Messe Wien Exhibition & Congress Center

Vienna, Austria

8-11 September 2021

International Myeloma Society

EXTENDED FOLLOW-UP SAFETY AND EFFICACY RESULTS OF BELANTAMAB MAFODOTIN (BELAMAF) 1.92 MG/KG OR 2.5 MG/KG COMBINED WITH POM AND DEX FOR THE TREATMENT OF RELAPSED/REFRACTORY MULTIPLE MYELOMA (Abstract ID: 1082298)

CMRG Canadian Myeloma RESEARCH GROUP
Transforming Myeloma Research

S. Trudel[1], A. McCurdy[2], H. Sutherland[3], M. Louzada[4], C.P. Venner[5], D. White[6], H. Mian[7], R. Kotb[8], I. Othman[9], F. Camacho[10], M Kardjadj[10], M Fu[10], E. Gul[10] and D. Reece[10]

[1]Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [2]The Ottawa Hospital, Ottawa, Ontario, Canada; [3]Vancouver General Hospital, BC Cancer, Vancouver, British Columbia, Canada; [4]London Health Sciences Centre, London, Ontario, Canada; [5]Cross Cancer Institute, University of Alberta, Edmonton, Alberta, Canada; [6]Dalhousie University and QEII Health Sciences Centre, Halifax, Nova Scotia, Canada; [7]Juravinski Cancer Centre, Hamilton, Ontario, Canada; [8]Cancer Care Manitoba, Winnipeg, Manitoba, Canada; [9]Allan Blair Cancer Centre, University of Saskatchewan, Regina, Saskatchewan, Canada; [10]Canadian Myeloma Research Group (CMRG), Ontario, Canada

INTRODUCTION

- Outcomes for patients (pts) with relapsed/refractory MM (RRMM) remain poor with the majority of pts unable to achieve deep and durable responses.
- Belantamab mafodotin (belamaf) is a first-in-class antibody-drug conjugate (ADC) targeting B-cell maturation antigen (BCMA) that has demonstrated clinically meaningful activity as monotherapy in RRMM.[1]
- Pre-clinical studies demonstrate that the immune mediated anti-myeloma activities of belamaf are enhanced by immunomodulatory drugs (IMiDs).[2] providing the rationale for combining belamaf with pomalidomide (POM).
- The Algonquin study is an ongoing Phase 1/2 trial designed to evaluate the recommended Part 2 dose (RP2D), safety, and preliminary efficacy of belamaf in combination with POM and dexamethasone (DEX) (B-Pd) pts with RRMM.
- The initial data from the dose-finding phase of the study identified 2.5 mg/kg in combination with standard dosing of POM/DEX as the maximum tolerated dose[3]

AIMS

Part 1: To determine the safety, tolerability and RP2D

Part 2: To evaluate clinical activity and confirm safety of B-Pd according to dosing schedule identified in Part 1

RESULTS

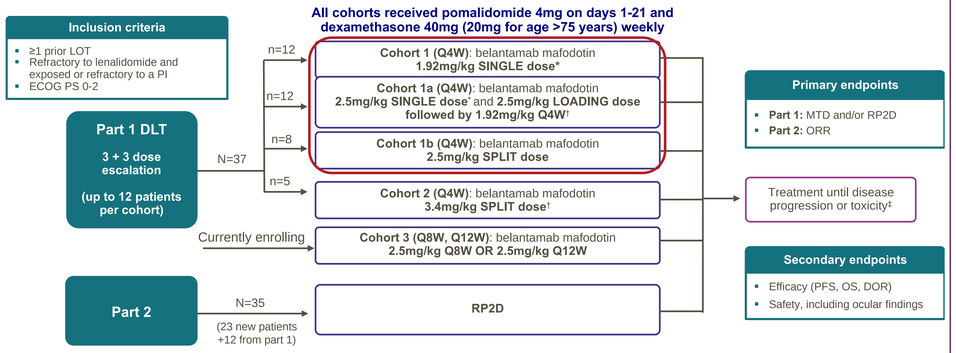
Patient Demographics and Disease Characteristics

- As of Aug 20, 2021, 32 pts were enrolled in Part 1 at doses of 1.92 or 2.5 mg/kg administered at each cycle (28 days) together with POM/DEX (Pd)
- Median age was 64 years and median prior lines of treatment was 3
- Consistent with inclusion criteria, 100% were PI and LEN exposed, 75% LEN and PI refractory while 31% were daratumumab (DARA) LEN, and PI refractory

