# MRD-Guided Frontline T-Cell Redirection therapy for Newly Diagnosed High-Risk Multiple Myeloma using Teclistamab-Daratumumab Intensification and Talquetamab-Daratumumab Early Rescue intervention: Primary endpoint of the Phase 2 GEM-TECTAL Trial

Paula Rodriguez-Otero[1], Enrique M Ocio[2], Albert Oriol[3], Eusebio Martin[4], Marta Sonia Gonzalez-Perez[5], María José Moreno[6], Mario Arnao[7], Laura Rosiñol[8], Roberto Maldonado[9], Joaquin Martínez-López[10], Verónica González-Calle[11], Joan Bladé[8], Juan Jose Lahuerta[10], Guntug Gungor, MD[12], Diptendu Santra, MD[13], Pavel Smirnov, MD[14], Margaret Doyle[15], Svetlana Gavrilov. MD, PhD[16], Maria Victoria Mateos[11], Jesús F San Miguel[1]

[1]Cancer Center Clinica Universidad de Navarra, Cima, IDISNA, Pamplona, Spain. [2]Hospital Universitario Marqués de Valdecilla (IDIVAL). Universidad de Cantabria. Santander. Spain. [3]Hospital Germans Trias i Pujol, ICO Badalona, Badalona, Spain. [4]University Hospital Virgen del Rocio, Sevilla, Spain. [5]Complejo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, Spain. [6]Hospital Universitari i Politecnic La Fe, Valencia, Spain. [7]Hospital Clinic, IDIBAPS, Barcelona, Spain. [8]Fundación PETHEMA, Grupo español de Mieloma. [9]Fundación PETHEMA, Grupo español de Mieloma. [10]Hospital Universitario 12 de Octubre, Madrid, Spain. [11]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain. [12]Johnson & Johnson, The Netherlands . [13]Parexel International, on behalf of Janssen-Cilag, Nottingham, United Kingdom. [14]Johnson & Johnson, Milan, Italy; [15]Johnson & Johnson, Dublin, Ireland; [16]Johnson & Johnson, Raritan, NJ, USA.



Presented by Paula Rodriguez-Otero at the IMS Annual meeting, Glasgow 23 – 26 September 2026

# Conflict of interest disclosure – Dr Paula Rodriguez-Otero

**Honoraria from lectures:** BMS, Johnson and Johnson, Sanofi, GSK, Abbvie, Menarini Steamline, and Pfizer.

**Participation in Ad Board meetings:** BMS, Johnson and Johnson, GSK, Sanofi, Kite Pharma, Abbvie, AstraZeneca, Oncopeptides, Menarini Steamline, H3Biomedicine, Pfizer, Regeneron, Roche.

**Consultant:** BMS, Johnson and Johnson, Abbvie, Roche, AstraZeneca, Regeneron and Pfizer

**Research funding:** Pfizer (institution)

**Travel Support**: Pfizer

# Background / Rationale

- Despite major advances in frontline therapy, patients with newly diagnosed **high-risk multiple myeloma** continue to experience inferior progression-free survival and a high risk of early relapse.
- **Persistent measurable residual disease (MRD) after initial therapy is one of the strongest predictors of poor outcomes, particularly in patients with additional high-risk features.**
- Teclistamab–daratumumab and talquetamab–daratumumab have demonstrated superior clinical outcomes in large randomized phase 3 trials in early-line relapsed multiple myeloma, providing a strong rationale for their evaluation in the frontline setting.

