·0–32·0)	17·0 (5·6–33·8)	20·6 (6·6–31·5)
Patients with CRS up to 1st full dose, no. (%)			
1st step-up dose	48 (34)	41 (27)	23 (29)
2nd step-up dose	70 (49)	63 (41)	34 (44)
3rd step-up dose	NA	55 (36)	1 (1)
1st full dose	38 (27)	22 (14)	22 (28)
Patients with CRS cycle 2+, no. (%)	5 (3)	5 (3)	2 (3)
Patients receiving supportive measures, no. (%)§	106 (74)	109 (71)	54 (69)
Acetaminophen	80 (56)	81 (53)	42 (54)
Tocilizumab¶	50 (35)	57 (37)	37 (47)
Corticosteroids	5 (3)	6 (4)	11 (14)
Oxygen	8 (6)	10 (6)	7 (9)
Nasal cannula low flow (≤6 L/min)	8 (6)	9 (6)	6 (8)
Face mask	0	0	1 (1)
Venturi mask	1 (1)	0	0
Other	0	1 (1)	0
Vasopressor‖	2 (1)	1 (1)	1 (1)
Patients with >1 CRS event, no. (%)	46 (32)	51 (33)	23 (29)
Grade worsened at subsequent event	6 (4)	7 (5)	3 (4)

*Con dos o tres dosis escalonadas. Relativo a la dosis más reciente.
‡Incluye SLC con fechas de inicio y finalización disponibles.
§Los pacientes podían recibir más de una terapia de soporte.
¶Tocilizumab se aconsejó para grado 2 y superior, pero se permitió en grado 1; el protocolo no recomendó el uso profiláctico de tocilizumab.
‖Sólo se utilizó un vasopresor.
Tabla S5 de Chari A, *et al.* Lancet Haematol 2025 Suppl.
Para mayor información los fármacos anteriormente mencionados, consultar sus respectivas fichas técnicas disponibles en CIMA.
CIMA: Centro de Información de Medicamentos; **CS:** cada semana; **C2S:** cada dos semanas; **IQR:** rango intercuartílico; **SLC:** síndrome de liberación de citoquinas; TRL: terapia redireccionadora de linfocitos T.
1. Chari A, *et al.* Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet Haematol 2025; 12: e269–81 Supplement.

ICANS en los grupos CS, C2S y TRL previos[1]

	0·4 mg/kg SC QW*,† (N=122)	0·8 mg/kg SC Q2W*,† (N=118)	Patients with previous TCR*,† (N=61)
Patients with ICANS, no. (%)	13 (11)	12 (10)	2 (3)
Grade 1	4 (3)	4 (3)	2 (3)
Grade 2	7 (6)	4 (3)	0
Grade 3	2 (2)	3 (3)	0
Grade 4	0	1 (1)	0
ICANS symptoms (≥2% in any cohort), no. (%)			
Confusional state	6 (5)	5 (4)	0
Disorientation	3 (2)	2 (2)	0
Somnolence	3 (2)	2 (2)	0
Depressed level of consciousness	3 (2)	1 (1)	0
Time to onset, hours, median (IQR)‡	23·6 (15·0–53·7)	31·9 (14·7–52·0)	81·6 (47·6–115·5)
Duration, hours, median (IQR)	15·5 (2·7–23·9)	7·8 (3·5–24·9)	25·3 (2·0–48·5)
Number of ICANS events, no. (%)	21	15	2
Recovered or resolved	18 (86)	12 (80)	2 (100)
Not recovered or not resolved	2 (10)	2 (13)	0
Recovering or resolving	1 (5)	0	0
Unknown	0	1 (7)	0
Concurrent CRS, no. (%)§			
Yes	14 (67)	10 (67)	2 (100)
No	7 (33)	5 (33)	0

*Con dos o tres dosis escalonadas.
†ICANS sólo se midió en la fase 2.
‡Relativo a la dosis más reciente.
§El SLC concurrente considera eventos ICANS que ocurren durante o dentro de los 7 días siguientes a la fecha de finalización del SLC.
Tabla S7 de Chari A, *et al.* Lancet Haematol 2025 Suppl.
CS: cada semana; **C2S:** cada 2 semanas; **ICANS:** síndrome de neurotoxicidad asociado a células inmunoefectoras; **IQR:** rango intercuartílico; **SC:** subcutáneo; **SLC:** síndrome de liberación de citoquinas; **TRL:** terapia redireccionadora de linfocitos T.
1. Chari A, *et al.* Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet Haematol 2025; 12: e269–81 Supplement.

