ABSTRACT/ POSTER 1546209

EFFECTIVENESS OF ANTI-B-CELL MATURATION ANTIGEN (BCMA)-TARGETING THERAPY AFTER SELINEXOR TREATMENT

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INTRODUCTION

- Multiple myeloma (MM) remains incurable, with the disease typically becoming refractory to three main classes of standard therapies: immunomodulatory drugs (IMiDs), proteasome inhibitors (PIs) and anti-CD38 monoclonal antibodies (αCD38 mAbs).
- Treatments with novel mechanisms of action, including the XPO1 inhibitor selinexor (Figure 1) and T-cell engaging anti-B-cell maturation antigen (αBCMA)-therapies (antibody drug conjugates [ADCs], bi-specific antibodies [BiS]), are increasingly used for treatment of relapsed and/or refractory MM (RRMM) after standard therapies have failed.

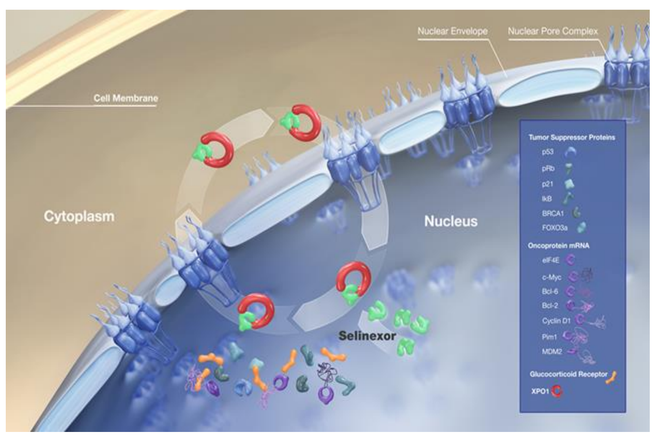


Figure 1. Selinexor mechanism of action

- Emerging data suggests a deleterious impact on T-cell function with certain MM treatments, including alkylators and PIs, leading to inferior clinical outcomes.[1,2]
- Reduced T-cell fitness may hamper the effectiveness of some therapies, including bispecific T-cell engagers, αCD38 mAbs, and chimeric antigen receptor T-cells.[3,4]
- The influence of selinexor-based treatment on T-cell function, which may alter the efficacy of αBCMA therapies following selinexor treatment, is unknown.
- Research in cell lines and animal models suggest that selinexor and other selective inhibitors of nuclear export (SINE) compounds have the potential to reduce T-cell exhaustion.[5,6]

METHODS

- We analyzed the effectiveness of non-cellular αBCMA (NCA) therapies in patients with MM treated in 4 clinical studies (STORM [NCT02336815]; STOMP [NCT02343042]; BOSTON [NCT03110562], XPORT-MM-028 [NCT04414475]) with selinexor + dexamethasone (Sd), with or without PIs, IMiDs, or αCD38 mAbs, followed by therapy with NCA.

Populations	STORM (Sd-80 BIW) (N = 202)	STOMP (Sd-based triplets and quads) (N = 246)	BOSTON (SVd) (N = 195)	XPORT (Sd-80 BIW, Sd-100 QW, Sd-40 BIW, SPd, or SVd) (N = 81)	Total (N = 724)
Patients with any on-study anti-MM therapy documented after selinexor, n (%)	124 (61.4)	148 (60.2)	99 (50.8)	33 (40.7)	404 (55.8)
Patients with non-CAR-T αBCMA after selinexor, n (%)	8 (6.5)	16 (10.8)	2 (2.0)	11 (33.3)	37 (9.2)

- After end of treatment with selinexor, survival follow-up data was collected every 3 months for 1 (STORM, STOMP, XPORT-MM-028) to ~3.5 years (BOSTON).