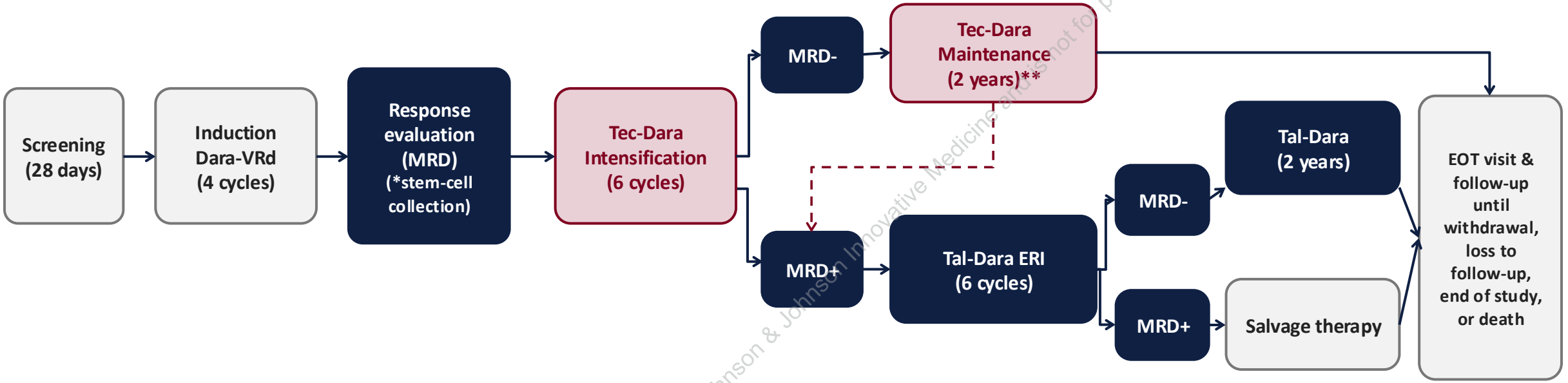
**Here, we present the primary endpoint results from the phase 2 GEM-TECTAL trial evaluating an MRD-guided frontline strategy with Tec-Dara intensification and Tal-Dara early rescue in patients with newly diagnosed high-risk multiple myeloma.**



Munshi NC, et al. Blood Adv. 2020 Dec 8;4(23):5988-5999; Raab MS et al, Nat Med. 2026 Jul;32(7):2440-2448; Costa LJ, N Engl J Med. 2026 Feb 19;394(8):739-752. Mina R et al, N Engl J Med. 2026 Aug 13;395(7):671-683

# Study Design and endpoints

Data cutoff: May 7, 2026






**Key inclusion criteria**

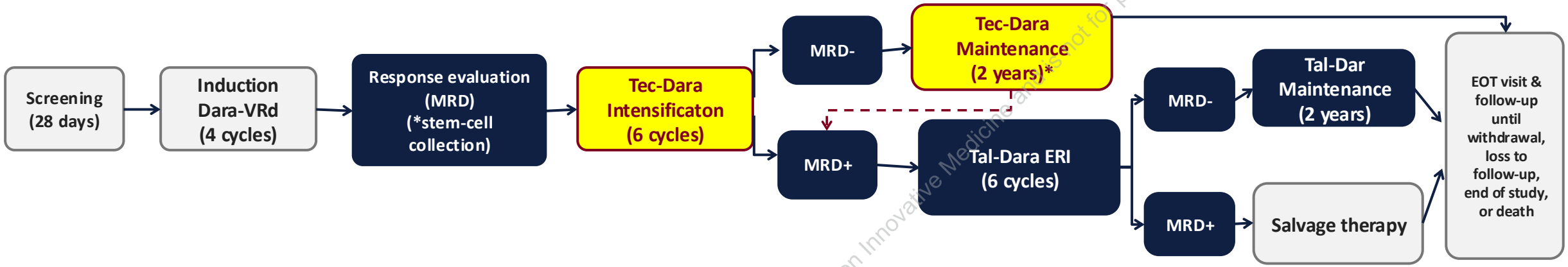
- NDMM, regardless of transplant elegibility.
- ECOG-PS modified frailty score 0-1
- ECOG 0-2
- High-risk was defined*:
  - Presence of HR-CA: del(1p), del(17p), t(4;14), t(14;16) or amp(1q)
  - R-ISS 3
  - Presence of EMD/PMD

