Effectiveness and Safety of Belantamab Mafodotin in Patients With Relapsed or Refractory Multiple Myeloma in Real-Life Setting: The ALFA Study

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Introduction

- Although the therapeutic landscape for multiple myeloma (MM) has expanded, treatment of patients with relapsed or refractory multiple myeloma (RRMM) remains challenging.
- Patients triple-refractory to immunomodulatory drugs, proteasome inhibitors (PIs), and anti-CD38 antibodies have few widely available therapeutic alternatives and poor prognosis.
- Belantamab mafodotin (BLMF), a first-in-class antibody-drug conjugate targeting B-cell maturation antigen (BCMA), demonstrated effectiveness and had a manageable safety profile in patients with RRMM in the DREAMM-2 trial.[1,2]

Objective

The aim of the ALFA study is to describe BLMF effectiveness and safety in patients with RRMM in a real-life setting.

Patients and methods

ALFA is a non-interventional, retrospective study of patients with RRMM who started BLMF in 46 centers in France during early access programs from April 27, 2020, to June 30, 2021.

Patient characteristics, overall response rate (ORR, ≥partial response [PR]), at least very good PR (≥VGPR), clinical benefit rate (CBR, ≥minimal response [MR]), progression-free survival (PFS) and overall survival (OS), and safety were assessed.

Effectiveness was evaluated in patients with at least one response assessment in the overall study population.

Safety was evaluated in patients who received at least one dose of BLMF.

Subgroup analyses for PFS and OS were performed according to best response, high cytogenetic risk, renal clearance, age at BLMF initiation, previous penta-exposure, delay since diagnosis, and number of prior lines of treatment.

Results

Table 1. Patient characteristics

Characteristic	Total (N=184)
Age at BLMF start, years, median (interquartile range, IQR)	70.3 (63.3–75.9)
≥75 years, n (%)	55 (29.9)
≥80 years, n (%)	20 (10.9)
Gender, n (%)	
Male	98 (53.3)
Eastern Cooperative Oncology Group - Performance Status (ECOG-PS) score at BLMF start, n (%)	
0	32 (20.5)
1	67 (42.9)
2	39 (25.0)
3	17 (10.9)
4	1 (0.6)
Not available	28
Ophthalmologic history, n (%)	
Yes	74 (47.7)
No	81 (52.3)
Not available	29
If yes, type (several choices available)	
Cataract	39 (52.7)
Keratitis/keratopathy	14 (18.9)
Dry eye syndrome	13 (17.6)
Glaucoma	7 (9.5)
Time since MM diagnosis, years, median (IQR)	6.1 (3.7–9.9)
≤3 years, n (%)	28 (15.3)
Extramedullary disease, n (%)*	
Yes	15 (8.3)
No	165 (91.7)
Not available	4
Renal clearance, n (%)	
≥90 mL/min	30 (19.4)
60–90 mL/min	51 (32.9)
30–60 mL/min	55 (35.5)
<30 mL/min	19 (12.3)
Not available	21
Cytogenetic abnormalities, n (%)	**N=87**
High risk†	27 (32.5)
Standard risk	33 (39.8)
No abnormalities	23 (27.7)
Not available	4
Number of previous lines received, n (%)	
≤2	10 (5.4)
3	21 (11.4)
4	46 (25)
≥5	107 (58.2)
Penta-exposed, n (%)‡	
Yes	145 (78.8)

*Based on the investigator's judgment; †Defined as del(17p) and/or t(4 :14) and/or (14 :16); ‡Previously exposed to at least 2 different PIs, 2 different immunomodulatory drugs, and 1 anti-CD38.

Between April 2020 and June 2021 (median duration of follow-up 7.8 months, defined as time from BLMF initiation to date of last news), 184 patients initiated BLMF (**Table 1**).

At initiation, median (IQR) age was 70 (63–76) years with 30% of patients aged 75 years or older; 36.5% had an ECOG PS ≥2; 47.7% had renal failure (clearance <60 mL/min), 8.3% had extramedullary disease, and 79% (n=145) were penta-exposed.

Cytogenetic profiles at initial diagnosis were available for 83 patients (45%), among whom 33% had high cytogenetic risk.

Median time from MM diagnosis to initiation of BLMF was 6 years, and 107 patients (58%) had received ≥5 prior lines of therapy.

48% had ophthalmologic history (cataract [52.7%], keratitis/keratopathy [18.9%]).

The median (range) dose at initiation was 2.5 (1.6–3.0) mg/kg.

The median (Q1, Q3) number of BLMF cycles received was 3 (2, 7).