Mediana de tiempo hasta la aparición, duración y tasas de resolución de EAs de interés en MonumenTAL-1

EA	Talquetamab 0,4 mg/kg CS (n = 143)	Talquetamab 0,8 mg/kg C2S (n = 143)	TRL (n = 51)
Disgeusia			
Mediana de tiempo hasta la aparición (días)[a]	20,0	15,0	12,5
Mediana de duración (días)[b]	95,0	102,0	130,0
Resueltos n,(%)[c]	58(45,7)	36(30,8)	17(37,0)
Disfagia			
Mediana de tiempo hasta la aparición (días)[a]	20,5	28,5	27,5
Mediana de duración (días)[b]	109,0	73,0	174,0
Resueltos n,(%)[c]	25(69,4)	29(72,5)	4(33,3)
Boca seca			
Mediana de tiempo hasta la aparición (días)[a]	26,0	22,0	18,5
Mediana de duración (días)[b]	57,0	89,0	58,5
Resueltos n,(%)[c]	20(50,0)	20(31,3)	13(40,6)
Trastornos cutáneos (eruptivos)			
Mediana de tiempo hasta la aparición (días)[a]	20,0	22,0	27,0
Mediana de duración (días)[b]	28,0	26,0	15,0
Resueltos n,(%)[c]	66(88,0)	47(72,3)	22(71,0)
Trastornos cutáneos (no eruptivos)			
Mediana de tiempo hasta la aparición (días)[a]	29,5	27,0	26,0
Mediana de duración (días)[b]	36,0	39,0	32,0
Resueltos n,(%)[c]	90(60,0)	99(57,2)	45(63,4)
Uñas			
Mediana de tiempo hasta la aparición (días)[a]	68,5	67,5	64,0
Mediana de duración (días)[b]	88,5	74,0	122,0
Resueltos n,(%)[c]	32(32,7)	25(25,5)	13(31,7)
Infections			
Mediana de tiempo hasta la aparición (días)[a]	148,0	108,0	96,0
Mediana de duración (días)[b]	11,5	12,0	12,0
Resueltos n,(%)[c]	207(90,4)	166(87,4)	82(89,1)
SLC			
Mediana de tiempo hasta la aparición (días)[a]	25,9	28,0	26,3
Mediana de duración (días)[b]	14,5	18,0	20,4
Resueltos n,(%)[c]	188(99,5)	189(100,0)	57(100,0)
ICANS[d]			
Mediana de tiempo hasta la aparición (días)[a]	23,6	31,9	115,5
Mediana de duración (días)[b]	15,5	7,8	48,5
Resueltos n,(%)[c]	18(85,7)	12(80,0)	1(100,0)

[a]Mediana del tiempo transcurrido hasta el inicio de la enfermedad calculada en relación con la dosis más reciente recibida.
[b]La mediana de la duración se basa en los eventos con hora/fecha de inicio y fin disponibles.
[c]Los pacientes podían tener más de 1 evento. Los porcentajes se calculan con el número de eventos como denominador.
[d]Dado que el ICANS sólo se evaluó en la fase 2 del ensayo, el número de pacientes incluidos en el análisis fue de 122, 109 y 34 en las cohortes de 0,4 mg/kg CS, 0,8 mg/kg C2S y en la que había recibido un tratamiento redireccionador de linfocitos T, respectivamente

Tabla 2 de Chari A, *et al.* Clin Lymphoma Myeloma Leuk. 2024.

