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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 of Sanofi Genzyme, we would like to supplement our previous submission for cemiplimab-rwlc in advanced CSCC with updated data with longer follow-up and more patients that was recently presented as a discussion at ASCO 2020. As cemiplimab is currently the preferred treatment option for patients that are no longer candidates for curative surgery and curative radiation, we respectfully request the panel to consider 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 amending SCC-3-6 and SCC-F to include cemiplimab, among systemic therapies, as the primary preferred treatment option for eligible adult patients with squamous cell skin carcinoma who are not candidates for further curative surgery and curative radiation. The current data for cemiplimab (including ORR, CR rate, and DOR) represent the largest data set with the longest follow up in locally advanced (inclusive of recurrent, locally recurrent, locally advanced) and metastatic CSCC.
- Consider amending footnote 1 on page SCC-F to include information that may help optimize patient management and ensure that patients with advanced CSCC derive the most benefit from the treatment with cemiplimab-rwlc. Recommended that treatment is continued until disease progression or unacceptable toxicity, specifically longer-term follow up in 1540 study results in increase rate of complete responses over time (with median time to complete response being approximately 11 months).

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 radiation[1].

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 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].

Long-term follow-up data for Study 1540 patients with metastatic CSCC (Group 1 and Group 3) and patients with locally advanced CSCC (Group 2), not candidates for surgery or radiation) with up to 3 years of follow-up showed continued complete responses, and a clinically meaningful survival and duration of response for cemiplimab-rwlc in patients with advanced cutaneous squamous cell carcinoma. Importantly, new insights from this longer-term follow up data include the following;

- Overall Complete Response (CR) rate is 16.1%
- CR rates increase overtime, with median time to CR is 11.2 months
- Median duration of response (DOR) still not reached
- Estimated median PFS 18.3 months
- Median OS has not been reached (K-M estimated OS at24 months is 73.3%)

A summary of the efficacy results is provided in the table below.

Table: Efficacy results – Study 1540 – metastatic CSCC by dosing group, locally advanced CSCC

	mCSCC cemiplimab: 3 mg/kg Q2W (Group 1) (N = 59) ICR	laCSCC cemiplimab: 3 mg/kg Q2W (Group 2) (N = 78) ICR	mCSCC cemiplimab: 350 mg Q3W (Group 3) (N = 56) ICR	Combined (N=193) ICR
Confirmed objective response rate (ORR)[a,b]				
ORR	50.8%	44.9%	42.9%	46.1%
95% CI for ORR	(37.5, 64.1)	(33.6, 56.3)	(29.7, 56.8)	(38.9-53.4)
Complete response (CR)[b]	16.9%	12.8%	16.1%	16.1%
Partial response (PR)	30.5%	32.1%	26.8%	30.1%
Stable disease (SD)	15.3%	34.6%	17.9%	23.8%
Progressive disease (PD)	16.9%	11.5%	25.0%	17.6%
Duration of response (DOR)[a,c]				
Median (range) (months)	NR (20.7-NE)	NR (18.4 – NE)	NR (NE-NE)	NR (28.8- NE)
K-M 12-month estimate of patients with ongoing response	89.5 (70.9–96.5)	83.2 (64.1–92.7)	91.7 (70.6–97.8)	87.8 (78.5-93.3)
K-M 24month estimate of patients with ongoing response	68.8 (46.9–83.2)	62.5 (38.4–79.7)	NE (NE–NE)	69.4 (55.6-79.6)
Time to response				
Median (months) IQR range	1.9 (1.8: 2.0)	1.9 (1.9: 3.8)	2.1 (2.1: 4.2)	2.1 (1.9- 3.7)

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Disease Control Rate [a,]				
	71.2 (57.9–82.2)	79.5 (68.8–87.8)	64.3 (50.4–76.6)	72.5 (65.7–78.7)
Durable Disease Control Rate [a,d]				
	61.0 (47.4–73.5)	62.8 (51.1–73.5)	57.1 (43.2–70.3)	60.6 (53.3-67.6)

Data cut-off was Sep 20, 2019. CI: confidence interval; ICR: Independent Central Review; NR: Not Reached; NE: Not Evaulable

a. In Groups 1, 2, and 3, median durations of follow-up were 18.5, 15.5, and 17.3 months, respectively.
b. Only includes patients with complete healing of prior cutaneous involvement; locally advanced CSCC patients in Study 1540 required biopsy to confirm complete response.
c. Based on Kaplan Meier estimates
d. Defined as proportion of patients without progressive disease for ≥105 days

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

- Rischin D, Khushalani NI, Schmults CD, et al. Phase II study of cemiplimab in patients (pts) with advanced cutaneous squamous cell carcinoma (CSCC): longer follow-up. J Clin Oncol. 2020;38(suppl 15):10018. doi:10.1200/JCO.2020.38.15_suppl.10018

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. Rischin D, Khushalani NI, Schmults CD, et al. Phase II study of cemiplimab in patients (pts) with advanced cutaneous squamous cell carcinoma (CSCC): longer follow-up. J Clin Oncol. 2020;38(suppl 15):10018. doi:10.1200/JCO.2020.38.15_suppl.10018
4. Migden MR, Khushalani N, Chang A, et al. Lancet Oncology 2020;21 P294-305