***Table 1**: Baseline patient characteristics.*

Characteristics (n=32)	(%)
Age, median (range), years	64 (36-81)
Previous regimens, median (range)	3 (1-5)
Stem cell transplant	62.5%
PI exposed/refractory	100% / 81.2%
LEN exposed/refractory	100% / 90.6%
DARA exposed/refractory	37.5% / 37.5%
LEN and PI refractory	75%
LEN, PI, and DARA refractory	31.2%
ISS Stage I/II/III/Unknown	32.2% / 34.4% / 15.6% / 18.7%
High-risk cytogenetics [del17p13, t(4;14), t(14;16)]	28.1%

METHODS



- Here we report updated tolerability and efficacy data for pts treated at each cycle with belamaf, 1.92 mg/kg (Cohort 1; n=12) or 2.5 mg/kg (Cohorts 1a and 1b; n=20) in combination with Pd

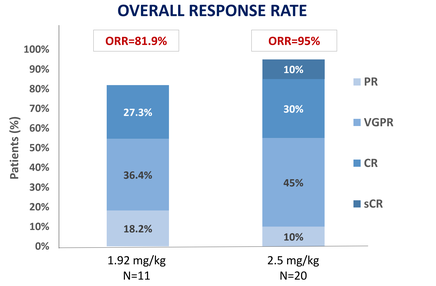
RESULTS

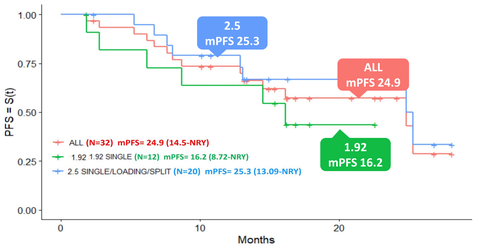
Clinical Efficacy

Patient Disposition

***Table 2**: Patient Disposition*

Treatment Status	1.92 mg/kg (Cohort 1) n=12	2.5 mg/kg (Cohorts 1a-b) n=20
Ongoing	5 (41.7%)	9 (45%)
Discontinued	7 (58.3%)	11 (55%)
Reason for discontinuation		
Disease progression	6 (50%)	8(40%)
Adverse event	0	1 (5%)
Decision by patient	1 (8.3%)	2 (10%)
Investigator decision	0	0
Exposure, # of cycles, median (range)	14 (2-24)	14.5 (3-30)
Duration of follow up, median (range), months	14.97 (1.84-22.60)	13.30 (2.40-28.16)





- 11 pts in the 1.92 mg/kg cohort and 20 pts in the 2.5 mg/kg cohorts were evaluable for response
- The ORR (≥PR)/VGPR rates in the 1.92 mg/kg and 2.5 mg/kg cohorts respectively were 82%/64% and 95%/85%
- The PFS was longer at 25.3 months in the 2.5 mg/kg group vs 16.2 months for pts that received the 1.92 mg/kg dose

RESULTS

Safety Overview

- AEs were reported by 100% of pts (N=32) and considered to be treatment-related in 91.7% and 85% of pts in the 1.92 and 2.5 mg/kg cohorts, respectively
- The most frequent ≥Gr 3 treatment emergent non-ocular AEs (TEAEs) were neutropenia, thrombocytopenia, neutropenia, dyspnea and lung infection (**Table 3**)
- At 12 months of treatment, ≥Gr 3 keratopathy (eye exam finding) and blurred visions were reported in 42.9%/28.6% of pts in the 1.92mg/kg (n=7) cohort and 100%/33.3% of pts treated at 2.5 mg/kg (n=15)
- SAEs were observed in 66.7% and 45% of pts in the 1.92 and 2.5 mg/kg cohorts, respectively and no Grade 5 AE was reported
- Only 1 pt discontinued treatment due to an AE of multifocal leukoencephalopathy this occurred in the 2.5 mg/kg cohort

