SEA-BCMA MONO- AND COMBINATION THERAPY IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: UPDATED RESULTS OF A PHASE 1 STUDY (SGNBCMA-001)

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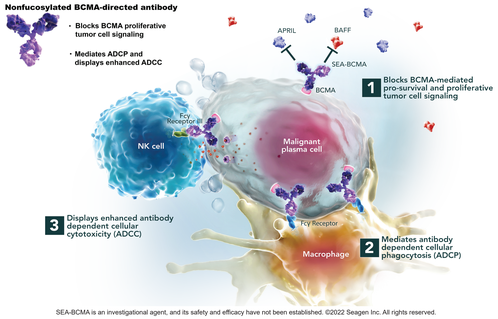
Background

- Despite recent progress in the treatment of triple-class R/R (R/R to a proteasome inhibitor, immunomodulatory drug and anti-CD38 antibody) MM, patients remain in need of novel therapies with manageable toxicity and non-cross-resistant mechanisms of action.
- B-cell maturation antigen (BCMA) is expressed in most MM plasma cells.[1]
- SEA-BCMA is an investigational, humanized, nonfucosylated IgG1 monoclonal antibody directed to BCMA.
- Preclinical data for SEA-BCMA demonstrate promising antitumor activity and versatile combinability.[2]
- SGNBCMA-001 Part A was comprised of both monotherapy dose escalation (100–1600 mg flat dosing by intravenous infusion) and dose expansion at the highest tolerated dose. SEA-BCMA 1600 mg Q2W was generally well-tolerated and showed initial antitumor activity with an ORR of 14% (95% CI: 2.9, 34.9; n=22).[3]
- Here, we evaluated intensive SEA-BCMA dosing (Part B) and the addition of dexamethasone (DEX; Part C) to further assess the safety, tolerability, and clinical activity. Preliminary data from Part D, testing the combination of SEA-BCMA, pomalidomide (pom), and DEX in an earlier line of therapy, are also presented.

SEA-BCMA Proposed Mechanism of Action

- A sugar-engineered antibody, the nonfucosylated Fc region of SEA-BCMA has increased affinity for activating FcγRIIIa and minimal affinity for inhibitory FcγRIIb.

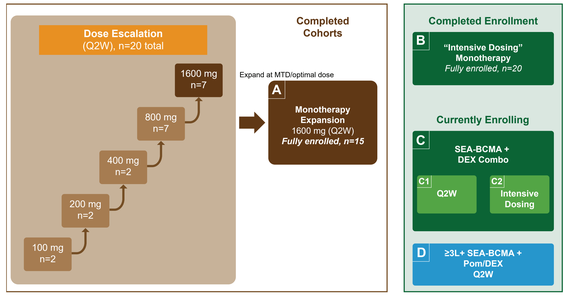


Methods

- SGNBCMA-001 (NCT03582033) is an ongoing phase 1, open-label, multicenter, dose escalation and expansion study to evaluate the safety, tolerability and antitumor activity of SEA-BCMA in adults with R/R MM not previously exposed to any other BCMA-directed therapy.
- Parts B and C enrolled patients who have received ≥3 prior lines of therapy for MM and are triple-class refractory. These expansion cohorts are testing
  - Intensive dosing (Part B; weekly induction dosing of SEA-BCMA for 8 weeks is followed by Q2W maintenance dosing) and
  - DEX (40 mg weekly) combination therapy with either standard SEA-BCMA dosing (Part C1) or intensive SEA-BCMA dosing (Part C2; 800 mg [dose level -1] or 1600 mg [dose level 1]).
- Part C2 has been amended to allow patients with prior exposure to BCMA-directed therapy and is continuing to enroll.
- Part D (testing the combination of SEA-BCMA with pom and DEX in patients who have received ≥2 prior lines of therapy) is enrolling.
- Responses are assessed per the 2016 International Myeloma Working Group criteria.

SEA-BCMA Study Schema

Currently Conducting 3 Expansion Cohorts in Parallel



Color Key: brown box=prior lines of therapy must include at least a PI, an IMiD, and an anti-CD38 antibody; green boxes=triple-class refractory cohorts, blue box=≥3L + at least 2 consecutive cycles of both lenalidomide and a PI + pom naïve

- Parts B and C aim to optimize clinical activity in patients with triple-class refractory MM
- Part D aims to assess potential IMiD synergy in earlier line of therapy
- **Updated data from Parts B and C, and preliminary data from Part D are presented therein**

