Submitted by:
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Dear NCCN Multiple Myeloma Guidelines Panel Members,

On behalf of Celgene Corporation, we respectfully request the NCCN Guidelines Panel for Multiple Myeloma review recently published data on the use of pomalidomide (POMALYST®) in combination with bortezomib and dexamethasone (PVd) in patients with relapsed/refractory multiple myeloma (rrMM).

Specific Changes:

We request consideration of a Category 1, Preferred Regimen recommendation for previously treated multiple myeloma to reflect the randomized Phase III study (OPTIMISMM [MM-007]) in patients with rrMM recently published in Lancet Oncology (Richardson et al., 2019).

FDA Clearance:

Pomalidomide is a thalidomide analogue indicated, in combination with dexamethasone, for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy (Celgene Corporation).

Bortezomib is indicated for the treatment of patients with multiple myeloma (Takeda Oncology).

PVd is not approved by the FDA for the treatment of patients with rrMM.

Rationale for Proposed Change:

The open-label, multicenter, randomized, Phase III study (OPTIMISMM) evaluated the safety and efficacy of PVd (n=281) vs. Vd alone (n=278) in 559 patients with rrMM (Richardson et al., 2019). The regimens included:

- Pomalidomide 4mg orally on Days 1-14 of a 21-Day cycle,
- Bortezomib 1.3 mg/m^2 on Days 1,4, 8, and 11 of a 21-Day cycle in Cycles 1-8 and on Days 1 and 8 after Cycle 8,
- Dexamethasone 20mg (or 10mg if >75 years) orally on Days 1, 2, 4, 5, 8, 9, 11, and 12 of a 21-Day cycle in Cycles 1-8 and on Days 1, 2, 8, and 9 after Cycle 8.

Patients included in the study received 1-3 prior lines of therapy (including ≥2 cycles of previous lenalidomide) and were pomalidomide naïve. Patients with prior bortezomib exposure were included if they had no disease progression at the bortezomib 1.3 mg/m^2 twice weekly dose or had progressed on lower dose.

Overall, 200 (71.2%) PVd and 191 (68.7%) Vd patients were lenalidomide refractory, and 212 (75%) PVd and 213 (77%) Vd patients received a prior proteasome inhibitor. Patients had received a median of 2 prior therapies, with 111 (39.5%) in the PVd arm and 115 (41.4%) in the Vd arm receiving one prior line of therapy. Of the patients who received one prior line of therapy, 64 (58%) in the PVd arm and 65 (57%) in the Vd arm were refractory to lenalidomide.

The primary endpoint was progression-free survival (PFS) and secondary endpoints included overall response rate (ORR) by IMWG criteria, overall survival (OS) and duration of response (DOR). Please see the following table for select efficacy results.

Table 1. Efficacy Results: PFS, ORR, OS, and DOR

	PVd	Vd	HR (95% CI), P-value
Median PFS, months			
Total population	11.20	7.10	0.61 (0.49, 0.77), P<0.0001
Lenalidomide refractory patients	9.53	5.59	0.65 (0.50, 0.84), P=0.0008
Patients who received 1 prior line of therapy	20.73	11.63	0.54 (0.36, 0.82), P=0.0027
Patients who were lenalidomide refractory and received 1 prior line of therapy	17.84	9.49	0.55 (0.33, 0.94), P =0.03
ORR			
≥ PR	82.2%	50.0%	P<0.0001
≥VGPR	52.7%	18.3%	P<0.0001
OS data has not matured at time of publication			
Median DOR, months (95% CI)			
	13.7 (10.9, 18.1)	10.9 (8.1, 14.8)	P=0.06

Median follow-up of 15.9 months

The most commonly reported (≥15% in either arm; PVd vs. Vd, respectively) grade 3/4 adverse events included neutropenia (42% vs. 9%), infections (31% vs. 18%), and thrombocytopenia (27% vs. 29%). Eight deaths were reported as treatment related: 6 (2%) in the PVd arm and 2 (1%) in the Vd arm. Serious adverse events were reported in 57% vs. 42% of patients in the PVd and Vd arms respectively. Second primary malignancies were reported in 3% of patients in the PVd arm and in 1% of patients in the Vd arm.

A copy of the OPTIMISMM publication is enclosed for your review. Your consideration of this submission is greatly appreciated.

Sincerely,

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Unicel-Anne Flores, PharmD
Manager, Global Medical Information

Amit Agarwal, MD, PhD
Executive Director, US Medical Affairs

REFERENCES

1. Celgene Corporation. Pomalyst (pomalidomide) [Package Insert]. Summit, NJ: Celgene Corporation. http://www.pomalyst.com/.
2. Takeda Oncology. Velcade® (bortezomib) [Package Insert]. Cambridge, MA: Takeda Oncology. https://www.velcade.com/files/PDFs/VELCADE_PRESCRIBING_INFORMATION.pdf. Accessed on May 13, 2019. Velcade is a registered trademark of Millennium Pharmaceuticals, Inc.
2. Richardson P., Oriol A, Beksac M, et al. Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial. Lancet Oncol. 2019. doi:10.1016/S1470-2045(19)30152-4.