

February 16, 2018

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### **NCCN Guidelines Panel: Kidney Cancer**

On behalf of Merck & Co., Inc., I respectfully request the NCCN Kidney Cancer Panel to review the enclosed information for KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V2.2019 for Kidney Cancer.

#### **Specific changes requested:**

We respectfully request the NCCN Kidney Cancer panel to consider adding KEYTRUDA (pembrolizumab) as a first-line treatment option for patients with advanced non-clear cell renal cell carcinoma (nccRCC).

#### **FDA Approval:**

KEYTRUDA (pembrolizumab) is not approved for the treatment of patients with advanced renal cell carcinoma, with the exception of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Please see enclosed prescribing information for other FDA-approved indications.<sup>1</sup>

#### **Rationale:**

KEYNOTE-427 (NCT02853344) cohort B (n=165) is a phase 2 study to evaluate the efficacy and safety of pembrolizumab as first-line monotherapy in advanced non-clear cell renal cell carcinoma. The primary objective is overall response rate (ORR) per RECIST v1.1 by blinded independent central review. Secondary endpoints included duration of response (DOR), disease control rate (DCR), PFS, OS and safety.<sup>2</sup>

Results below were based on a median follow-up of 11.1 months (range, 0.9-21.3 month) with a data cutoff date of September 7, 2018:

- ORR was 24.8% (41/165) (95% CI, 18.5-32.2) with 4.8% complete response (CR) and 20% partial response (PR). Median DOR was not reached (range, 2.8 to 15.2+ months) with response  $\geq$  6 months in 81.5% of responders based on KM estimates. Responses were observed in all subgroups of papillary, chromophobe and unclassified histology.
- ORR in the intermediate/poor IMDC risk patients (112/165) was 23.2% (95% CI, 15.8-32.1) with 2.7% CR and 20.5% PR. ORR in the favorable IMDC risk patients (53/165) was 28.3% (95% CI, 16.8-42.3) with 9.4% CR and 18.9% PR.
- Median PFS was 4.1 months (95% CI, 2.8-5.6 months). Median OS was not reached (95% CI, not reached). One year estimated PFS and OS were 23% and 72%, respectively.
- Treatment related adverse events (TRAE) of any grade occurred in 64% of patients with grade 3-5 occurring in 11%. Ten patients (6%) discontinued treatment due to a TRAE. There were 2 TRAE death (pneumonitis and cardiac arrest). Safety profile in KEYNOTE-427 cohort B was similar to the previously described safety profile of pembrolizumab in other tumor types.<sup>2</sup>

**To assist the committee with their review, I have included the following resources:**

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc
2. McDermott D, et al. Pembrolizumab monotherapy as first-line therapy in advanced non-clear-cell renal cell carcinoma (nccRCC): results from cohort B of KEYNOTE-427. Presented at the 2019 ASCO GU Annual Meeting; Feb 14-16, 2019; San Francisco, CA.

Thank you for considering this request. Please contact me for any additional information.

Sincerely,

A handwritten signature in black ink, appearing to read 'S. Giffin', with a horizontal line extending to the right.

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