# Belantamab mafodotin, lenalidomide and dexamethasone in transplant-ineligible patients with newly diagnosed multiple myeloma: part 1 results of a phase I/II study

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## Supplementary methods

*Time to endpoints*

All time to event endpoints were calculated from the time of randomization. Progression-free survival (PFS) was calculated until the date of disease progression or death from any cause, whichever occurred first. Time to progression (TTP) was calculated until the date of myeloma progression, whereas overall survival (OS) was calculated until the date of death due to any cause. Patients who did not experience any event at the time of the analysis were censored at the date of their last available disease assessment denoting absence of progression (for PFS/TTP) or last follow-up (for OS).

*Statistical analysis*

No formal statistical hypothesis was to be tested for this study; therefore, no sample size calculation was performed. The analysis is based on descriptive statistics. Categorical variables are expressed with absolute and relative frequencies, while the continuous ones were described with median (range) or mean with standard deviation. For the PFS and TTP estimates, survival analysis techniques were employed using the Kaplan-Meier (KM) method. As per protocol, the analysis is performed in the dose limiting toxicity (DLT) population. This is defined as all patients who had received ≥1 belamaf dose and who were followed up for ≥4 weeks or patients who could not be followed up for ≥4 weeks due to toxicity reasons (i.e., death/treatment discontinuation). As per study design, for patients who received ≥1 belamaf dose but were not part of the DLT population, a new patient was enrolled in replacement; safety data of the replaced patients were to be analyzed separately, however, no such patients exist. Statistical analysis was conducted using SAS (version 9.4). The data cut-off date for this analysis was June 5$^{th}$, 2023. All authors had access to primary clinical trial data.

*Data Sharing Statement*

Individual participant data will not be shared until the final analysis of the phase 2 portion of the BelaRd study. The study protocol is uploaded separately.

**Table S1 Key patient eligibility criteria**

| **Inclusion criteria** |
|---|
| Age ≥18 years old |
| Multiple myeloma diagnosis according to the International Myeloma Working Group (IMWG) criteria (CRAB-SLiM criteria)[26] |
| Measurable disease, defined as at least one of the following:<br>• Urine M-protein excretion ≥200 mg/24h<br>• Serum M-protein concentration ≥0.5 g/dL<br>• Involved serum free light chain (sFLC) level ≥10 mg/dL, with an abnormal sFLC ratio (<0.26 or >1.65) |
| Eastern Cooperative Oncology Group performance status of 0 to 2 |
| Adequate organ function, defined as follows:<br>• Absolute neutrophil count ≥1.5 × $10^9$/L without granulocyte colony-stimulating factor support<br>• Hemoglobin ≥ 8.0 g/dL<br>• Platelet count ≥75 x $10^9$/L or ≥50 x $10^9$/L if bone marrow is >50% involved by plasma cells, no transfusions allowed to reach these numbers<br>• Total bilirubin ≤1.5 × upper limit of normal (ULN)<br>• Alanine aminotransferase ≤2.5 × ULN<br>• Estimated glomerular filtration rate ≥30 mL/min/1.73 $m^2$, calculated using the Modified Diet in Renal Disease formula |
| **Exclusion criteria** |
| • Patients who were assigned a IMWG frailty score of 0 were deemed ineligible for this study due to potential eligibility for proceeding to high dose therapy and autologous stem cell transplantation |
| • Presence of another primary malignancy |
| • Uncontrolled active infection, including active hepatitis or HIV infection |
| • Severe heart failure |
| **Additional information** |
| All patients were assessed at baseline for frailty according to IMWG frailty index based on age, Activities of Daily Living (ADL) score, Instrumental Activities of Daily Living score and comorbidities (Charlson Comorbidity Index)[27] |
| Contraception is used throughout the study |

**Table S2 Adverse events included in the evaluation of dose-limiting toxicities**

| **Hematological toxicities** |
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| • ≥ Grade 3 febrile neutropenia lasting more than 48h despite adequate treatment<br>• Grade 4 thrombocytopenia with platelet count ≤25 $\times 10^9$/L accompanied by clinically significant bleeding |
| **Non-hematological toxicities** |
| • Any ≥Grade 3 toxicity which is more severe than expected for an individual agent, or which does not resolve with appropriate supportive treatment within 48h<br>• Any ≥ Grade 3 non-hematologic laboratory value if the abnormality leads to hospitalization<br>• Grade 4 corneal events<br>• Any organ-specific toxicities, including liver toxicity meeting prespecified liver stopping criteria |