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P884 BELANTAMAB MAFODOTIN PLUS LENALIDOMIDE AND DEXAMETHASONE IN TRANSPLANT INELIGIBLE PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA: UPDATED RESULTS FROM THE PHASE 1/2 BELARD STUDY

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background:

Belantamab mafodotin (belamaf; GSK2857916) is a multi-modal antibody-drug conjugate that targets BCMA, which has shown efficacy and a manageable safety profile in pretreated patients (pts) with multiple myeloma (MM). Also, preclinical data demonstrate synergy between belamaf and lenalidomide, suggesting added benefit in the combination of belamaf plus lenalidomide and dexamethasone (Rd).

Aims:

We present updated safety and efficacy results of belamaf-Rd in transplant ineligible (TI), newly diagnosed MM (NDMM) pts.

Methods:

The ongoing, prospective, open-label, phase 1/2 BelaRd study (NCT04808037) aims to enroll 66 pts with TI NDMM, with ECOG-PS ≤2 and adequate organ function. Part 1 evaluates the safety/tolerability of three belamaf doses (2.5, 1.9, 1.4 mg/kg, Q8W) plus Rd in 36 pts, and establishes the recommended phase 2 dose (RP2D). Part 2 evaluates the safety and efficacy of the RP2D in 2 groups (15 pts each) and assesses 2 sets of guidelines for ocular adverse events (OAEs) to identify the optimal way to manage belamaf-related corneal damage. Eye examinations include Snellen best corrected visual acuity (BCVA) and corneal examination (slit lamp examination). Ocular symptoms are classified by Common Terminology Criteria for Adverse Events (CTCAE) v5.0. This descriptive analysis presents the updated safety and efficacy results for all Part 1 pts (cut-off date 15/12/22).

Results:

Of the 36 pts [mean age: 73 years; male: 19 (53%)] in Part 1, 31 (86%) are still on treatment, while 5 (14%) have discontinued [4 pts due to belamaf-unrelated adverse events (AEs); 1 pt withdrew consent]. The median belamaf administrations and number of cycles reached were 6 (2-10) and 15 (3-22), respectively, while the median follow-up time was 15 months (3-23). The most common (≥ 10% of patients) non-ocular ≥ Gr3 treatment-emergent adverse events (TEAEs) were fatigue (21 pts, 58%), rash (6 pts, 17%), diarrhoea (5 pts, 14%) and COVID -19 infection (4 pts, 11%), while no ≥ Gr3 thrombocytopenias and infusion-related reactions were reported. Regarding ocular manifestations suggesting an impairment in vision, from a total of 499 ocular assessments, Gr2 and Gr3 BCVA changes were noted in 164 (33%) and 54 (11%), while a meaningful BCVA decline (worse than 20/50 in the better seeing eye) was observed in 38 (8%), with a median time to resolution of 1 month. In terms of ≥ Gr2 symptoms directly related to decreased vision, blurred vision and visual impairment were observed in 38 (8%) and 98 (20%) with a median time to resolution of 2 months. In terms of other ≥Gr2 ocular symptoms, observed in ≥10% of assessments, dry eye was noted in 96 (20%), with a median time to resolution of 3 months. Regarding

corneal findings, in 501 slit lamp examinations, Gr2 and Gr4 keratopathy was observed in 55 (11%) and in 2 (<1%), respectively, with a median time to resolution of 4 months. The overall response rate [partial response (PR) or better] was 100.0% [36 pts; stringent complete response: 14% (5 pts); complete response: 19% (7 pts); very good partial response: 47% (17 pts); PR: 19% (7 pts)], with median time to first response of 1 month.

Summary/Conclusion:

Part 1 of the BelaRd study showed that the belamaf-Rd combination is safe and effective in TI NDMM pts. The frequency of meaningful decline in the pts' vision was minimal, and OAEs had only a minor impact on the pts' daily functioning. Furthermore, rapid and deep responses were observed in all cohorts, with all pts achieving ≥PR.

Table 1. Characteristics of patients at baseline and after treatment

	Overall	Cohort 1 (2.5 mg/kg)	Cohort 2 (1.9 mg/kg)	Cohort 3 (1.4 mg/kg)
Patients	**36**	**12**	**12**	**12**
Age in years, median (range)	72.5 (64.0-86.0)	75.0 (66.0-86.0)	74.5 (68.0-82.0)	69.0 (64.0-79.0)
Presence of high-risk cytogenetics*, n (%)	3 (8.3)	1 (8.3)	2 (16.7)	0 (0.0)
Presence of lytic bone lesions, n (%)	19 (52.8)	7 (58.3)	7 (58.3)	5 (41.7)
Intended dose intensity (mg/kg/Q4W)	-	1.25	0.95	0.7
Actual dose intensity (mg/kg/Q4W), median (range)	0.7 (0.4-1.7)	0.9 (0.6-1.7)	0.7 (0.5-1.0)	0.5 (0.4-0.7)
Relative dose intensity (%), median (range)	72.2 (46.4-102.2)	68.4 (46.4-102.2)	71.6 (55.0-100.0)	76.2 (57.3-91.8)
Gr≥3 Infections and Hematologic and belamaf related OAEs, n (%)				
Covid-19	4 (11.1)	2 (16.7)	0 (0.0)	2 (16.7)
Lower Respiratory Tract Infection	1 (2.8)	0 (0.0)	0 (0.0)	1 (8.3)
Pneumonia	1 (2.8)	1 (8.3)	0 (0.0)	0 (0.0)
Thrombocytopenia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Febrile Neutropenia	1 (2.8)	0 (0.0)	1 (8.3)	0 (0.0)
Leukopenia	2 (5.6)	2 (16.7)	0 (0.0)	0 (0.0)
Neutropenia	3 (8.3)	1 (8.3)	1 (8.3)	1 (8.3)
Dry Eye	1 (2.8)	1 (8.3)	0 (0.0)	0 (0.0)
Keratopathy	2 (5.6)	1 (8.3)	0 (0.0)	1 (8.3)
Vision Blurred	3 (8.3)	2 (16.7)	0 (0.0)	1 (8.3)
Visual Acuity Reduced	18 (50.0)	5 (41.7)	6 (50.0)	7 (58.3)
Visual Impairment	4 (11.1)	3 (25.0)	0 (0.0)	1 (8.3)
OSDI assessments reported ADL difficulties 'most' or 'all' of the time (Q6-Q9)/ Total OSDI assessments (%)**	12/465 (2.6)	6/146 (4.1)	3/173 (1.7)	3/146 (2.1)
Number of belamaf doses skipped due to OAE/Number of planned doses (%)	86/298 (28.9)	34/98 (34.7)	28/106 (26.4)	24/94 (25.5)
At least VGPR, n (%)	29 (80.6)	9 (75.0)	11 (91.7)	9 (75.0)
At least CR, n (%)	12 (33.3)	6 (50.0)	4 (33.3)	2 (16.7)

*High risk cytogenetics defined as Del 17p, t(14:16) or t(4:14)
**Related to OSDI items Q6-Q9
ADL, activities of daily living; CR, complete response; Gr, grade; n, number of subjects; OAE, ocular adverse event; OSDI, Ocular Surface Disease Index; Q4W, every 4 weeks; VGPR, very good partial response