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Analysis of second primary cutaneous squamous cell carcinoma (CSCC) tumors (SPTs) reported during the C-POST trial, a randomized phase III study of adjuvant cemiplimab vs placebo (pbo) for high-risk CSCC

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Background

The primary analysis of the phase 3 C-POST trial (NCT03969004) demonstrated that cemiplimab is the first systemic adjuvant therapy to improve disease-free survival (DFS; HR 0.32 vs pbo) in patients (pts) at high risk of CSCC recurrence after surgery and radiotherapy. We report results of CSCC SPTs that arose during the study period.

Methods

A secondary objective of C-POST was to compare the effect of adjuvant cemiplimab vs pbo on the cumulative incidence of SPTs. SPTs were defined as invasive CSCC lesions in the skin unrelated to the index high-risk CSCC. SPTs were managed by local modality therapy as part of routine clinical practice and were not DFS events per protocol. Pts could have multiple SPTs during the study.

Results

From Jun 2019 to Aug 2024, 415 pts were enrolled (209 cemiplimab; 206 pbo). There were 191 SPTs occurring in 68 pts during the study period (on-treatment plus follow-up; Table). Although the number (nbr) of pts with ≥1 SPT was similar in each arm (n=31 cemiplimab; n=37 pbo), the total nbr of SPTs and the annualized SPT rate were lower in the cemiplimab arm (68 SPTs; 0.63 [95% CI: 0.36–1.11]) vs the pbo arm (123 SPTs; 1.20 [0.59–2.44]). In a post-hoc analysis in which first SPTs were counted as DFS events, efficacy still favored cemiplimab (HR 0.43; 95% CI: 0.30–0.60).Table: 1603MO

	Cemiplimab (n=209)	Pbo (n=206)
Total SPTs, n	68	123
Total pt-years followed	412.4	331.0
SPT rate		
Unadjusted [†]	0.2	0.4
Adjusted annualized (95% CI) [‡]	0.63 (0.36–1.11)	1.20 (0.59–2.44)
Pts with ≥1 SPT, n (%)	31 (15)	37 (18)
Pts by number of SPTs, n (%)		
1	17 (8)	25 (12)
2	6 (3)	4 (2)
3	2 (1)	1 (<1)
4	1 (<1)	2 (1)
5	4 (2)	0

	Cemiplimab (n=209)	Pbo (n=206)
6	0	1 (<1)
7	0	2 (1)
9	1 (<1)	0
16	0	1 (<1)
43	0	1 (<1)

†Total SPTs during the study period divided by total pt-years followed. ‡Via negative binomial model: response variable: total SPTs during the study period; covariates: treatment arm, anatomic region of resected high-risk tumor, geographic region; offset variable: log-transformed standardized observation duration.

Conclusions

Cemiplimab may be associated with a lower incidence and rate of SPTs in a subset of pts with high-risk CSCC. The robust efficacy signal with cemiplimab vs pbo is maintained in a post-hoc analysis in which first SPTs were included as DFS events.

Clinical trial identification

NCT03969004.

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Legal entity responsible for the study

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Disclosure

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