CS: cada semana; **C2S:** cada 2 semanas; **EAs:** eventos adversos; **ICANS:** síndrome de neurotoxicidad asociado a células inmunoefectoras; **SLC:** síndrome de liberación de citoquinas

Perfil de seguridad de talquetamab*

EAs asociados al GPRC5D[1]

Dermatológicos

Trastornos eruptivos

Trastornos cutáneos no eruptivos

Toxicidad ungueal

Boca seca / Xerostomía

Orales

Disgeusia

Disfagia

Pérdida de Peso

Relacionados con el TCR[1]

SLC

ICANS

Infecciones[1]

Infecciones

*Para mayor información acerca del perfil de seguridad, consultar secciones 4.4 y 4.8 de la Ficha Técnica

EAs: eventos adversos; **GPRC5D:** miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; **ICANS:** síndrome de neurotoxicidad asociado a células inmunoefectoras; **SLC:** síndrome de liberación de citoquinas; **TCR:** receptor de células T.

Para mayor información acerca del perfil de seguridad de talquetamab® consultar sección 4.4 y 4.8 de la Ficha Técnica.

1. Chari A, *et al.* Clinical Management of Patients With Relapsed/Refractory Multiple Myeloma Treated With Talquetamab. Clin Lymphoma Myeloma Leuk 2024;24(10):665-693.e14.

No se observó un incremento de las infecciones de grado 3/4 con un seguimiento mayor[1*]

GPRC5D se expresa predominantemente en células con fenotipo de células plasmáticas y tiene poca o ninguna expresión en células B normales, células T, células *natural killers*, monocitos, granulocitos y progenitores de médula ósea, a diferencia de CD38 y BCMA.[2]

- En la cohorte quincenal de talquetamab (N = 154), se produjeron infecciones de grado 3 o 4 en el **18 %**[3&]

- **Un 14% de la cohorte quincenal de talquetamab necesitó inmunoglobulina intravenosa[1^]**

Nuevas infecciones de grado ≥3 a lo largo del tiempo en la cohorte quincenal[1^]

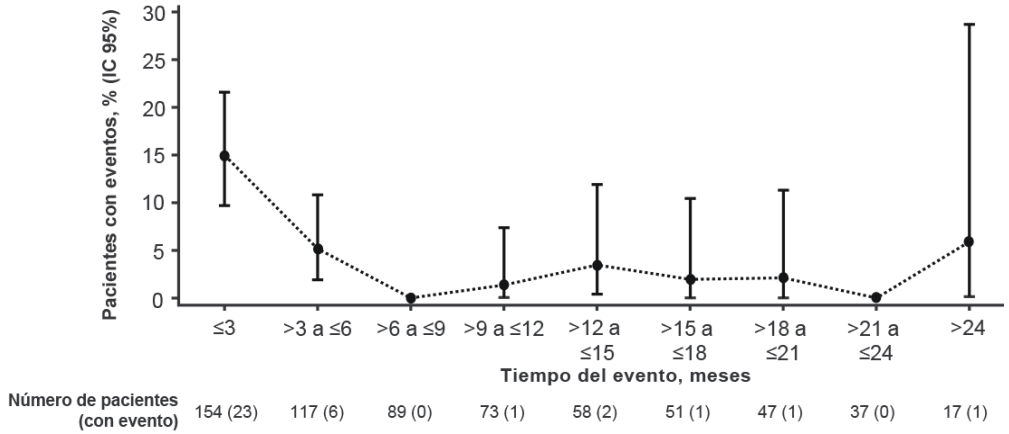
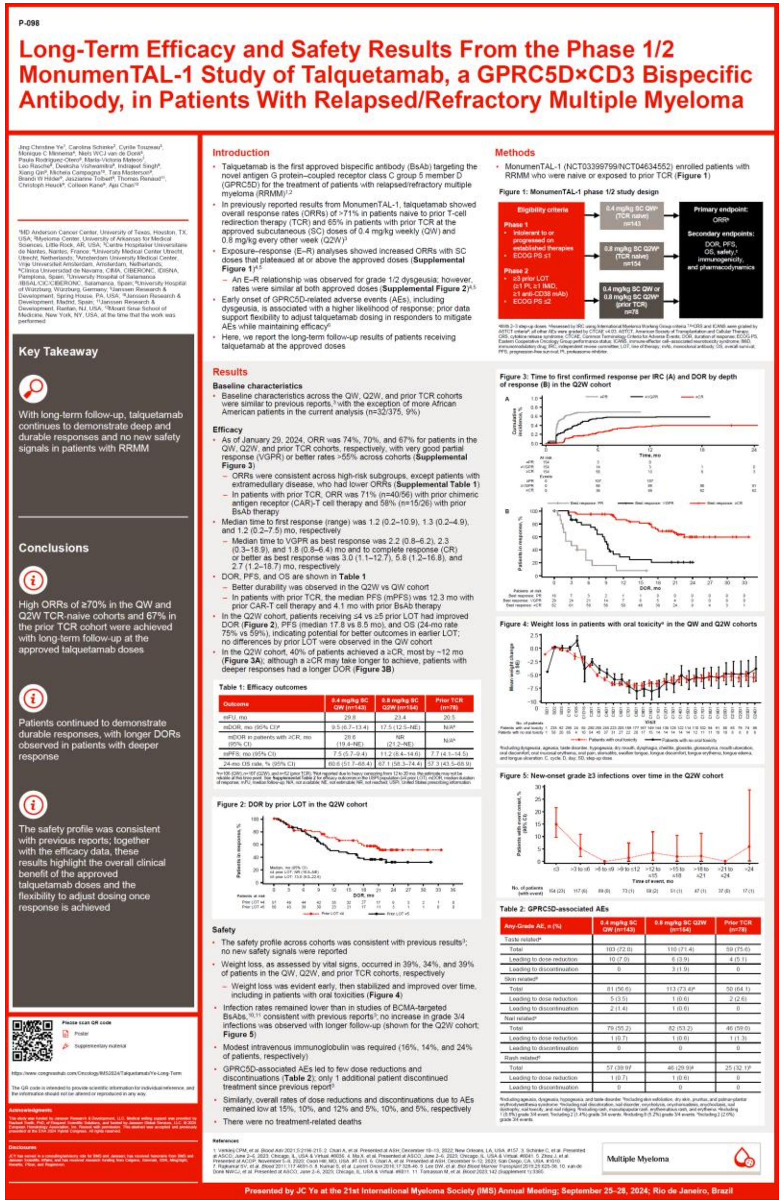


