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NCCN Guidelines Panel: Merkel Cell Carcinoma

On behalf of the Pfizer and EMD Serono Alliance, we respectfully request the NCCN Merkel Cell Carcinoma (MCC) Panel consider the enclosed retrospective observational study data¹ supporting the use of avelumab for the treatment of locally advanced MCC.

Specific Changes Requested: We request the panel consider the following:

MCC-D – “Principles of Systemic Therapy”

- **“Local Disease: Recurrent locally advanced”: recommend inclusion of “Avelumab” as a consideration if curative surgery and curative RT are not feasible**
- **“Regional Disease: For recurrent regional disease”: recommend inclusion of “Avelumab” as a consideration if curative surgery and curative RT are not feasible**

FDA Clearance (Merkel Cell Carcinoma)²:

Avelumab (BAVENCIO®) is FDA-approved for the treatment of adults and pediatric patients 12 years and older with metastatic MCC under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Rationale: Avelumab is an intravenous programmed death ligand-1 (PD-L1) blocking antibody approved by the FDA based on the JAVELIN Merkel 200 trial to treat adults and pediatric patients 12 years and older with metastatic MCC (mMCC).² Response rates to avelumab were comparable between patients with locally advanced MCC (laMCC) and mMCC in a retrospective observational study of patients initiating first line therapy.¹

The following resources are submitted in support of this requested change:

1. Cowey et al. Real-world clinical outcomes with first-line avelumab in locally advanced/metastatic Merkel cell carcinoma in the USA: SPEAR-Merkel. Future Oncol 2021 Mar 12.
2. BAVENCIO® (avelumab) prescribing information. EMD Serono, Inc. and Pfizer Inc.



The basis of this request is the results from the Study Informing Treatment Pathway Decisions in Merkel Cell Carcinoma (SPEAR-Merkel). This was a retrospective, observational, descriptive study of patients with laMCC or mMCC initiating 1L avelumab between March 1, 2017 and March 31, 2019 in the US Oncology Network who had a diagnosis of laMCC or mMCC and received avelumab as first line therapy during the study period. A total of 148 adult patients initiated systemic treatment for MCC during this time. Patients with laMCC were further described as patients with nonmetastatic disease and evidence of nodal involvement in the same region as the primary tumor, locally recurrent disease, high-risk locally advanced disease or unresectable disease prior to the initiation of therapy. Patients with evidence of distant metastases or disseminated disease to the initial/primary site of diagnoses prior to the initiation of first line therapy were characterized as mMCC.

Among the overall 1L avelumab population, nine patients (three with laMCC, six with mMCC) achieved a best overall response of CR and nine (three with laMCC, six with mMCC) achieved a best overall response of R-NOS. The real-world overall response rate (rwORR) in the overall 1L avelumab population was 64.3% (n = 18/28; 95% CI: 44.1–81.4%). The rwORR was 66.7% (n = 6/9; 95% CI: 29.9–92.5%) in patients with laMCC and 63.2% (n = 12/19; 95% CI: 38.4–83.7%) in patients with mMCC. The median DOR was 15.5 months (95% CI: 7.5 months–NR) in the overall 1L avelumab population, NR in patients with laMCC and 9.6 months (95% CI: 2.6–15.5 months) in patients with mMCC. In the overall 1L avelumab population, the median PFS was 11.4 months (95% CI: 5.3 months–NR) and the median OS was 20.2 months (95% CI: 11.1 months–NR). Neither the median PFS nor the median OS was reached in patients with laMCC. In patients with mMCC, the median PFS was 10.0 months (95% CI: 2.8 months–NR) and the median OS was 20.2 months (95% CI: 10.0 months–NR).

During 1L avelumab treatment, 32.1% of patients had ≥ 1 ED visit and 42.9% had ≥ 1 hospitalization; 3.6% (n = 1) and 10.7% (n = 3), respectively, were treatment related. The most common reasons for ED visits in the overall 1L avelumab population were pain (14.3%), gastrointestinal (diarrhea, nausea and vomiting) and dyspnea (10.7% each). The most common reasons for hospitalizations included infection-related (17.9%), gastrointestinal (10.7%) and cardiovascular (7.1%) adverse events.

We greatly appreciate the Panel's thorough consideration of the data the inclusion of avelumab as an option for patients with locally advanced disease for whom curative surgery and curative radiation are not feasible.

Best regards,

Constantin and Kirk

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