***Table 3**: Most frequent non-corneal AEs*

AE	1.92 mg/kg (Cohort 1) N=12		2.5 mg/kg (Cohorts 1a-b) N=20	
AEs ≥25%	**Any Gr**	**≥Gr 3**	**Any Gr**	**≥Gr 3**
Thrombocytopenia	7 (58.3%)	5 (41.7%)	9 (45%)	4 (20%)
Neutropenia	7 (58.3%)	6 (50%)	13 (65%)	10 (50%)
Dyspnea	3 (25%)	3 (25%)	5 (25%)	3 (15%)
Lung infection	3 (25%)	3 (25%)	5 (25%)	1 (5%)
Fever	7 (58.3%)	0 (0%)	8 (40%)	0 (0%)
Constipation	6 (50%)	0 (0%)	5 (25%)	0 (0%)
Fatigue	6 (50%)	0 (0%)	13 (65%)	0 (0%)
Nausea	3 (25%)	0 (0%)	4 (20%)	0 (0%)
Cataract	4 (33.3%)	0 (0%)	7 (35%)	0 (0%)

***Table 4**: Most frequent corneal AEs and resulting dose modifications*

Corneal AEs (Total)	1.92 mg/kg (Cohort 1) N=12		2.5 mg/kg (Cohorts 1a-b) N=20	
n(%)	**Any Gr**	**≥Gr 3**	**Any Gr**	**≥Gr 3**
Keratopathy	11 (91.7%)	5 (41.7%)	20 (100%)	14 (70%)
Blurred vision	10 (83.3%)	4 (33.4%)	18 (60%)	9 (45%)
Dose holds	7 (58.3%)		20 (100%)	
Median dose holds (range)	6 (1-8)		5 (1-16)	
Dose delays/ reductions	2 (16.7%) / 0 (0%)		4 (20%) / 11 (55%)	
Corneal AEs (12 months)	**N=7**		**N=15**	
Keratopathy	7 (100%)	3 (42.9%)	15 (100%)	15 (100%)
Blurred vision	7 (100%)	2 (28.6%)	14 (93.3%)	5 (33.3%)

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 Pd
  - The most common AEs are thrombocytopenia, neutropenia and corneal events (keratopathy and blurred vision)
  - ≥Gr 3 keratopathy were higher with the 2.5 mg/kg dose; however, symptoms of ≥Gr 3 blurred vision were similar between the two groups for patients that had received 12 cycles of treatment
- Both dose cohorts (1.92 and 2.5 mg/kg) demonstrated deep and durable responses; however, the the 2.5 mg/kg dose appears to have better efficacy
- Alternative dosing schedules with the 2.5 mg/kg dose to optimize efficacy and safety are under evaluation

REFERENCES

[1]Lonial et al, *Lancet Oncol*.2020;21(2):207; [2] Tai et al, *Blood*..2014;123(20):3128; [3]Trudel et al, ASH 2020; 725a

ACKNOWLEDGEMENTS

Study is funded by GlaxoSmithKline (ID: 205207).

CONTACT INFORMATION

suzanne.trudel@uhn.ca.

DISCLOSURES: TRUDEL: Consultancy: Celgene, AMGEN, GSK; Honoria: Celgene, Janssen, Takeda, Amgen, Sanofi, Karyopharm; Grant funding: Celgene, Amgen, Janssen, GSK, Genentech; LOUZADA: Honoraria and consultancy: Janssen, Celgene, Pfizer, Amgen, Takeda; SUTHERLAND: Research funding: Janssen, GSK, Karyopharm; Consultancy: Celgene, Amgen, Janssen; WHITE: Honoraria: Amgen, Celgene, Janssen, Sanofi, Takeda; VENNER: Honoraria: Janssen, Amgen, Takeda; Research funding: Celgene, Amgen; KOTB: Research funding: Merck; Shares: Karyopharm; Honoraria: Celgene, Janssen, Amgen, Takeda, Merck; OTHMAN: Honoraria: Celgene, Janssen, Sanofi, Novartis, Takeda, Roche; MIAN: Honoraria: Janssen, Amgen, Takeda, Celgene; KARDJADJ: None; FU: None; GUL: None; CAMACHO: consulting: Janssen, AbbVie, Bausch-Health; REECE: Research funding: Otsuka, Celgene, Janssen, Takeda, Merck, BMS, Millennium; Consultancy: Celgene, Janssen, Amgen, Karyopharm, Takeda; Honoraria: Celgene, Janssen, Amgen, Takeda