RESULTS

Table 1. Patient characteristics and demographics*

	Patients with Non-CAR T-Cell Anti-BCMA Therapy After Selinexor (N = 37)
Age (Years)[1], median (range)	68.0 (40-87)
Sex, N (%)	
Male	21 (56.8)
Female	16 (43.2)
Duration from last dose of selinexor to first anti-BCMA therapy (weeks), median (range)	8.0 (2-117)
Baseline ECOG performance status, N (%)	
0	14 (37.8)
1	18 (48.6)
2	4 (10.8)
Missing	1 (2.7)
Number of prior lines of therapy, median (range)	5.0 (2-11)
Previously exposed to αCD38 mAb (daratumumab or isatuximab), n (%)	30 (81.1)
Refractory to, n (%):	
PI (bortezomib, carfilzomib, or ixazomib)	30 (81.1)
IMiD (thalidomide, lenalidomide, or pomalidomide)	29 (78.4)
αCD38 mAb (daratumumab or isatuximab)	27 (73.0)
αCD38 mAb, PI, and IMiD	21(56.8)
≥2 Pis, ≥2 IMiDs, and αCD38 mAb	8 (21.6)

Abbreviations: αCD38 mAb=anti-CD38 monoclonal antibody; ECOG=Eastern Cooperative Oncology Group; IMiD=immunomodulatory drug; PI=proteasome inhibitor; POM=pomalidomide; SEL=selinexor.
* Results are as of August 1, 2022 for ongoing studies STOMP and XPORT-MM-028.
[1]Age at screening.

Table 2. Selinexor-based regimens

	Patients with Non-CAR T-Cell Anti-BCMA Therapy After Selinexor (N = 37)
Selinexor combination, n (%)	
Sd-80 BIW, Sd-100 QW, or Sd-40 BIW	12 (32.4)
Sd 80 BIW	9 (24.3)
Sd 100 QW	2 (5.4)
Sd 40 BIW	1 (2.7)
SVd	9 (24.3)
SPd	6 (16.2)
SDd	3 (8.1)
SKd	5 (13.5)
SNd	2 (5.4)

Abbreviations: BIW=twice weekly, d=dexamethasone, D=daratumumab, K=carfilzomib, N=ixazomib, P=pomalidomide, QW=once weekly, S=selinexor, V=bortezomib.

Table 3. Non-cellular anti-BCMA therapies

	Patients with Non-CAR T-Cell Anti-BCMA Therapy After Selinexor (N = 37) n (%)
Belantamab mafodotin*	28 (75.7)
Teclistamab	2 (5.4)
SEA-BCMA	2 (5.4)
AMG 701	1 (2.7)
Elranatamab	1 (2.7)
MEDI2228	1 (2.7)
Investigational†	3 (8.1)

* One patient received 2 NCAs, belantamab and teclistamab.
† Two had αBCMA bispecific antibodies and 1 had αBCMA bispecific T-cell engager (BiTE).

Efficacy

- The median overall survival from initiation of NCA was 12.0 months (95% CI: 9.4, NE) with a median follow-up of 7.8 months (Figure 2 & Table 4).
- Median time to treatment discontinuation (TTD) with NCA was 3.1 months (95% CI: 2.1, NE) (Figure 3 & Table 4).
- A trend for longer overall survival and TTD was seen for the other NCAs compared with bela-maf (Table 4).

Table 4. Efficacy of NCAs after selinexor-based regimens

	Any NCA after selinexor (N = 37)	Bela-maf after selinexor (N=28)	NCA except bela-maf after selinexor (N=10)
OS, median (months) (95% CI)	12.0 (9.4, NE)	11.3 (6.6, NE)	NR (9.4, NE)
Median follow-up (months)	7.8	7.8	9.1
TTD, median (months) (95% CI)	3.1 (2.1, NE)	3.1 (1.4, NE)	8.7 (1.9, NE)

NE, not evaluable; NR, not reached; OS, overall survival; TTD, time to treatment discontinuation.