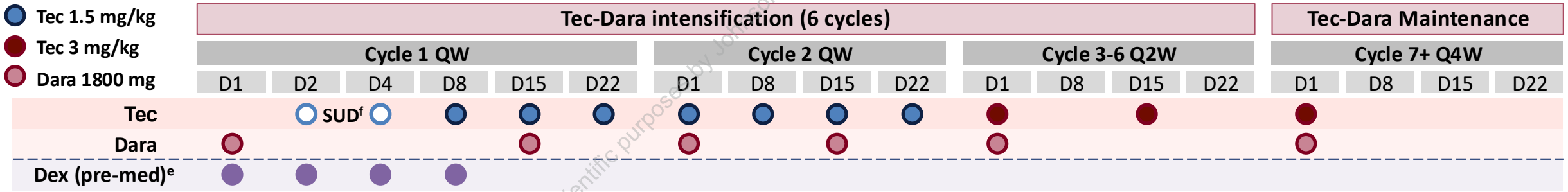
**Primary endpoint:**
MRD negative CR rate after 6 cycles of Tec-Dara intensification [NGF, $10^{-6}$)

**Secondary objectives include**: MRD- CR after D-VRD induction, MRD conversion after Tec-D intensification and Tal-D early rescue intervention, MRD assessed with alternative techniques, resurgence of MRD, time-to-event data (PFS, OS, DoR) and safety

* Approximately 50% of patients were planned to have ultra-HR disease defined as: R-ISS III, ≥2 HR-CA, or HR-CA+EMD.
**Patients who convert to MRD+ or relapse from CR at any time during Tec-Dara maintenance
High-risk cytogenetic abnormalities were assessed by FISH. High-risk cytogenetic abnormalities were defined using a cutoff of 20% for deletions and 10% for translocations.
NDMM: newly diagnosed multiple myeloma; HR-CA: high risk cytogenetic abnormalities. EMD: extramedullary disease, PMD: paramedullary disease. ERI: Early rescue intervention

# Study Treatments: Tec-Dara Intensification and maintenance



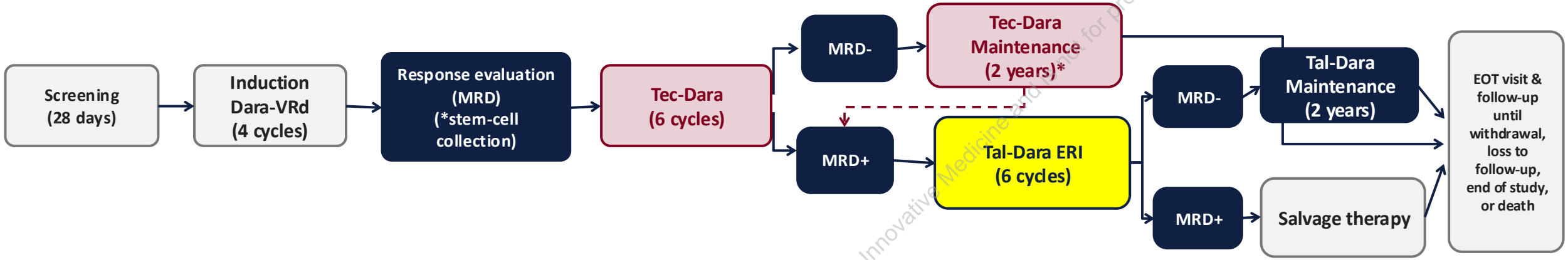



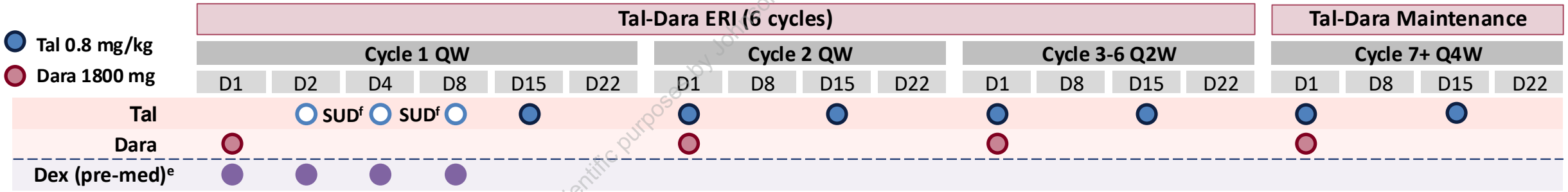

[f]SUD 1: 0.06 mg/kg C1D2; SUD 2: 0.3 mg/kg C1D4

**Tec-Dara regimen aligns with approved RRMM Tec-Dara; steroid-free after 2 cycles with monthly dosing after 6 cycles**

Dara-VRD: Daratumumab, bortezomib, lenalidomide, dexamethasone. MRD: minimal residual disease. Tec-Dara: teclistamab, daratumumab. Tal-Dara: talquetamab, daratumumab. EOT: end-of-treatment. ERI: Early rescue intervention. SUD: Step-up dose. QW: weekly. Q2W: Every other week. D: day.

