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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 V4.2018 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 clear cell renal cell carcinoma.

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 (PI).[1]

Rationale:
KEYNOTE-427 (NCT02853344) cohort A (n=110) is a phase 2 study that evaluated the efficacy and safety of pembrolizumab as first-line monotherapy in advanced clear cell renal cell carcinoma. The primary objective was overall response rate (ORR) per RECIST v1.1 by blinded independent central review. Secondary endpoints included duration of response (DOR), PFS, OS and safety.[2]

Results were based on a median follow-up of 12.1 months with a data cutoff date of March 12, 2018:

- ORR was 38.2% (42/110) (95% CI, 29.1-47.9) with 2.7% complete response (CR) and 35.5% partial response (PR). A total of 14.5% (16/110) of patients experienced a tumor burden reduction ≥80%. Median DOR was not reached (range, 1.4+ to 12.5+ months) with response ≥6 months in 74.8% of responders based on KM curve.
- ORR in intermediate/poor IMDC risk patients (n=69) was 42% (95% CI, 30.2-54.5) with 2.9% CR and 39.1% PR. The median DOR was not reached for intermediate/poor patients (range, 2.3+ to 11.2+ months) with response ≥6 months in 71.6% of responders based on KM curve.
- ORR in the favorable IMDC risk patients (n=41) was 31.7% (95% CI, 18.1-48.1) with 2.4% CR and 29.3% PR. The median DOR was also not reached for favorable patients (range, 1.4+ to 12.5+ months) with response ≥6 months in 76.5% of responders based on KM curve.
- Median PFS was 8.7 months (95% CI, 6.7-12.2 months). Median OS was not reached (95% CI, not reached).
- Treatment related adverse events of any grade occurred in 80% of patients with grade 3/4 occurring in 21.8%. Twelve patients (10.9%) discontinued treatment due to a treatment-related adverse event. High dose steroids (40 mg prednisone or equivalent/day) were administered in 14 patients. There was one death due to treatment-related pneumonitis.
- Safety profile in KEYNOTE-427 cohort A was similar to the previously described safety profile of pembrolizumab in other tumor types.

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

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

2. McDermott DF, Lee J-L, Szczylik C, et al. Pembrolizumab monotherapy as first-line therapy in advanced clear-cell renal cell carcinoma (accRCC): results from cohort A of KEYNOTE-427. Presented at the 2018 ASCO Annual Meeting; June 1-5, 2018; Chicago, IL.

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

Sincerely,

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