Figura 5 de Jing C, *et al.* IMS 2024

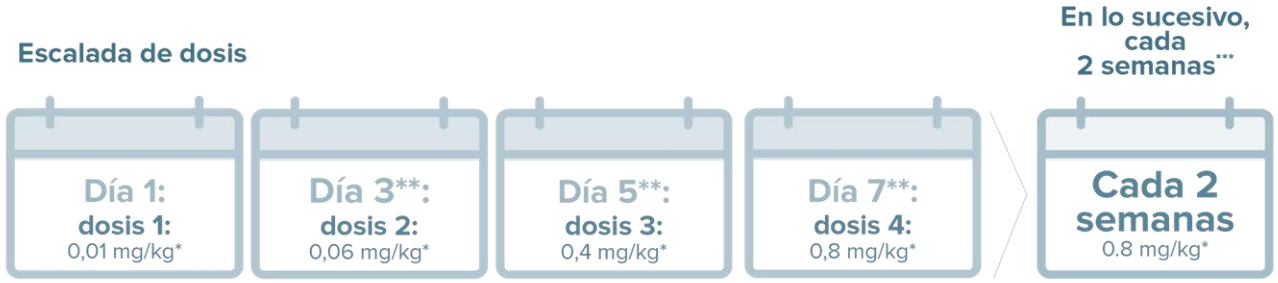
*Para mayor información acerca del perfil de seguridad de talquetamab® consultar sección 4.4 y 4.8 de la Ficha Técnica.
^La mediana de seguimiento para la dosis quincenal fue de 23,4 meses. Dato extraído de la Tabla 1 del póster P-098 de Jing C, *et al.* Póster presentado en IMS 2024. Póster completo disponible AQUÍ
[&]La mediana de seguimiento para la dosis quincenal fue de 19,4 meses.[3]
BCMA: antígeno de maduración de células B; **BsAb:** anticuerpo biespecífico; **CD38:** *cluster of differentiation* 38; **CS:** cada semana; **C2S:** cada 2 semanas; **GPRC5D:** miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; **IV:** intravenosa; **TRL:** tratamiento redireccionador de linfocitos T.
1. Jing C, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P-098 presentado en 21st International Myeloma Society (IMS) Annual Meeting; 25-28 septiembre 2024; Río de Janeiro, Brasil; **2.** Rodríguez Otero P, *et al.* GPRC5D as a novel target for the treatment of multiple myeloma: a narrative review. Blood Cancer Journal 2024;14:24; **3.** Chari A, *et al.* Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet Haematol 2025; 12: e269–81