# Study Treatments: Tal-Dara early rescue intervention and maintenance




[f]SUD 1: 0.01 mg/kg C1D2; SUD 2: 0.06 mg/kg C1D4; SUD 3: 0.4 mg/kg C1D8

**Tal-Dara regimen aligns with RRMM dosing and schedule steroid-free after 2 cycles with Q2W dosing**

Dara-VRD: Daratumumab, bortezomib, lenalidomide, dexamethasone. MRD: minimal residual disease. Tec-Dara: teclistamab, daratumumab. Tal-Dara: talquetamab, daratumumab. EOT: end-of-treatment. ERI: Early rescue intervention. SUD: Step-up dose. QW: weekly. Q2W: Every other week. D: day.

# Baseline Characteristics

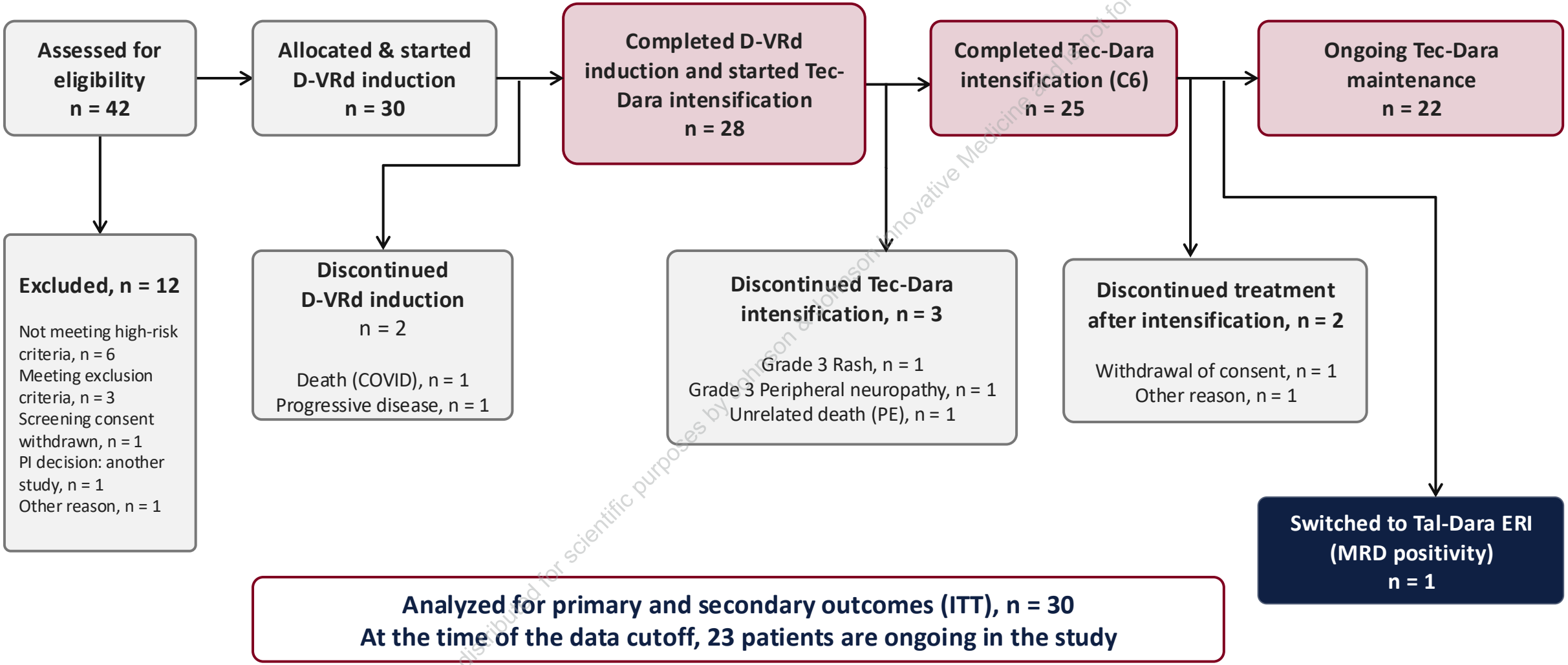
| Characteristic | Overall population (N = 30) |
|---|---|
| **Age**, median (range), years | **70 (48–77)** |
| Age ≥ 70 years, n (%) | **17 (56.7)** |
| Male **sex**, n (%) | **15 (50.0)** |
| **ECOG, n (%)** | |
| 0-1 | **28 (96.6)** |
| 2 | **1 (3.4)** |
| **Charlson CCI, n (%)** | |
| ≤ 1 | **18 (60.0)** |
| > 1 | **3 (10.0)** |
| Not available | **9 (30.0)** |
| **ISS, n (%)** | |
| 1 | **10 (33.3)** |
| 2 | **11 (36.7)** |
| 3 | **8 (26.7)** |
| R-ISS, n (%) | |
| 1 | **7 (23.3)** |
| 2 | **18 (60.0)** |
| 3 | **5 (16.7)** |