Figure 2. Overall survival after NCA therapy

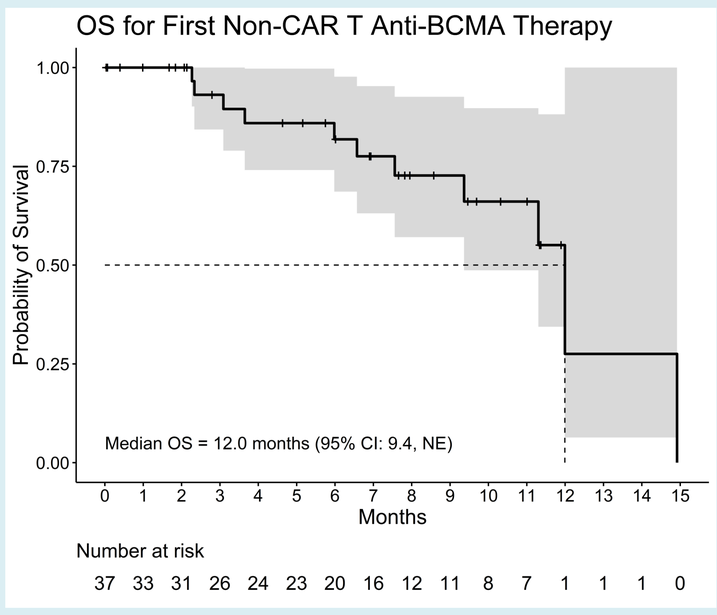
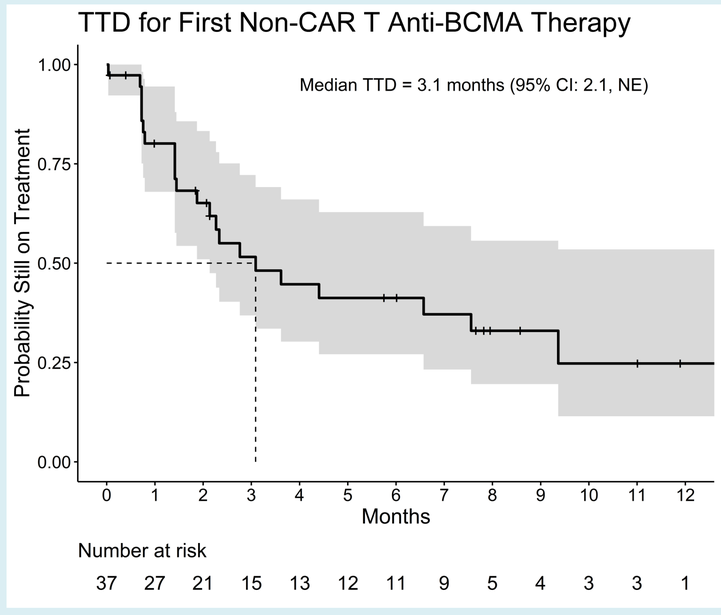


Figure 3. Time to discontinuation of NCA therapy



Safety

- The trials did not record treatment-emergent adverse events (TEAEs) that occurred when the patients started on αBCMA therapy.
- The most common TEAEs that occurred in ≥ 25% of patients on selinexor regimens prior to starting an αBCMA therapy included fatigue (any grade, 23 [62.2%]/grade 3/4, 5 [13.5%], nausea (23 [62.2%]/2 [5.4%]), decreased appetite (20 [54.1%]/1 [2.7%]), thrombocytopenia (19 [51.4%]/12 [32.4%]), anemia (17 [45.9%]/5 [13.5%]), weight decreased (15 [40.5%]/0), diarrhea (13 [35.1%]/3 [8.1%]), constipation (12 [32.4%]/0), asthenia (12 [32.4%]/1 [2.7%]), cough (10 [27.0%/0), dyspnea (10 [27.0%]/1 [2.7%]).

CONCLUSIONS

- **In this cohort of heavily-pretreated patients with MM who received a selinexor regimen prior to NCA, overall survival was in the range of 1 year, akin to historical results seen with ADCs.**
- **The 8-week median time between administration of selinexor and NCAs suggests that selinexor, with various partner agents, did not negatively impact overall survival with subsequent NCA therapy, including bela-maf, bispecific antibodies, and BiTEs.**

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