Phase 1 / 2 Study of Belantamab mafodotin in Combination with Pomalidomide and Dexamethasone: Results for Part 1 Dose Finding

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INTRODUCTION

- Outcomes for patients (pts) with relapsed/refractory multiple myeloma (RRMM) remain poor with the majority of pts unable to achieve deep and durable responses.
- Belantamab mafodotin (Belamaf:GSK2857916) is a BCMA-directed antibody-drug conjugate(ADC) with an afucosylated, humanised, anti-BCMA monoclonal IgG1 conjugated to monomethyl auristatin F (MMAF)
- Belamaf specifically binds to BCMA, eliminating myeloma cells by multimodal mechanisms, including delivery of MMAF to BCMA-expressing malignant plasma cells, enhanced antibody-dependent cellular cytotoxicity (ADCC)/antibody-dependent cellular phagocytosis (ADCP) activity and immunogenic cell death[1]
- It showed clinically meaningful single agent activity with a manageable safety profile in pts with RRMM[2,3]
- The immune mediated anti-MM activities of belamaf can be further enhanced by immunomodulatory drugs (IMiDs) as has been demonstrated with other mAb-IMID combinations making this treatment strategy particularly attractive
- The ability of IMiDs to enhance immune responses including ADCC forms the basis for combining belantamab with pomalidomide (POM) and dexamethasone (DEX)

OBJECTIVES

Part 1: To determine the safety, tolerability and recommended part 2 dose (RP2D)

Part 2: To evaluate clinical activity and confirm safety of belamaf administered in combination with POM and DEX according to dosing schedule identified in Part 1

METHODS

Study Population

Key Eligibility Criteria

- ≥ 2 prior lines of treatment, lenalidomide (LEN) refractory, proteasome inhibitor (PI) exposed and progressed on or within 60 days of last MM therapy
- Measureable disease by IMWG 2016 criteria; an ECOG PS 0–2 and adequate organ function (including kidney)

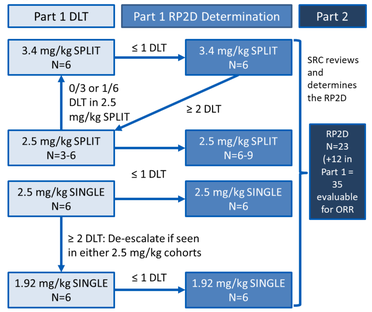
Study Endpoints

- **Part 1**: Define the maximum tolerated dose (MTD)/RP2D
- **Part 2**: Assess efficacy: overall response rate (ORR), PFS, DOR, OS and safety [% of pts with adverse events (AEs)]

Table 1: *Treatment regimens for each dose cohort.*

Dose Level	Belantamab mafodotin IV Q4W	POM PO Days 1-21	DEX PO Days 1, 8, 15, 22
2b	3.4 mg/kg SPLIT Days 1 and 8	4 mg QD	40 mg ≤ 75 years old 20 mg > 75 years old
1b	2.5 mg/kg SPLIT Days 1 and 8		
1a	2.5 mg/kg SINGLE Day 1		
-1a	1.92 mg/kg SINGLE Day 1		

Figure 1*: Trial design.*



Study Design

- **Part 1**: dose escalation accomplished using standard 3+3
- Belamaf dose of 1.92 mg/kg may be tested if starting dose level of 2.5 mg/kg is not tolerated or ≥ 2 DLT observed
- Up to 12 pts maybe enrolled per cohort to better inform dose for Part 2
- **Part 2**: expansion N=23 (+12 in Part 1) for ORR determination (IMW 2016 criteria)

RESULTS

Patient Demographics and Disease Characteristics

- As of Feb 1, 2020, 24 patients were enrolled in Part 1 and had completed the 28-day DLT observation period (**Table 2**)
- Median age was 62.4 years and the median prior lines of treatment was 3 (range:2-5)
- Consistent with inclusion criteria, 100% were PI and LEN exposed, 75% LEN and PI refractory while 37.5% were daratumamab (DARA) refractory
- 41.7% were considered high risk by FISH cytogenetics (del17p13. t(4;14) and/or t(14;16)

Table 2: *Baseline patient characteristics.*

Characteristics (N=24)	%
Age, median (range), years	62.5 (range 36-78)
Previous regimens, median (range)	3 (range 2-5)
Stem cell transplant	58.3%
PI exposed (refractory)	100 (83.3)
LEN exposed (refractory)	100 (87.5)
DARA exposed (refractory)	37.5 (37.5)
LEN and PI refractory	75
LEN, PI, and DARA refractory	33%
ISS stage I/II/III	50/50/0
High-risk cytogenetics [del17p13, t(4;14), t(14;16)]	5/12 (41.7%)