| Characteristic | Overall population (N = 30) |
|---|---|
| **EMD/PMD, n (%)** | 19 (63.3) |
| Bone plasmacytoma, n (%) | 18 (60.0) |
| Extramedullary, n (%) | 1 (3.3) |
| **High-risk cytogenetic abnormalities, n (%)** | **21 (70.0)** |
| del(17p), n (%) | 6 (22.2) |
| del(1p) | 9 (36.0) |
| amp(1q) | 16 (64.0) |
| t(4;14) | 7 (25.0) |
| t(14;16) | 6 (22.2) |
| **≥2 high-risk cytogenetic abnormalities, n (%)** | **10 (33.3)** |
| **Ultra-high-risk disease, n (%)** | **21 (70.0)** |
| **IMS/IMWG Consensus genomic staging*, n (%)** | **19 (63.3% )** |

High-risk cytogenetic abnormalities included del(17p), t(4;14), t(14;16), del(1p) and/or amp(1q). High-risk cytogenetic abnormalities were defined using a cutoff of 20% for deletions and 10% for translocations. R-ISS: revised international staging system. Ultra-high-risk disease was defined as R-ISS III, ≥2 HRCA, or HRCA plus EMD/PMD.
Abbreviations: EMD, extramedullary disease; PMD, paramedullary disease.
* TP53 mutations, biallelic 1p deletion was not performed in this study.