P-098
Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma
Introduction
Methods
Figure 1: MonumenTAL-1 phase 1/2 study design
Key Takeaway
With long-term follow-up, talquetamab continues to demonstrate deep and durable responses and no new safety signals in patients with RRMM
Results
Baseline characteristics
Efficacy
Table 1: Efficacy outcomes
Figure 2: DOR by prior LOT in the Q2W cohort
Safety
Conclusions
High ORRs of ≥70% in the QW and Q2W TCR-naive cohorts and 67% in the prior TCR cohort were achieved with long-term follow-up at the approved talquetamab doses
Patients continued to demonstrate durable responses, with longer DORs observed in patients with deeper response
The safety profile was consistent with previous reports; together with the efficacy data, these results highlight the overall clinical benefit of the approved talquetamab doses and the flexibility to adjust dosing once response is achieved
Figure 4: Weight loss in patients with oral toxicity in the QW and Q2W cohorts
Figure 5: New-onset grade ≥3 infections over time in the Q2W cohort
Table 2: GPRC5D-associated AEs
Multiple Myeloma
Presented by JC Ye at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

TALVEY® es un anticuerpo biespecífico listo para usar por vía SC[1]

Fase de escalada de dosis para reducir el riesgo de SLC[1&]

Pauta posológica quincenal (cada 2 semanas)[1]



Basado en la ficha técnica de TALVEY®.[1]

*La dosis se basa en el peso corporal actual y se debe administrar por vía SC.

Los pacientes deben ser tratados con TALVEY® hasta la progresión de la enfermedad o toxicidad inaceptable.[1]

Se indicará a los pacientes que deben permanecer cerca de un centro sanitario y que **serán supervisados durante las 48 horas siguientes a la administración de todas las dosis** dentro de la fase de escalada de dosis de TALVEY® para detectar signos y síntomas de SLC y de ICANS.[1#]

TALVEY®, UN ANTICUERPO BIESPECÍFICO QUE OFRECE UNA PAUTA POSOLÓGICA QUINCENAL DESDE EL INICIO^[1]

[&]Para mayor información acerca de la pauta posológica autorizada de TALVEY®, consultar sección 4.2 de la ficha técnica. Para mayor información de los medicamentos previos al tratamiento, consultar sección 4.2 de la ficha técnica e información disponible AQUÍ.
**La dosis se puede administrar entre 2 y 4 días después de la dosis anterior y se puede administrar hasta 7 días después de la dosis anterior para permitir la resolución de las reacciones adversas.
***Dejar transcurrir un mínimo de 12 días entre las dosis quincenales (cada 2 semanas).
[#]A los pacientes con SLC o ICANS de grado 2 o superior se les debe indicar que permanezcan cerca de un centro sanitario y se deben monitorizar durante 48 horas para detectar signos y síntomas después de la siguiente dosis de TALVEY®.
^Tras el escalado de dosis.
ICANS: Síndrome de Neurotoxicidad Asociado a Células Inmunoefectoras; **SLC:** Síndrome de Liberación de Citoquinas.
1. Ficha Técnica TALVEY®.

Conclusiones:

PERFIL DE EFICACIA ELEVADO CON RESPUESTAS TEMPRANAS Y DURADERAS[1-3ъ]

- TRG: 69,5 % con la pauta quincenal[1]
- Tasa SG: 67,1 % pacientes vivos a los 24 meses[3#]

VERSATILIDAD: TALVEY® PUEDE USARSE CON/SIN TRL PREVIO[1]

- TRG de ≈70 % tanto en pacientes sin TRL previo como en aquellos expuestos previamente[1¶]

PERFIL DE SEGURIDAD CONSISTENTE CON LOS ANÁLISIS PREVIOS[1‡]

- Tasas de infecciones relativamente bajas[2ϕ]

FLEXIBILIDAD[ʃ] DE DOSIFICACIÓN:[5]