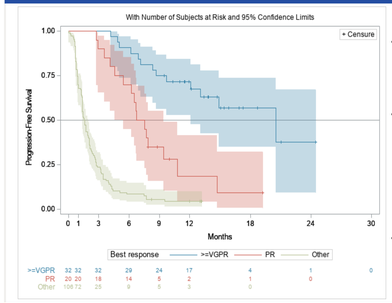
Table 2. Response rate (overall, clinical benefit)

	Total (N=184)
Best response to treatment, n (%)	
Very good partial response	33 (20.4)
Partial response	20 (12.3)
Minimal response	6 (3.7)
Stable disease	43 (26.5)
Progressive disease	60 (37)
Not available	22
Overall response rate, n (%)	
Yes	53 (32.7)
Not available	22
Clinical benefit (at least minimal response), n (%)	
Yes	59 (36.4)
Not available	22
At least stable disease (SD), n (%)	
Yes	102 (63.0)
Not available	22

162/184 patients (88%) had at least one response assessment available in the overall study population (**Table 2**):

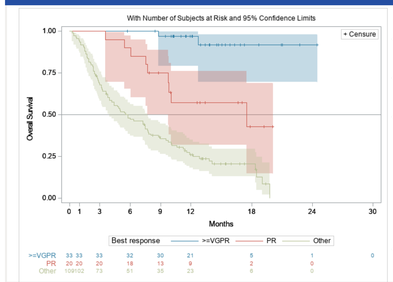
- The ORR was 32.7% (≥VGPR 20.4%, PR 12.3%) and the CBR was 36.4% (MR 3.7%).
- No major difference was found regarding subgroups of interest except for patients with extramedullary disease (ORR and CBR in this subgroup were 0%).

Figure 1. PFS according to best response to BLMF



- The median PFS (mPFS) for the whole population was 2.4 months (95% Confidence Interval 1.9–3.2).
- According to the best response, mPFS was 20.6 months (95% CI 12.1–not reached) in patients with ≥VGPR, 7.1 months (95% CI 4.6–9.4) in patients with PR, and 1.6 months (95% CI 1.4–2.0) in the other patients; *P*<0.01 (**Figure 1**).
- No differences were found in subgroups of interest.

Figure 2. OS according to best response to BLMF



- The median OS (mOS) was 8.8 months (95% CI 6.3–11.6).
- mOS was not reached in patients with ≥VGPR.
- mOS was 17.5 months (95% CI 7.7–not reached) in patients with PR and 5.6 months (95% CI 3.9–7.7) in the other patients; including mOS at 14.1 months in MR, 9.5 months in stable disease, and 3.3 months in progressive disease (**Figure 2**).
- No differences were found in subgroup of interest.

Table 3. Safety

	Total (N=184)
Number of patients with at least one ophthalmologic adverse event (AE), n (%)	103 (56)
Yes	81 (44)
No	
If yes, grade of ophthalmologic AE	**N=103**
Grade 1	30 (42.9)
Grade 2	20 (28.6)
Grade 3	15 (21.4)
Grade 4	5 (7.1)
Type of ophthalmologic AE, n (%)	
Keratopathy/keratitis	77 (41.8)
Grade 3–4	15 (8.2)
Decreased visual acuity	20 (10.9)
Grade 3–4	2 (1.1)
Other ocular disorders	24 (13.0)
Grade 3–4	4 (2.2)
At least one ophthalmologic AE resulting in discontinuation of treatment (temporary or permanent), n (%)	40 (21.7)
Yes	144 (78.3)
No	
At least one ophthalmologic AE resulting in:	21 (11.4)
Temporary interruption, n (%)	23 (12.5)
Permanent discontinuation, n (%)	

Adverse events (AEs) were reported in 159 patients (86.4%).

The most frequent AEs were ocular AEs, reported in 56.0% of patients (n=103). Most ocular AEs were of Grade 1 or 2 (71.5%) (**Table 3**).

41.8% had keratitis/keratopathy (all grades) and 8.2% had keratitis/keratopathy with a Grade 3–4.

10.9% had decreased visual acuity (all grades) and 1.1% had decreased visual acuity with a Grade 3–4.

13.0% had other ocular symptoms (all grades) and 2.2% had these symptoms with a Grade 3–4.

Ocular AEs led to dose modification, temporary interruption, and permanent discontinuation in 19.6%, 11.4%, and 12.0% of patients, respectively.

Among 29 patients with a delay in perfusion due to ocular AEs, the median duration was 32 days.

Among other AEs, thrombocytopenia occurred in 13.6% of patients and infusion reaction was reported in 3.3% of patients.

Conclusions

The results of the ALFA study were consistent with the DREAMM-2 trial[1] in an overall older and more frail population. In the ALFA overall population, the ORR was 32.7%, CBR was 36.4%, mPFS was 2.4 months, and mOS was 8.8 months.

In patients ≥VGPR to BLMF, mPFS was 20.6 months and mOS was not reached.

No new safety concerns were identified. These data, presented from the largest real-life study conducted to our knowledge, confirm previous results.

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