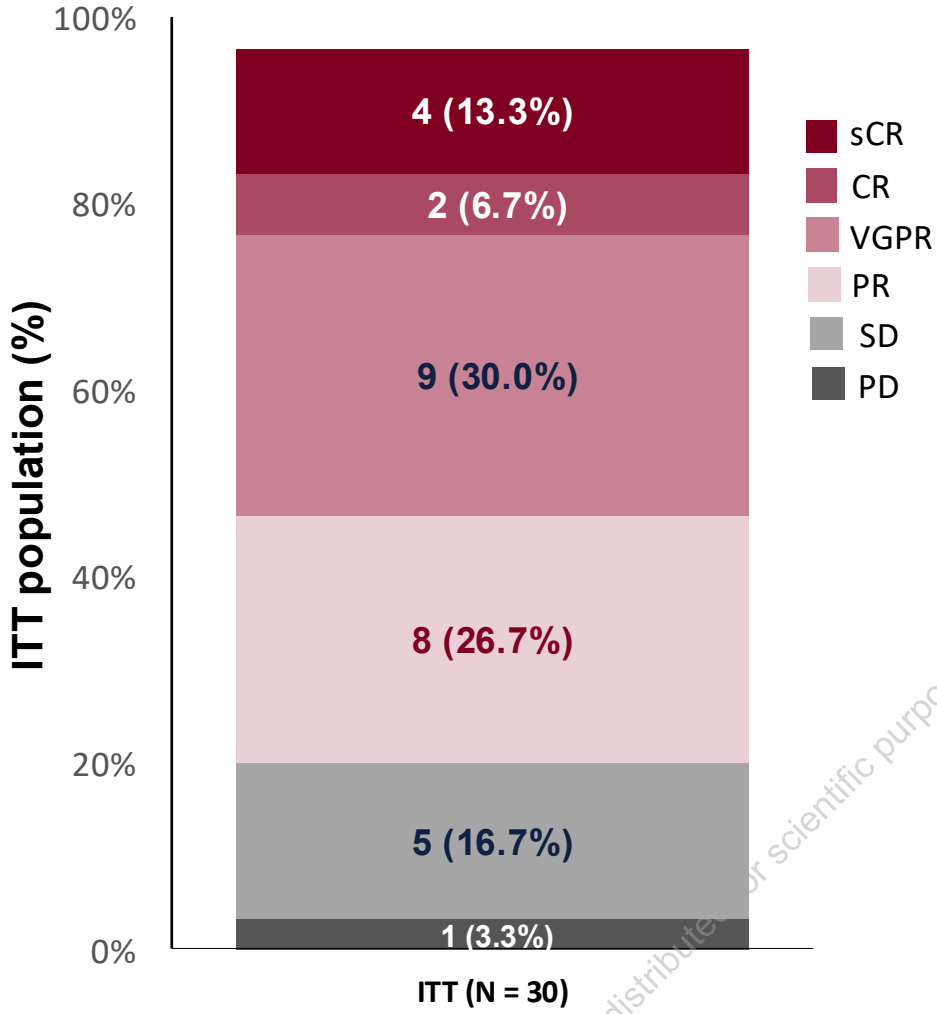
# Patient Disposition

Data cutoff: May 7, 2026
Median follow-up : 9.8 months.




D-VRd: daratumumab, bortezomib, lenalidomide and dexamethasone; ITT: intention-to-treat; MRD: measurable residual disease; PI: principal investigator; Tal-Dara: talquetamab-daratumumab; Tec-Dara: teclistamab-daratumumab.PE: pulmonary edema.

