SEA-BCMA, an Investigational Nonfucosylated Monoclonal Antibody: Ongoing Results of a Phase 1 Study in Patients with Relapsed/Refractory Multiple Myeloma (SGNBCMA-001)

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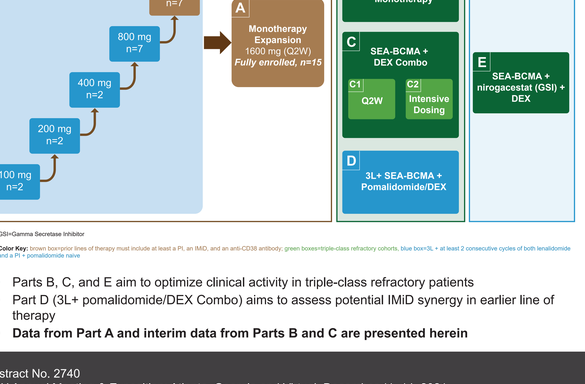
Background

- Despite recent progress in the treatment of triple-class R/R (relapsed/refractory to a proteasome inhibitor, immunomodulatory drug or anti-CD38 antibody) MM, patients remain in need of novel therapies with manageable toxicity and non-cross-resistant mechanisms of action.
- 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]
- Here, we present preliminary clinical safety and ongoing antitumor activity data from the first-in-human Phase 1 clinical trial. Data from a biomarker analysis are presented on poster #1197.

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 first-in-human safety, tolerability and antitumor activity of SEA-BCMA in adults with R/R MM not previously exposed to any other BCMA-directed therapy.
- Here, we present preliminary data from Parts A, B, and C:
  - Part A tested monotherapy safety and tolerability with dose escalation (100–1600 mg flat dosing Q2W by intravenous infusion), and dose expansion at the highest tolerated dose.
  - Parts B and C aim to optimize clinical activity by testing intensive dosing (Part B; Q1W induction dosing of SEA-BCMA for 8 weeks is followed by Q2W maintenance dosing) and DEX combination therapy with either standard SEA-BCMA dosing (Part C1) or intensive SEA-BCMA dosing (Part C2) in patients who have received ≥3 prior lines of therapy for MM and are triple-class refractory.
- Additional combination cohorts are ongoing (Part D SEA-BCMA/pomalidomide/DEX) or planned (Part E SEA-BCMA/nirogacestat/DEX).
- Responses are assessed per the 2016 International Myeloma Working Group criteria.

SEA-BCMA Study Schema

Currently Conducting 3 Expansion Cohorts in Parallel

GSI=Gamma Secretase Inhibitor

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 + pomalidomide naive

- Parts B, C, and E aim to optimize clinical activity in triple-class refractory patients
- Part D (3L+ pomalidomide/DEX Combo) aims to assess potential IMiD synergy in earlier line of therapy
- **Data from Part A and interim data from Parts B and C are presented herein**

Results

1 Demographics and Disease Characteristics

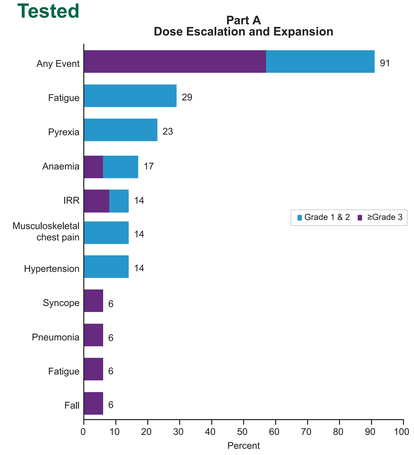
Patient Characteristic	Part A (N=35)	Part B (N=12)	Part C1 (N=12)	Total (N=59)
Age (years)				
Median (Min–Max)	71.0 (51–84)	71.0 (57–82)	68.5 (48–76)	71.0 (48–84)
Age, n (%)				
≥ 65	28 (80)	10 (83)	9 (75)	47 (80)
Gender, n (%)				
Female	16 (46)	5 (42)	7 (58)	28 (47)
Male	19 (54)	7 (58)	5 (42)	31 (53)
ECOG Performance Status, n (%; Eligibility: 0–1)				
1	31 (89)	11 (92)	10 (83)	52 (88)