Patient Disposition

- Pts were enrolled at the following dose levels and schedules: 1.92 SINGLE (n=11), 2.5 SINGLE (n=7), 2.5 SPLIT (n=3), 3.4 SPLIT (n=3)
- As of the data cutoff, 2 pts had discontinued treatment due to disease progression (n=1), pt decision (n=1); 22 pts were ongoing

Table 3: *Treatment disposition.*

Patient Disposition	Total (N=24)
Dose Cohort	
2b: 3.4 SPLIT	3
1b: 2.5 SPLIT	3
1a: 2.5 SINGLE	7
-1a: 1.92 SINGLE	11
Ongoing	22
Discontinued	2
Progression	1
Patient decision	1
Median number of cycles, n (range)	4.5 (1-14)

Dosing Limiting Toxicities (DLTs)

- Two DLTs of Grade 3 corneal events were reported, 1 each in the 2.5 SINGLE and 3.4 SPLIT dosing cohorts (**Table 4**)

Table 4: *DLT by dose cohort.*

Dose Cohort	DLT
1a: 2.5 SINGLE	1 patient: Gr 3 corneal toxicity
2b: 3.4 SPLIT	1 patient: Gr 3 corneal toxicity

Safety

- AEs were reported by 22 (91.7%) pts and considered to be treatment-related in 19 (79.2%)
- The most frequent treatment emergent AEs (TEAEs) (≥25%) were keratopathy leading to decreased visual acuity and blurred vision, thrombocytopenia, neutropenia, fatigue, fever, glaucoma, diarrhea, constipation, dyspnea, and rash (**Table 5**)
- Grade 3/4 occurring in ≥10% of pts were thrombocytopenia, neutropenia and corneal events (**Table 6**)
- Serious AEs were noted in 10 (41.7%) pts and are listed in **Table 7**
- No pt discontinued treatment due to AEs and there were no Grade 5 AEs

Table 5: *Most frequent TEAEs.*

Common (≥25% All Grade) TEAEs	%
Corneal toxicity	62.5
Thrombocytopenia	50
Neutropenia	50
Decreased visual acuity	45.8
Fatigue	41.7
Fever	33.3
Blurred vision	29.2
Glaucoma	29.2
Diarrhea	29.2
Constipation	25
Dyspnea	25
Rash	25

Table 6: *Most frequent Grade 3/4 TEAEs.*

Common (≥10% Grade 3/4) TEAEs	%
Corneal events	37.5
Neutropenia	33
Thrombocytopenia	29.2

Table 7: *Number of serious adverse events.*

SAE Term	Events
Fever	7
Non-cardiac chest pain	2
Bronchitis	1
Hypokalemia	1
Infusion related reaction	1
Febrile neutropenia	1
Pneumonia	1
RSV infection	1
Spinal cord compression	1
Cellulitis	1

Clinical Efficacy

- 18 pts were evaluable for confirmed response (**Figure 2**)
- The ORR (≥PR) across all cohorts was 83.3% (5 PR, 9 VGPR and 1 sCR) noting short follow-up in some cohorts
- The ORR for cohort 1a (2.5 mg/kg SINGLE) with the longest follow-up, was 100% (6 VGPR and 1 sCR), with all patients continuing beyond 12 cycles (**Figure 3**)

Figure 2: *Confirmed responses.*

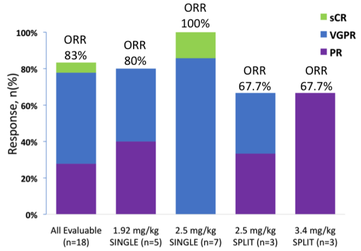
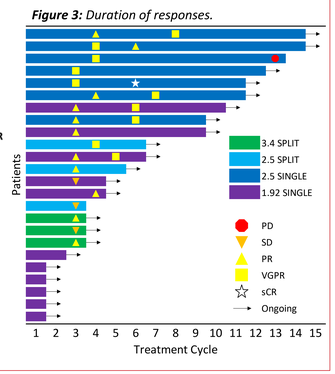


Figure 3: *Duration of responses.*



CONCLUSIONS

- Belamaf given in combination with POM and DEX demonstrates a manageable safety profile that is consistent with the known safety profiles of belamaf and POM
  - The most common AEs are thrombocytopenia, neutropenia and corneal events (keratopathy)
  - Keratopathy is a well described toxicity of MMAF-ADCs and resulted in blurred vision and decreased visual acuity but did not lead to treatment discontinuation
- The R2PD is pending completion of the current treatment cohorts
- Belamaf shows promising preliminary clinical activity in combination with POM and DEX
- Responses are deep and durable when administered in combination with POM and DEX dosed as 2.5 mg/kg IV on day 1 of each 28-day cycle; whereas assessment of clinical activity in the other cohorts is immature
- Overall, the results are promising and warrant further evaluation

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DISCLOSURES

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