# GEM-TECTAL:
# biespecíficos en primera línea en pacientes con HR-NDMM

# GEM-TECTAL: Teclistamab y talquetamab + Dara en HR-NDMM

- Población: pacientes con MM de alto riesgo en primera línea. Incluye pacientes candidatos y no candidatos.

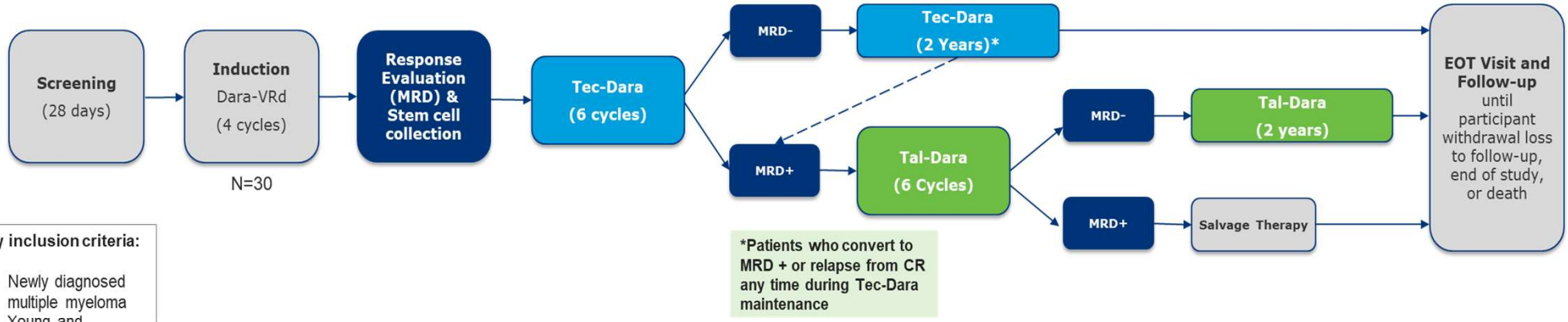
- Definición de alto riesgo:

  - High-risk FISH: del(17p), del(1p), t(4;14), t(14;16) and 1q amplifications.
  - R-ISS 3
  - Presence of extramedullary disease, defined as presence of paramedullary lesions or extramedullary plasmacytoma.

  Note: In order to have a representative population with high-risk features, 50% of patients included will have ultra-high risk disease defined as:
  - R-ISS 3
  - Double hit (at least two high-risk cytogenetic abnormalities)
  - One high-risk cytogenetic abnormality + extramedullary disease.

- N=30 pacientes. Prueba de concepto para un futuro fase III.

# GEM-TECTAL: Diseño del estudio




**Key inclusion criteria:**

- Newly diagnosed multiple myeloma
- Young and transplant-eligible or elderly-fit participants
- ECOG 0-1
- High-risk:
  1. FISH del(1p), del(17p), t(4;14), t(14;16), 1q amp
  2. R-ISS 3
  3. Presence of EMD

***Patients who convert to MRD + or relapse from CR any time during Tec-Dara maintenance**

**Disease Assessments**

- CRR, MRD-negativity rate, MRD conversion, sustained MRD negativity
- MRD- participants will be defined as those with negative MRD by NGF with a sensitivity level of $10^{-6}$ and complete metabolic response by PET-CT (Deauville score ≤ 3)

**Time-to-event Data**

- PFS, EFS, TNT, DoR and OS

**Safety and Tolerability until Death, Withdrawal of consent, or End of Study**

- Incidence of adverse events (AEs)
- Changes in laboratory parameters and vital signs

**Exploratory analysis**

# GEM-TECTAL: Objetivos

| Objective | Endpoint |
|---|---|
| **Primary** | |
| **To evaluate efficacy in terms of MRD negative CR rate after Tec-Dara intensification** | MRD measured by NGF (sensitivity level of $10^{-6}$) and FDG PET-CT scan using the Deauville score and CR evaluated per IMWG 2016 response criteria after 6 cycles of Tec-Dara therapy |
| **Secondary** | |
| **To evaluate MRD negative CR rate after D-VRD induction** | MRD measured by NGF (sensitivity level of $10^{-6}$) and FDG PET-CT scan using the Deauville score and CR evaluated per IMWG 2016 response criteria after 4 cycles of D-VRD induction |
| **To evaluate MRD negativity after Tec-Dara intensification using alternative methods** | MRD negative rates measured by NGS, and QIP-MS-FLC after 6 cycles of Tec-Dara therapy |
| **To evaluate MRD conversion after early rescue intervention with Tal-Dara** | Percentage of patients converting from positive MRD to negative MRD evaluated by NGF, NGS, QIP-MS-FLC and FDG-PET-CT scan. |
| **To evaluate MRD conversion after Tec-Dara intensification** | Percentage of patients converting from positive MRD after D-VRD induction to negative MRD evaluated by NGF, NGS, QIP-MS-FLC and FDG-PET-CT scan after Tec-Dara intensification. |
| **To evaluate sustained MRD negativity during maintenance treatment in both Tec-Dara and Tal-Dara treatment arms** | Proportion of patients with persistent MRD negative disease at month 6, 12, 18 and 24 of maintenance treatment in both Tec-Dara and Tal-Dara treatment, by NGF, NGS, QIP-MS-FLC and FDG-PET-CT scan and annually thereafter |
| **To assess reappearance of MRD positivity or relapse from CR in patients during the Tec-Dara treatment** | Proportion of patients relapsing from MRD negative CR to MRD positive or who relapse from CR (not fulfilling criteria for disease progression) during any phase of Tec-Dara treatment (intensification or maintenance) |
| **To assess Time to event data** | PFS, EFS, TNT, DoR and OS |
| **To assess the safety of the treatment described in the protocol** | Incidence of treatment-emergent adverse events |
| **Exploratory analysis** | |
| **Immune profiling and genetic characterization** | Analysis of immune subpopulation and genetic markers. |

# GEM-TECTAL: Situación

- **Todos los centros iniciados (10 centros)**
  - Hospital Clinic Barcelona
  - ICO Badalona
  - Complejo Hospitalario Universitario de Santiago
  - Hospital 12 de Octubre
  - Hospital Virgen de la Arrixaca
  - Clinica Universidad de Navarra
  - Hospital Universitario de Salamanca
  - H. U. Marqués de Valdecilla
  - H. U. Virgen del Rocío
  - H. U. La Fe

- 3 pacientes incluidos (2 en tratamiento, 1 pendiente de iniciar)
- 6 fallos de screening:
  - 4 no alto riesgo
  - 3 HR pero que finalmente no fueron incluidos

- **Circuito centralizado de FISH en los tres centros de PETHEMA para poder acelerar la inclusión.**