# Response After D-VRd induction (ITT)



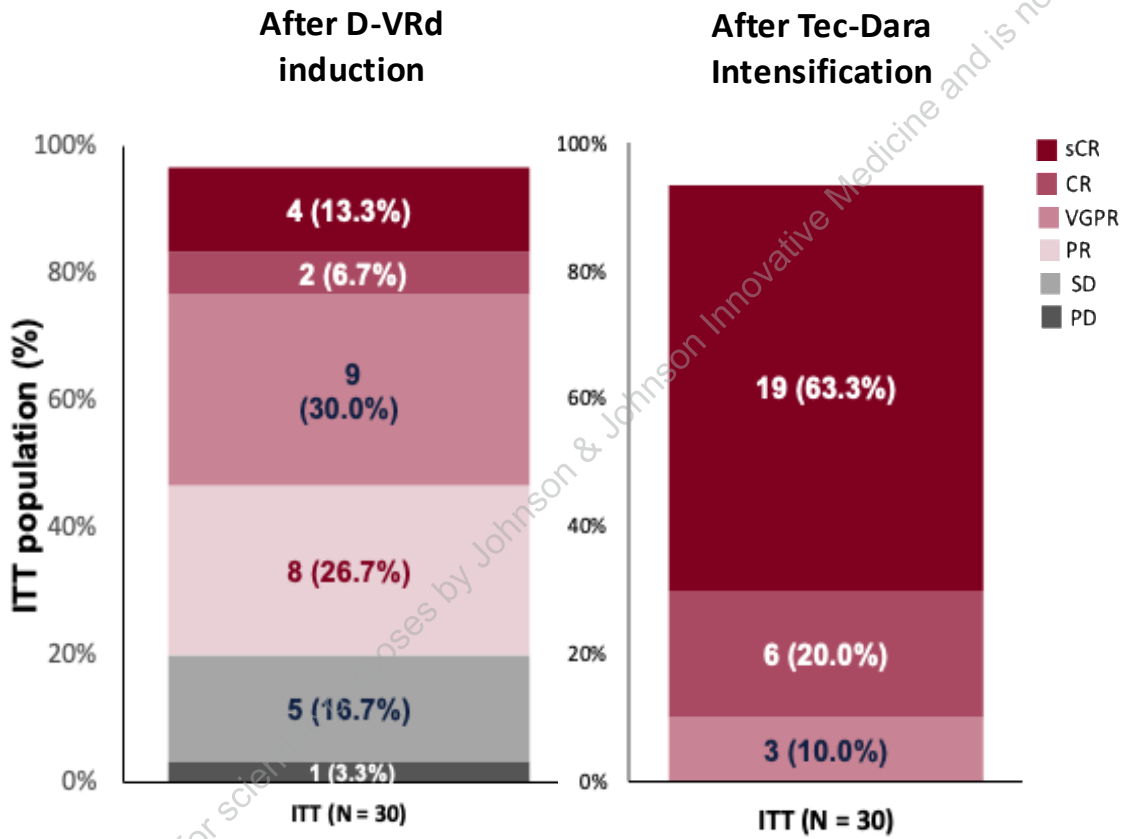

**ORR 23/30 (76.7%) · ≥CR 6/30 (20%)**
**≥VGR 15/30 (50%)**

| MRD at cycle 4 of induction | Overall population (N = 30) |
|---|---|
| MRD negative CR ($10^{-6}$), n (%) | 4 (13.3) |
| MRD negative ($10^{-6}$) in patients with at least VGPR, n (%) | 7 (23.3) |

MRD was assessed by Next-generation Flow cytometry using EuroFlow standards. Sensitivity level was $10^{-6}$. Patients with unavailable or not evaluable samples were considered MRD positive. All percentages are given based on ITT population (n=30

One patient was not evaluable for response due to death from COVID-19 pneumonia during induction. Percentages are based on the ITT population (N = 30).
Response evaluation was performed following IMWG 2016 response criteria. sCR: stringent complete response. CR: complete response. VGPR: very Good partial response. PR: partial response. SD: stable disease. PD: progressive disease.

# Response after Tec-Dara intensification (ITT)




**Tec-D intensification deepened responses in all treated patients, with 100% achieving ≥VGPR and 83.3% achieving CR/sCR after 6 cycles.**

Dashed branches indicate patients who did not start intensification. Flow width is proportional to patient count.
Percentages are based on the ITT population (N = 30). Response evaluation was performed following IMWG 2016 response criterio.
sCR: stringent complete response. CR: complete response. VGPR: very Good partial response. PR: partial response. SD: stable disease. PD: progressive disease.

# MRD-Negative CR After Tec-D Intensification ($10^{-6}$, NGF)

***PRIMARY ENDPOINT***

| | n/N (%) |
|---|---|
| Complete response | **25 / 30 (83.3)** |
| **MRD negative CR** | **22 / 30 (73.3)** |
| MRD neg in patients with ≥VGPR | **24 / 30 (80)** |
| MRD negative among CR patients | **22 / 25 (88)** |

***MRD negative CR after induction was 13.3% (4/30)***

**The primary endpoint analysis showed an MRD-negative CR rate of 73.3% in the ITT population (22/30); 22 of the 25 patients achieving CR were MRD-negative.**



MRD-negative CR was assessed after 6 cycles of Tec-Dara intensification. Percentages are based on the indicated denominator.
MRD was assessed by Next-generation Flow cytometry using EuroFlow standards. Sensitivity level was $10^{-6}$. Patients with unavailable or not evaluable samples were considered MRD positive. CR: complete response. MRD-neg: MRD negativity at $10^{-6}$. VGPR: Very good partial response.