Abbreviations

3L, ≥2 lines of prior therapy; BCMA, B-cell maturation antigen; CI, confidence interval; CR, complete response; DEX, dexamethasone; DLT, dose-limiting toxicity; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; IMiD, immunomodulatory drug; IRR, infusion related reaction; MM, multiple myeloma; MR, minimal response; MTD, maximum tolerated dose; n, number of patients with disease characteristic; OR, overall response; ORR, overall response rate; PD, progressive disease; PI, proteasome inhibitor; pom, pomalidomide; PR, partial response; Q2W, once every 2 weeks; R/R, relapsed/refractory; SAE, serious adverse event; SD, stable disease; sFLC, serum free light chain; TEAE, treatment emergent adverse event; triple-class R/R, R/R to a proteasome inhibitor, immunomodulatory drug and anti-CD38 antibody; VGPR, very good partial response

References

1. Seckinger A, Delgado JA, Moser S, et al. Cancer Cell. 2017;31(3):396-410
2. Van Epps H, Anderson M, Yu C, et al. Cancer Res July 1 2018 (78) (13 Supplement) 3833; DOI: 10.1158/1538-7445.AM2018-3833
3. Hoffman JE, Lipe B, Melear J, et al.; Blood 2021; 138 (Supplement 1): 2740. doi: https://doi.org/10.1182/blood-2021-146047

Disclosures

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Results

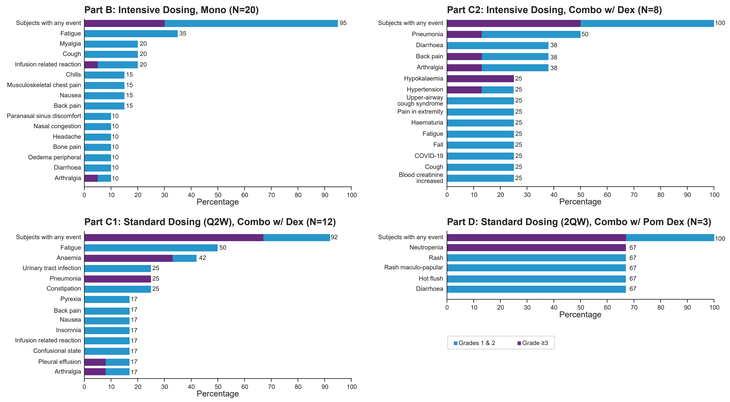
Demographics and Disease Characteristics

Patient Characteristic	Part A (N=35)	Part B (N=20)	Part C1 (N=12)	Part C2 (N=8)	Part D (N=3)
Age (years)					
Median (Min–Max)	71.0 (51–84)	74.0 (57–91)	68.5 (48–76)	72.5 (68–83)	75.0 (68–76)
Age, n (%)					
≥65	28 (80)	18 (90)	9 (75)	8 (100)	3 (100)
Gender, n (%)					
Female	16 (46)	7 (35)	7 (58)	2 (25)	1 (33)
Male	19 (54)	13 (65)	5 (42)	6 (75)	2 (67)
ECOG Performance Status, n (%; Eligibility: 0–1)					
1	32 (91)	17 (85)	9 (75)	7 (88)	2 (67)
Number of prior systemic therapies for myeloma					
Median (Min–Max)	6.0 (3–15)	4.5 (3–10)	5.0 (3–10)	5.0 (3–6)	4.0 (2–5)
Refractory, n (%)					
To PI	25 (71)	19 (95)	12 (100)	8 (100)	3 (100)
To IMiD	26 (74)	19 (95)	12 (100)	8 (100)	2 (67)
To anti-CD38 antibody	26 (74)	20 (100)	12 (100)	8 (100)	2 (67)
Triple class refractory	23 (66)	19 (95)	12 (100)	8 (100)	1 (33)
Intolerant of any above classes	9 (26)	4 (20)	4 (33)	2 (25)	1 (33)
Extramedullary disease, n (%)					
Presence of bone lesions indicated by skeletal survey	23 (66)	9 (45)	7 (58)	7 (88)	–
Soft tissue plasmacytomas identified by radiography	5 (14)	–	–	1 (13)	–

Note: Parts A and D enrolled triple-class exposed, while Parts B and C required triple-class refractory.

Updated Safety Data Show SEA-BCMA was Generally Well-Tolerated

Parts B (Intensive Dosing), C1 (Combination Therapy with DEX), and C2 (Intensive Dosing Combination Therapy with DEX) Show Similar Tolerability with no DLTs Observed



- In Part A SEA-BCMA was generally well-tolerated with a single DLT (prolonged IRR) observed, and the MTD was not identified in the 5 dose levels tested.[3]
- Part B completed the safety run-in (n=6) and completed enrollment at 1600 mg SEA-BCMA intensive dosing.
- Part C1 completed the safety run-in (n=6) and continued enrollment for SEA-BCMA 1600 mg Q2W + DEX.
- Part C2 dose optimization is completing safety run-ins at 800 mg SEA-BCMA intensive dosing (dose level –1) and at 1600 mg SEA-BCMA intensive dosing (dose level 1).
- No DLTs were observed in Part B, the safety run-in portions of either Part C1 or C2 thus far, and among the first 3 patients in Part D; safety and tolerability were similar to that observed in Part A.
- No patients in Parts B, C2, and D discontinued treatment due to TEAEs. In Part C1, 1 patient discontinued treatment due to a TEAE unrelated to SEA-BCMA. The majority of treatment discontinuations were due to PD.
- No deaths related to SEA-BCMA occurred during the study to date; all deaths within 30 days of SEA-BCMA dosing were due to myeloma.

