

May 2, 2017

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**NCCN Guidelines Panel: Multiple Myeloma**

On behalf of Merck & Co., Inc., I respectfully request the NCCN Panel for Multiple Myeloma to review the enclosed information with KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V3.2017 for Multiple Myeloma.

Specific changes requested:

We respectfully request the panel to consider adding KEYTRUDA (pembrolizumab), in combination with pomalidomide and low-dose dexamethasone, for the treatment of patients with relapsed/refractory multiple myeloma.

FDA approval:

KEYTRUDA (pembrolizumab) is not approved for the treatment of patients with multiple myeloma. For additional information on FDA-approved indications, please see enclosed prescribing information (PI).<sup>1</sup>

Rationale:

In a single-center, phase II study, 48 patients with relapsed/refractory multiple myeloma (RRMM) received pembrolizumab 200 mg IV every 2 weeks, pomalidomide 4 mg orally daily for 21 days and dexamethasone 40 mg orally weekly; cycles were repeated every 28 days for 2 years and responding patients continued on monthly pembrolizumab with pomalidomide and dexamethasone. Patients had a median of 3 (range: 2-5) lines of therapy, median age 64 (range: 35-83) years and had received both immune modulatory agent and proteasome inhibitor; 73% were refractory to both; 31 patients had prior ASCT and 30 patients had high-risk cytogenetics.<sup>2</sup>

Treatment-related adverse events grade 3 and higher occurred in 42% of patients, including neutropenia (42%), anemia (21%), lymphopenia (15%), hyperglycemia (21%) and pneumonia (15%). Autoimmune adverse events included pneumonitis (13%) and hypothyroidism (10%), mostly grade ≤2. Objective responses occurred in 60% of patients including: sCR/CR (8%), VGPR (19%) and PR (33%); median duration of response was 14.7 months (95% CI 7.9-17.5). At a median follow-up of 15.6 months, median progression free survival was 17.4 months (95% CI 11.7-18.8) and median overall survival was not reached (95% CI 18.9-NR). Pembrolizumab, pomalidomide and low-dose dexamethasone showed acceptable safety and durable responses in RRMM patients.<sup>2</sup>

The following resources are submitted to assist the committee with their review:

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Badros A *et al.* Pembrolizumab, Pomalidomide and Low Dose Dexamethasone for Relapsed/Refractory Multiple Myeloma. Blood First Edition Paper, prepublished online May 1, 2017; DOI 10.1182/blood-2017-03-775122

Thank you for considering this request. Below is my contact information should you need to contact me for additional information.

Sincerely,

A handwritten signature in black ink, appearing to read 'Maria Rivas', with a stylized, cursive script.

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