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NCCN Guidelines Panel: B-Cell Lymphomas

On behalf of Merck & Co., Inc., I respectfully request the NCCN Panel for B-Cell Lymphomas to review the enclosed information with KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V3.2017 for B-Cell Lymphomas, more specifically for primary mediastinal large B-cell lymphoma.

Specific changes requested:

We respectfully request the panel to consider adding KEYTRUDA (pembrolizumab) for the treatment of patients with relapsed/refractory primary mediastinal large B-cell lymphoma.

FDA approval:

KEYTRUDA (pembrolizumab) is not approved for the treatment of patients with primary mediastinal large B-cell lymphoma. For additional information on FDA-approved indications, please see enclosed prescribing information (PI).[1]

Rationale:

There are limited treatment options for relapsed/refractory primary mediastinal large B-cell lymphoma (rrPMBCL) and prognosis is generally poor with overall response rates (ORR) of 0 to 25% and 2-year overall survival of 15%. PMBCL frequently involves overexpression of PD-L1, potentially making PMBCL particularly susceptible to PD-1 blockade. A multicenter, international, multicohort, open-label phase 1b trial (KEYNOTE-013) evaluated safety and antitumor activity of pembrolizumab in patients with rrPMBCL. At time of data cutoff (May 27, 2016), 18 patients (median age 30; median 3 prior lines of therapy) had been enrolled and treated, of whom 17 were included in the efficacy analyses. Eleven patients (61%) experienced drug-related adverse events (DRAEs), mostly grade 1-2; most commonly reported DRAEs were hypothyroidism, diarrhea, nausea, fatigue, pyrexia, and decreased appetite (n=2 patients each). No patient discontinued treatment due to adverse events; there were no treatment-related deaths. ORR was 41% (7/17) with 2 patients achieving CR and 5 PR; 6 additional patients (35%) had stable disease. Of patients evaluable by imaging, 13/16 (81%) had decreases in target lesions. With a median follow-up of 11.3 months (range, 3.4 to 27.4 months), median duration of response was not reached. Two patients reached the maximum 2-year treatment duration and remained in remission. Median overall survival was not reached and all responders were still alive at data cutoff. The results in these heavily pretreated rrPMBCL patients showed that PD-1 blockade with pembrolizumab has a manageable safety profile and promising antitumor activity.[2]

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

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.

2. Zinzani PL *et al*. Safety & tolerability of pembrolizumab in patients with relapsed/refractory primary mediastinal large B-cell lymphoma. Blood First Edition Paper, prepublished online May 10, 2017; DOI 10.1182/blood-2016-12-758383

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

Sincerely,

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