# Safety During Tec-D Intensification

*Safety population, N = 28*

**During induction, the safety profile was consistent with D-VRd**

| AE Term | Any grade, n (%) | Grade 1-2, n (%) | Grade 3-4, n(%) |
|---|---|---|---|
| Any TEAE, n (%) | **27 (96.4)** | | |
| **Infections, n (%)** | **22 (78.6)** | **18 (64.3)** | **4 (14.3)** |
| CRS, n (%) | **7 (25)** | **7 (25) (grade 1)** | **-** |
| ICANS, n (%) | **1 (3.6)** | **1 (3.6) (grade 2)** | **-** |
| Neutropenia, n (%) | **13 (46.4)** | **2 (7.1)** | **11 (39.3)** |
| Diarrhea, n (%) | **7 (25)** | **7 (25)** | **-** |

- **7 patients had 9 CRS events, all grade 1.**
  - Median duration: 1 day
  - 1 patient received Tocilizumab.
- **TEAE leading to teclistamab discontinuation: 2 patients (7.1%)**
  - 1 grade 3 rash related to teclistamab.
  - 1 grade 3 sensory/motor neuropathy related to Teclistamab.

**Tec-D intensification showed a manageable safety profile, with a low rate of treatment discontinuation and no treatment-related deaths.**

Percentages are based on the 28 patients who received Tec-D intensification. NR, not reported; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event.

# Infections during Tec-D Intensification

*Safety population, N = 28*

| Infections | Any grade, n (%) | Grade 1-2, n (%) | Grade 3-4, n(%) |
|---|---|---|---|
| **Infections, n (%)** | **22/28 (78.6)** | **18 (64.3)** | **4 (14.3)** |
| Upper respiratory infection, n (%) | **15 (53.6)** | **13 (46.4)** | **2 (7.1)** |
| COVID-19, n (%) | **2 (7.14)** | **2 (7.14)** | **0** |
| Lower respiratory infection* | **3 (10.7)** | **0 (0)** | **3 (10.7)** |
| CMV infection | **1 (3.6)** | **0** | **1 (3.6)** |
| CMV reactivation | **1 (3.6)** | **1 (3.6)** | **0** |
| Other | **4 (14.3)** | **4 (14.3)** | **0** |

- 2 deaths during D-VRd induction: pulmonary edema (n=1), COVID-19 pneumonia (n=1).
- **No deaths related to infections during Tec-Dara Intensification**
- **21/28 (75%) patients received Immunoglobulin replacement therapy (IGRT).**
- No discontinuations of Teclistamab due to infections

**Infections were frequent but predominantly low grade, with no grade 4/5 events, or treatment discontinuations, consistent with the established safety profile of Tec-Dara.**

*Includes Grade 3 rinovirus infection, Lower respiratory viral infection. Other infections include: Conjuntivitis, Rhinitis, urinary tract infection and varivella (all events were grade 2) Percentages are based on the 28 patients who received Tec-D intensification. NR, not reported; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event.

# Conclusions

- **GEM-TECTAL enrolled an exclusively high-risk population**: 70% of patients had ultra-high-risk disease and 33% harbored two or more adverse cytogenetic abnormalities.
- Despite this unfavorable risk profile, **Tec-D intensification substantially deepened responses**, with all 28 treated patients achieving at least VGPR.
- The **primary endpoint analysis showed an MRD-negative CR rate of 73.3% in the ITT population** (22/30); 22 of the 25 patients achieving CR were MRD-negative.
- Tec-D intensification demonstrated a **manageable safety profile, with a low rate of treatment discontinuation and no treatment-related deaths.**

***Early incorporation of Tec-D intensification within an MRD-guided strategy induced deep responses and high MRD-negative CR rates, supporting further evaluation of a fully immune-based, bispecific antibody–centered, transplant-free approach for newly diagnosed, difficult-to-treat high-risk multiple myeloma.***

# Aknowlegedments

We sincerely thank:

- The patients and their families for their trust, commitment, and participation.
- The investigators and study teams at all participating PETHEMA/GEM centers.
- The study coordinators, research nurses, pharmacists, data managers, and operational teams for their essential contributions.
- Johnson & Johnson for its scientific collaboration and support of the GEM-TECTAL study.

GEM-TECTAL is a collaborative study conducted by PETHEMA/GEM in collaboration and with the financial support from Janssen Pharmaceutica NV, a member of the Johnson & Johnson group of companies