Patient Characteristic	Part A (N=35)	Part B (N=12)	Part C1 (N=12)
Number of prior systemic therapies for myeloma			
Median (Min–Max)	6.0 (3–15)	5.0 (3–10)	5.0 (3–10)
Refractory, n (%)			
To PI	24 (69)	11 (92)	12 (100)
To IMiD	25 (71)	11 (92)	12 (100)
To anti-CD38 antibody	25 (71)	11 (92)	12 (100)
Triple class refractory	22 (63)	11 (92)	12 (100)
Intolerant of any above classes	9 (26)	2 (19)	4 (33)
Extramedullary disease, n (%)			
Presence of bone lesions indicated by skeletal survey	23 (66)	8 (67)	7 (58)
Soft tissue plasmacytomas identified by radiography	5 (14)	–	–

Note: Part A enrolled triple-class exposed, while Parts B and C1 required triple-class refractory.

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

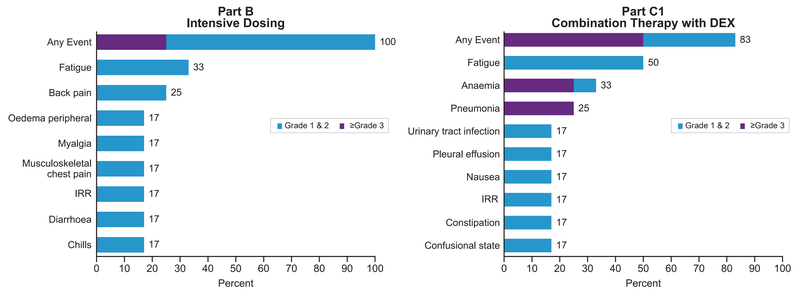
In Part A SEA-BCMA was Generally Well-Tolerated with a Single DLT (Prolonged IRR) Observed, and the MTD was not Reached in the 5 Dose Levels Tested



The most frequent TEAEs are listed; TEAE ≥ Grade 3 and SAEs are listed for events observed in ≥2 patients.

- The MTD was not reached in the 5 dose levels tested during dose escalation (100, 200, 400, 800, or 1600 mg Q2W; n=2, 2, 2, 7, and 7, respectively).
- At 800 mg, 1 of 7 patients reported a Grade 3 prolonged IRR, which met DLT criteria by lasting >24 hours despite supportive care. This constituted the single DLT observed during dose escalation.
- Dose expansion (n=15) proceeded at 1600 mg Q2W.
- Following a safety monitoring review, premedication with acetaminophen + antihistamine was introduced to mitigate IRRs in expansion cohorts.

Parts B (Intensive Dosing) and C1 (Combination Therapy with DEX) Completed Parallel Safety Run-ins at the 1600 mg Dose with no DLTs Observed and with Similar Tolerability



TEAE are listed for events observed in ≥2 patients.

- Part B completed the safety run-in (n=6) and continued enrollment at the 1600 mg Q1W dose.
- Part C1 completed the safety run-in (n=6) and continued enrollment for SEA-BCMA 1600 mg Q2W + DEX.
- No DLTs were observed in the completed safety run-in portions of either Part B or Part C1; safety and tolerability were similar to that observed in Part A.
- No patients discontinued treatment due to SEA-BCMA-related TEAEs. The majority of treatment discontinuations was 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.

