BELANTAMAB MAFODOTIN IN COMBINATION WITH VRD FOR THE TREATMENT OF NEWLY DIAGNOSED TRANSPLANT ELIGIBLE MULTIPLE MYELOMA PATIENTS: RESULTS FROM THE PHASE II, OPEN LABEL, MULTICENTER, GEM-BELA-VRD TRIAL

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INTRODUCTION

The use of bortezomib, lenalidomide and dexamethasone (VRd) as induction triplet has resulted in deep and durable responses in newly diagnosed transplant-eligible multiple myeloma (NDTE MM) patients, as shown by the Spanish group in the GEM2012 trial. (1)

The addition of anti-CD38 monoclonal antibodies to VRd deepen responses without impairing safety. (2)

The BCMA antibody-drug conjugated belantamab mafodotin (belamaf) is approved for relapsed and refractory MM, but its role in the frontline setting is not established. (3)

AIM

To evaluate safety of a phase II, open label, multicenter, non-randomized single arm clinical trial (GEM-BELA-VRd) (NCT04802356), after **4 cycles of induction** with belantamab (belamaf) in combination with bortezomib, lenalidomide and dexamethasone (VRd) in NDTE MM.

RESULTS

Basal characteristics are detailed in Table 1. Half of patients were women and the median age at diagnosis was 58 years old (27-74).

Table 1. Basal characteristics of 40 NDTE MM patients	
Age (median, range)	58 (27-74)
ECOG (no., %)	
0	20 (52.6)
1	15 (39.15)
2*	3 (7.9)
Subtype MM (no., %)	
Ig G	26 (65.0)
Ig A	10 (25.0)
BJ	4 (10.0)
Subtype light chain (no., %)	
Kappa	26 (65.0)
Lambda	14 (35.0)
ISS (no., %)	
I	25 (65.8)
II	8 (21.1)
III*	5 (13.2)
Serum M-prot (mean, SD)	2.1 (2.0)
Urine M-prot (mean, SD)	0.4 (0.9)
Cytogenetics (no., %)	
del17p	2/10 (20.0)
t(4;14)	2/13 (15.4)
t(14;16)	0
Extramedullary soft-tissue plasmacytomas (no, %)	7 (17.5)

** 2 cases missing*

Ocular toxicity was the most frequent AE. Thirty-eight patients (95%) presented ocular symptoms, the most frequent one was blurred vision (Table 2). Table 3 shows incidence of keratopathy (KVA scale) at 4 weeks after first belamaf dose and 4 weeks after second dose, and 2nd dose administration of belamaf in Table 4.

Table 2. Ocular symptomatology during the first 4 cycles of induction with Belamaf-VRD (CTCAE v. 4.0)	Any Grade n (%)	G 3-4 n (%)
Blurred vision	31 (77.5)	11 (27.5)
Eye irritation	23 (57.5)	4 (10.0)
Dry eye	20 (50.0)	4 (10.0)
Photophobia	10 (25.0)	0
Other	9 (22.5)	1 (2.5)
Eye pain	3 (7.5)	0
Eye pruritus	2 (5)	1 (2.5)
Dyplopia	1 (2.5)	0
Foreign body sensation	1 (2.5)	0

Table 3. Keratopathy by KVA scale		
Keratopathy	**4 weeks from 1st belamaf dose (C2 VRD)**	**4 weeks from 2nd planned belamaf dose (C4 VRD)**
None	**16 (40)**	**8 (20)**
Any grade	**24 (60.0)**	**32 (80.0)**
Mild	12 (50.0)	12 (37.5)
Moderate	11 (45.8)	17 (53.1)
Severe	1 (4.2)	3 (9.4)

Table 4. Second dose administration of belamaf	
Full dose (no., %)	24 (60.0)
Reduced dose (*1.9 mg/kg*) (no., %)	9 (22.5)
Withdrawn (no., %)	7 (17.5)

Hematological toxicity was reported in 24 patients (60%). Neutropenia and thrombocytopenia were the most frequent hematological AEs.

Infection was the most frequent **non-hematological AEs**, described in Table 5.

Table 5. Hematological and non-hematological AEs during the first 4 cycles of induction with Belamaf-VRD (CTCAE v. 4.0)	Any Grade n (%)	G 3-4 n (%)
Hematological toxicity		
Neutropenia	8 (20.0)	5 (12.5)
Thrombocytopenia	8 (20.0)	3 (7.5)
Anemia	4 (10.0)	1 (2.5)
Non-hematological toxicity		
Infections	22 (55.0)	9 (22.5)
-Respiratory infections	20 (50.0)	9 (22.5)
-Pneumonia	8 (20.0)	7 (17.5)
COVID pneumonia	3 (7.5)	3 (7.5)
-Urinary infections	1 (2.5)	0
-Catheter infections	1 (2.5)	0
Skin toxicity	14 (35.0)	6 (15.0)
Peripheral neuropathy	13 (27.5)	0

Table 6. Efficacy after 4 cy of Belamaf-VRD	
ORR	32/39 (82.1%)
CR	5/39 (12.8%)
MRD negativity	4/5 (80%)
Not evaluable	1/5
6-mo PFS	89.3%

Outcomes after 4 cycles of Belamaf-VRD induction are detailed in Table 6 for 39 evaluable patients with a median follow-up of 6 months (3-12).

In all, 2 patients died, both due to COVID-19 pneumonia and 1 progressed resulting in a 6-month PFS: 89.3% [95% CI (87.2 - 91.3)]

METHOD

- 50 patients were planned to be recruited in this phase II, open label, multicenter, non-randomized single arm clinical trial (GEM-BELA-VRd). **40 patients** had already completed the four induction cycles and were included in this analysis.
- Study design is detailed in Figure 1.
- Primary endpoint was safety, evaluated in terms of incidence of adverse events (AEs) [according to CTCAE v. 4.0], of ocular events (OEs) [according to Visual Acuity - KVA scale] and of deaths after first 4 induction cycles.
- Main key secondary endpoints were overall response rate (ORR), complete response rate (CR), and progression-free survival (PFS).
- Cut-off date: July 7th 2022

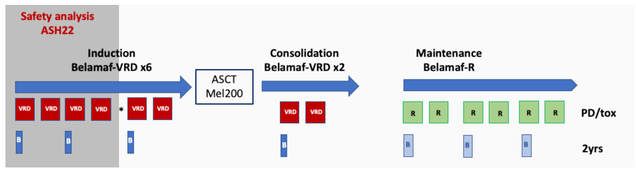

Figure 1. GEM-BELA-VRd study design and treatment schedule and dosing

CONCLUSIONS

The results of adding belamaf to VRD seem encouraging, although ocular toxicity is a concern.

The study is ongoing with belamaf as part of the maintenance.

Longer follow-up will confirm whether the combination improves outcomes in NDTE MM patients.

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