



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 interim data from the Phase III MAIA study (MMY3008; NCT02252172) on the use of lenalidomide (REVLIMID®) in combination with daratumumab and dexamethasone (DRd) in patients with transplant-ineligible newly diagnosed multiple myeloma (NDMM).

Specific Changes:

We request consideration of a Category 1, Preferred Regimen recommendation for primary therapy in non-transplant candidates with multiple myeloma and an update within the discussion section to reflect the interim results from the Phase III MAIA study abstract published in the journal Blood described below (Facon et al., 2018).

FDA Clearance:

Lenalidomide is a thalidomide analogue indicated for the treatment of patients with multiple myeloma in combination with dexamethasone. Please see the enclosed lenalidomide prescribing information for additional approved indications (Celgene Corporation).

Daratumumab is a CD38-directed cytolytic antibody indicated in combination with bortezomib, melphalan and prednisone for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant; in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy; in combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor (PI); and as a monotherapy for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy, including a PI and an immunomodulatory agent, or who are double-refractory to a PI and an immunomodulatory agent (Janssen Biotech).

DRd is not approved by the FDA for the treatment of transplant-ineligible NDMM.

Rationale for Proposed Change:

The open-label, multicenter, randomized, international Phase III MAIA study evaluated the safety and efficacy of DRd (n=368) compared to lenalidomide in combination with dexamethasone (Rd; n=369) in 737 patients with transplant-ineligible NDMM (Facon et al., 2018). All patients (median age 73 [range: 45-90 years]), 44% of patients \geq 75 years), were randomized to receive DRd or Rd and were treated until disease progression or unacceptable toxicity. The primary endpoint was progression-free survival (PFS), and key secondary endpoints included overall response rate (ORR), minimal residual disease (MRD)-negativity rate, complete response (CR) rate, very good partial response (VGPR) rate, overall survival (OS) and safety.

The prespecified interim analysis occurred after 239 PFS events on September 24, 2018 with a median follow up of 28 months. Median PFS was not reached for the DRd arm and was 31.9 months for the Rd arm (HR 0.55 [95% CI 0.43 – 0.72]; $P < 0.0001$) indicating a 45% reduction in the risk of progression or death in patients who received DRd. Patients with \geq CR included 47.6% in the DRd arm vs. 24.7% in the Rd arm (odds ratio [OR] 2.75; [95% CI 2.01 – 3.76]; $P < 0.0001$). Patients with \geq VGPR included 79.3% in the DRd arm vs. 53.1% in the Rd arm (OR 3.4 [95% CI 2.45-4.72]; $P < 0.0001$). A total of 19% of patients have died (HR for OS 0.78 [95% CI 0.56-1.1]); follow up is ongoing. Patients in the DRd arm reported higher rates (\geq 5% difference) of grade 3/4 pneumonia, neutropenia, and leukopenia.

A copy of the MAIA abstract, recently presented at the 60th American Society of Hematology (ASH) annual 2018 meeting, is enclosed for your review. Your consideration of this submission is greatly appreciated.

Sincerely,



Katherine Kim, PharmD
Associate Director, Global Medical Information



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

REFERENCES

1. Celgene Corporation. Revlimid (lenalidomide) [Package Insert]. Summit, NJ: Celgene Corporation. <http://www.revlimid.com/>.
2. Janssen Biotech. Darzalex[®] (daratumumab) [Package Insert]. Horsham, PA: Janssen Biotech. <http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX-pi.pdf>. Accessed on February 20, 2019. Darzalex is a registered trademark of Johnson & Johnson.

3. Facon T, Kumar SK, Plesner T, et al. Phase 3 Randomized Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Patients with Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplant (MAIA) [abstract]. *Blood*. 2018;132(suppl 1): LBA-2.