- Primer y único anticuerpo biespecífico dirigido contra GPRC5D4 aprobado para el MMRR[†] con posibilidad de dosificación quincenal desde el inicio[5]

ъCon una mediana de seguimiento de 23,4 meses, la mediana de tiempo hasta la primera respuesta (intervalo) fue de 1,3 (0,2-4,9) meses en la cohorte tratada con TALVEY® SC 0,8 mg/kg C2S.[1] Se observó una mayor durabilidad de la respuesta en la cohorte quincenal vs. la cohorte semanal. Con una mediana de seguimiento de 23,4 meses, en la cohorte quincenal se obtuvo una mediana de duración de la respuesta de 17,5 meses (12,5-NE) vs. 9,5 (6,7-13,4) con la cohorte semanal que tuvo una mediana de seguimiento de 29,8 meses.[1]
#Tasa de SG a los 24 meses (IC95 %): 67,1 % (58,3–74,4) TALVEY® 0,8 mg/kg cada 2 semanas.[3]
¶TRG: 74,1 % en pacientes con la pauta de dosificación de TALVEY® semanal, 69,5 % con la pauta quincenal y 66,7 % en pacientes que habían recibido una TRL previa.[1] Dato extraído de la Figura 2 de Rasche L, *et al.* Póster P915 EHA 2024. Póster completo disponible AQUÍ
‡Mediana de seguimiento de 23,4 meses en la cohorte quincenal vs. 29,8 meses en la cohorte semanal.[1] Para mayor información acerca del perfil de seguridad de TALVEY® consultar sección 4.4 y 4.8 de la Ficha Técnica.
ϕTras una mediana de seguimiento de 19,7 meses, ocurrieron infecciones de grado 3/4 en el 18 % de los pacientes tratados con la dosis de quincenal de TALVEY®.[2,4]
ʃPosibilidad de administración semanal o quincenal tras la fase de escalado de dosis. Para mayor información acerca de la posología y forma de administración consultar sección 4.2 de la Ficha Técnica.
†Autorizado por la Comisión Europea el 21 de agosto de 2023.[6]
CD38: *cluster of differentiation;* **CS:** cada semana; **C2S:** cada 2 semanas; **EAs:** eventos adversos; **GPRC5D:** miembro D del grupo 5 de la familia C del receptor acoplado a proteína G; **IC:** intervalo de confianza; **SC:** subcutáneo; **SG:** supervivencia global; **TRG:** tasa de respuesta global; **TRL:** tratamiento redireccionador de linfocitos T.

1. Rasche L, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P915 presentado en: European Hematology Association (EHA) 2024 Hybrid Congress;13-16 de junio 2024; Madrid, España; **2.** Touzeau C, *et al.* Pivotal Phase 2 MonumenTAL-1 Results of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, for Relapsed/Refractory Multiple Myeloma. Presentación oral presentada en: European Hematology Association (EHA) 2023 Hybrid Congress; 8-11 de junio 2023; Frankfurt, Alemania; **3.** Jing C, *et al.* Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5DxCD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma. Póster P-098 presentado en 21st International Myeloma Society (IMS) Annual Meeting; 25-28 septiembre 2024; Río de Janeiro, Brasil; 4. Chari A, *et al.* Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet Haematol 2025; 12: e269–81 **5.** Jakubowiak A, *et al.* Updated Results of Talquetamab, a GPRC5DxCD3 Bispecific Antobody, in Patients With Relapsed/Refractory Multiple Myeloma With Prior Exposure to T-Cell Redirecting Therapies: Results of the Phase 1/2 MonumenTAL-1 Study. Póster 3377 presentado en 65th American Society of Hematology (ASH) Annual Meeting; 9-12 diciembre 2023; San Diego, CA. EEUU; **6.** EMA. TALVEY®.European Commission Decision. Disponible en: https://www.ema.europa.eu/en/medicines/human/EPAR/talvey#authorisation-details Último acceso: abril 2025

Ficha técnica

Ficha Técnica disponible en el siguiente link:

https://static.janssen-emea.com/sites/default/files/Spain/SMPC/ES-PL-0233.pdf

Para más información, acceda a
la Ficha Técnica a través del QR

GRACIAS

Johnson&Johnson

CP-494019 Abril 2025. JANSSEN-CILAG S.A.