TEAEs Leading to Dose Reduction or Dose Delay Were Infrequent Across All Cohorts

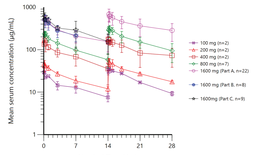
AEs Leading to Dose Reduction or Delay			
SEA-BCMA	Part A (N=35) n (%)	Part B (N=12) n (%)	Part C1 (N=12) n (%)
Dose Reduction - TEAE by Preferred Term			
Any Event	2 (6)	0 (0)	1 (8)
IRR	2 (6)	0 (0)	0 (0)
Peripheral sensory neuropathy	0 (0)	0 (0)	1 (8)
Dose Delay - TEAE by Preferred Term			
Any Event	3 (9)	0 (0)	0 (0)
Depressed level of consciousness	1 (3)	0 (0)	0 (0)
Neutrophil count decreased	1 (3)	0 (0)	0 (0)
Procedural complication	1 (3)	0 (0)	0 (0)

- SEA-BCMA dose reductions (3/59, 5%) or delays (3/59, 5%) due to TEAEs were infrequent across all study parts.

3 Pharmacokinetic Analysis

Serum SEA-BCMA Exposures Increased Proportionally with Increasing Dose with a Half-life of Approximately 10 Days

SEA-BCMA Mean Serum Concentration (µg/mL ± SD) Over Time

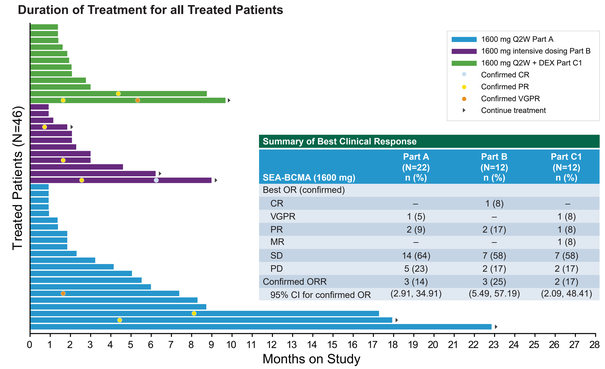


- SEA-BCMA PK reaches steady state at Cycle 2.
- PK accumulation over Cycles 1 and 2 (corresponding to 4 weeks) was approximately 40-90%, 60-110%, 10-60% for $AUC_{0\text{-}14day}$, C_{trough}, and C_{max}, respectively.
- Presence of ATAs was assessed in samples from 43 patients on monotherapy; all ATA samples tested at any visit during the study returned negative.
- The PK profile of SEA-BCMA in combination therapy with DEX is comparable to monotherapy and is unaltered with a change in schedule from Q2W to Q1W.

4 Preliminary Results for SEA-BCMA Antitumor Activity

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

Duration of Treatment for all Treated Patients



Summary of Best Clinical Response			
SEA-BCMA (1600 mg)	Part A (N=22) n (%)	Part B (N=12) n (%)	Part C1 (N=12) n (%)
Best OR (confirmed)			
CR	–	1 (8)	–
VGPR	1 (5)	–	1 (8)
PR	2 (9)	2 (17)	1 (8)
MR	–	–	1 (8)
SD	14 (64)	7 (58)	7 (58)
PD	5 (23)	2 (17)	2 (17)
Confirmed ORR	3 (14)	3 (25)	2 (17)
95% CI for confirmed OR	(2.91, 34.91)	(5.49, 57.19)	(2.09, 48.41)

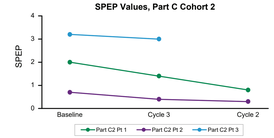
- For Part A, 3 patients in Part A remain on treatment (2 PR and 1 SD). Across all dose escalation levels, 10 of 35 patients (29%) had a duration on SEA-BCMA study treatment of at least 6 months.
- In Part B, 3 patients remain on treatment to date (1 CR, 1 PR and 1 SD).
- One Part C1 patient (PR) remains on treatment.

