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NCCN Guidelines Panel: Non-Melanoma Skin Cancer

Dear NCCN Guidelines Non-Melanoma Skin Cancer Panel:

On behalf of Regeneron Pharmaceuticals, Inc. and Sanofi Genzyme, we respectfully request the NCCN Guideline Panel on Non-Melanoma Skin Cancer/ Squamous Cell Skin Cancer to review a supplement our previous submission (16 June 2019) with updated data for cemiplimab-rwlc in advanced CSCC. These data provide additional evidence of the activity of cemiplimab-rwlc in advanced CSCC, namely when used in neoadjuvant setting for Stage III/IV CSCC (M0). We request the panel to consider these data when updating the NCCN Squamous Cell Skin Cancer guidelines based in part on the data provided.

Specific changes requested:

Within the NCCN Squamous Cell Skin Cancer Guidelines (Version 1.2020):

- Consider cemiplimab-rwlc in the discussion section for neoadjuvant systemic therapy for Stage III/IV (M0) CSCC of the head and neck (page MS-24 of the V1.2020)
- In principles of treatment for Squamous Cell Skin Cancer (SCC-D), consider stating that neoadjuvant anti-PD-1 systemic therapy may be an appropriate consideration in the management of some patients with stage III/IV (M0) CSCC

These changes may help guide management of patients in which neoadjuvant systemic therapy may mitigate loss of function and/or disfigurement that may be associated with CSCC lesions in the head and neck area.

FDA Clearance:

- LIBTAYO® (cemiplimab-rwlc) is approved by the FDA for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or patients with locally advanced CSCC who are not candidates for curative surgery or curative radiation¹.

Rationale:

Libtayo® (cemiplimab-rwlc) is approved for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or patients with locally advanced CSCC who are not candidates for curative surgery or curative radiation based on the results from 2 prospective, multi-cohort clinical trials (Study 1423 [NCT02383212], Study 1540 [NCT02760498]) in patients with metastatic (nodal and/or distant) CSCC or locally advanced CSCC who were not candidates for surgery or radiation^{1,2}.

At ESMO 2019, data from an ongoing Phase II study of neoadjuvant cemiplimab prior to surgery in patients with stage III/IV (M0) cutaneous squamous cell carcinoma of the head and neck (NCT03565783) conducted at MDACC were presented. This study included patients with stage III/IV(M0) CSCC, with measurable disease per RECIST 1.1, and for whom curative intent surgery or radiation were planned. 20 patients were enrolled and completed the study. The overall response rate (ORR) by RECIST was 30% (6 partial response, 12 stable disease, 2 progressive disease). However, the pathologic complete response (pCR, defined as 0% viable tumor cells) was observed in 11 (55%) patients and major pathologic response (MPR, defined as $\leq 10\%$ viable tumor cells) in an additional 3 (15%) patients, for an overall pathological response rate of 70%³. Moreover, 11 (55%) patients who obtained a pCR or MPR did not receive planned radiotherapy after surgery based on these pathologic responses and judgement of the multidisciplinary tumor board (MDT) at MDACC³. No recurrences have been observed with a median follow up of 3.8 months (range: 1.5-11.2). There were no grade ≥ 3 AEs, no surgical delays and no loss of opportunity for curative surgery³.

Additionally, post-hoc analysis from the laCSCC cohort of pivotal study 1540 demonstrated worse ORR and worse disease control among those patients considered poor candidates for surgery due to two or more prior CSCC surgeries.⁴ These data, taken together with data from phase II study of neo-adjuvant cemiplimab-rwlc, suggest that treating CSCC earlier in its natural history (ie, stage III/IV, prior to planned surgery) with anti-PD-1 therapy may lead to improved outcomes for patients.

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

- R. Ferrarotto, et al. Phase II Study of Neoadjuvant Cemiplimab Prior to Surgery in Patients with Stage III/IV (M0) Cutaneous Squamous Cell Carcinoma of the Head and Neck (CSCC-HN).
- Migden MR, Khushalani N, Chang A, et al. Lancet Oncology 2020;21 P294-305

We appreciate the opportunity to provide this information for review by the NCCN Guidelines Non-Melanoma Skin Cancer Panel. Thank you for your time and consideration of this request.

Sincerely,

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Clinical References:

1. Regeneron, Sanofi Genzyme. LIBTAYO® (cemiplimab-rwlc) [US prescribing information].
2. Migden MR, Rischin D, et al. PD-1 Blockade with Cemiplimab in Advanced Cutaneous Squamous Cell Carcinoma. *N Engl J Med*. 2018 Jun 4. doi: 10.1056/NEJMoa1805131.
3. Gross N, et al. *Annals of Oncology* 2019;30 (Supplement 5, Page v910)
4. Migden MR, Khushalani N, Chang A, et al. *Lancet Oncology* 2020;21 P294-305
5. Migden MR, et al. *J Clin Oncol* 2019;37 (suppl; abstr 6015);