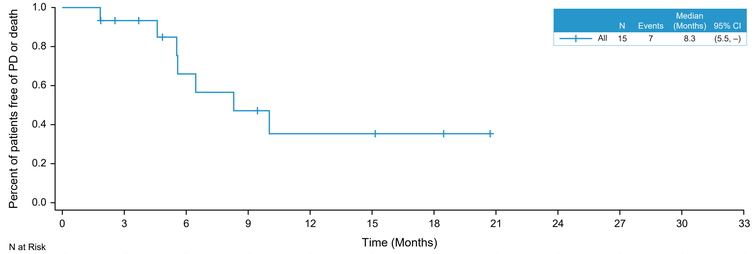
Preliminary Results for SEA-BCMA Antitumor Activity and DOR

SEA-BCMA Demonstrated Single Agent Activity and Response Rates Increased with Intensive Dosing and Combination Therapy

	Standard Q2W Dosing SEA-BCMA 1600 mg		Intensive Dosing (Weekly x 2 Cycles, Then Q2W) SEA-BCMA		
	Part A Monotherapy[a] (N=22)	Part C1 + DEX (N=12)	Part B Monotherapy (N=20)	Part C2 + DEX (N=8)	Part D Q2W + pom/DEX (N=3)
Best overall response (confirmed), n (%)					
Stringent complete response	0	1 (8)	1 (5)	0	2 (67)
Complete response	0	0	0	0	0
Very good partial response	1 (5)	0	0	1 (13)	0
Partial response	2 (9)	1 (8)	3 (15)	2 (25)	1 (33)
Minimal response	1 (5)	1 (8)	1 (5)	0	0
Stable disease	13 (59)	7 (58)	11 (55)	5 (63)	0
Progressive disease	5 (23)	2 (17)	4 (20)	0	0
Overall response rate (ORR), n (%)	3 (14)	2 (17)	4 (20)	3 (38)	3 (100)
95% CI[b] for ORR	(2.9, 34.9)	(2.1, 48.4)	(5.7, 43.7)	(8.5, 75.5)	(29.2, 100)
ORR by dosing schedule, n (%)	**5 (15)**		**7 (25)**		

a Escalation and Expansion Phase dosed at 1600 mg.
b Two-sided 95% exact confidence interval, computed using the Clopper-Pearson method (1934).

Duration of Response (Overall)



- Both intensive SEA-BCMA dosing (Part B) and the addition of DEX (Part C1) showed increased ORR relative to Q2W monotherapy (Part A).
- For the combination of the intensive SEA-BCMA dosing schedule and the addition of DEX (Part C2), the ORR across both SEA-BCMA dose levels (800 mg [n=3] and 1600 mg [n=5]) was 38% (n=8; 95% CI: 8.5, 75.5).
- The combined ORR of both intensive dosing cohorts Parts B and C2 relative to standard dosing (Q2W) cohorts Parts A [1600 mg SEA-BCMA] and C1 were 25% versus 15%, respectively.
- The overall median DOR from 15 patients with a confirmed response across Parts A (1600 mg SEA-BCMA), B, C1, C2, and D was 8.3 months (95% CI: 5.5, –).
- In Part A, the median DOR was 10 months (95% CI: 5.6, –), 1 patient remains on treatment. In Part B, the median DOR was 6.5 months (95% CI: 1.8, –); 4 patients remain on treatment, including 2 responders. In Part D, the median DOR was 8.3 months (95% CI: –, –); 2 responding patients remain on treatment.
- In Parts C1 and C2, the median DOR was not yet reached (1 responding patient remains on treatment in Part C1, and 2 responding patients remain on treatment in Part C2).

Conclusions

- Updated results for SEA-BCMA continue to demonstrate a favorable safety profile and combination potential.
- Encouraging preliminary data suggest that both the intensive dosing schedule and combination with DEX may increase clinical activity over Q2W monotherapy.
- Part C2 and Part D (testing the combination of SEA-BCMA with pomalidomide and DEX), are enrolling.
- SEA-BCMA shows potential to provide R/R MM patients with the option of a novel therapy with manageable toxicity and combinability in regimens with other classes of myeloma therapies.

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