5 Preliminary Data from Part C2 Dose Level -1

Safety Run-in (n=3): Intensive Dosing SEA-BCMA + DEX Appears Safe and Active; No DLTs observed

	Baseline		Cycle 1		Cycle 2		Study Status
Pt #	SPEP (g/dL)	sFLC (mg/dL)	SPEP (g/dL)	sFLC (mg/dL)	Best OR (confirmed)	SPEP (g/dL)	Best OR (unconfirmed)	On Cycle
1	2.0	–	1.4	–	MR	0.8	PR	3
2	0.7	–	0.4	–	MR	0.3	PR	2
3	3.2	741.6	3.0	595.2	SD	TBD	TBD	1

- **Both patients who completed Cycle 2 have achieved unconfirmed PR**
- Pt #1: 70-year-old male with IgG lambda R/R MM
  - 30% SPEP reduction after Cycle 1 → 60% SPEP reduction after Cycle 2 → on treatment Cycle 3
- Pt #2: 74-year-old male with IgG kappa R/R MM
  - 42% SPEP reduction after Cycle 1 → 57% SPEP reduction after Cycle 2 → on treatment Cycle 3
- Pt #3: 83-year-old male with IgG lambda R/R MM
  - 6% SPEP reduction / 20% sFLC reduction after Cycle 1 → on treatment Cycle 2



Conclusions

- Preliminary results for SGNBCMA-001 suggest an acceptable safety profile and combination potential.
- SEA-BCMA shows initial antitumor activity in a heavily pre-treated late-line R/R MM patient population as a single agent.
- Preliminary data from expansion cohorts suggest that both the SEA-BCMA intensive dosing schedule and combination with DEX may further increase clinical activity.
- A new expansion cohort (Part C2) combines these 2 strategies (SEA-BCMA intensive dosing schedule and combination with DEX) and is currently enrolling.
- Additional combination expansion cohorts are ongoing (SEA-BCMA + pomalidomide + DEX; Part D) or planned (SEA-BCMA + nirogacestat + DEX; Part E).
- SEA-BCMA shows potential to provide R/R MM patients with the option of a novel therapy with manageable toxicity and a non-cross-resistant mechanism of action.

Abbreviations

3L+= 2 lines of prior therapy; ATA=anti-therapeutic antibody; BCMA=B-cell maturation antigen; CI=confidence interval; CR=complete response; DEX=dexamethasone; DLT=dose-limiting toxicity; ECOG=Eastern Cooperative Oncology Group; GSI=Gamma Secretase Inhibitor; 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; PK=pharmacokinetic; PR=partial response; Pt=patient; Q1W=weekly; Q2W=once every 2 weeks; R/R=relapsed/refractory; triple-class R/R=R/R to a proteasome inhibitor, immunomodulatory drug or anti-CD38 antibody; SD=stable disease; SAE=serious adverse event; sFLC=serum free light chain; SPEP=serum protein electrophoresis; TBD=to be determined; TEAE=treatment emergent adverse event; VGPR=very good partial response

References

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2. Van Epps H, Anderson M, Yu C, et al. Abstract 3833: SEA-BCMA: A highly active enhanced antibody for multiple myeloma. Cancer Res July 1 2018 (78) (13 Supplement) 3833; DOI: 10.1158/1538-7445.AM2018-3833

Disclosures

This study is sponsored by Seagen Inc., Bothell, WA, USA. The institutions of **JEH, BL, JM, ML, MAS, RN, MT, CAY, DJG,** and **AA** received research funding from Seagen Inc. **HL, YW** and **PH** are employees of and hold ownership interest in Seagen Inc. Other disclosures: **JEH** BMS, Celgene. **BL:** Seagen Inc. **JM:** Janssen, AstraZeneca, TG Therapeutics. **ML:** Alnylam, Bristol Myers Squibb, Caelum, Celgene, GlaxoSmithKline, Janssen Pharmaceuticals, Karyopharm, Kite, Kura Oncology, Oncopeptides, Pfizer, Sanofi, Takeda. **MAS:** nothing to disclose. **RN** BMS, GSK, Janssen, Karyopharm, Takeda. **MHT** nothing to disclose. **CAY** Seagen Inc. **DJG** Seagen Inc., Celgene, BMS, Janssen Biotech, GSK, Neoleukin Therapeutics, SpringWorks Therapeutics, Legend Biotech, Juno Therapeutics; **AA** nothing to disclose.

Abstract No. 2740
ASH Annual Meeting & Exposition; Atlanta, Georgia and Virtual, December 11–14, 2021