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C-POST phase 3 trial of adjuvant (adj) cemiplimab (cemi) vs placebo (pbo) for high-risk cutaneous squamous cell carcinoma (CSCC): Updated overall survival (OS) and outcomes from circulating tumour DNA (ctDNA) analyses

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Background

The phase 3 C-POST trial (NCT03969004) established adj cemi as a new standard of care for patients (pts) with high-risk CSCC, demonstrating increased disease-free survival (DFS) for adj cemi vs pbo (HR, 0.32; $P<0.001$) with median 24 mo of follow-up (f/u). At primary analysis, OS data were immature and favoured cemi vs pbo (HR, 0.86); an update 6 mo later showed an OS HR of 0.78 (median f/u, 30 mo). We present updated OS and DFS data, and results from an exploratory analysis evaluating the association between baseline (BL) ctDNA and DFS.

Methods

Pts with high-risk CSCC (per nodal and/or non-nodal criteria; N=415) after surgery and postoperative radiotherapy were randomised 1:1 to cemi (n=209) or pbo (n=206). Key endpoints were DFS (primary), OS, and safety. After the DFS primary endpoint was reached, the study continued in a blinded manner to obtain unbiased long-term outcomes. During enrolment, a protocol amendment implemented collection of peripheral blood samples at BL for ctDNA-based minimal residual disease (MRD) analysis using a tumour-informed, ultrasensitive next-generation sequencing assay. Data cutoff: May 29, 2026.

Results

At a median f/u of 43.8 mo, OS HR was 0.63 (95% CI, 0.36-1.11) with adj cemi vs pbo, with 51 death events (cemi, 21; pbo, 30). The DFS HR was 0.46 (95% CI, 0.31-0.67). Median OS and DFS are not presented because f/u time is not long enough. Grade ≥ 3 treatment-emergent adverse events occurred in 25.4% and 17.2% of pts in the cemi and pbo arms, respectively. Among pts with ctDNA data (cemi, 93; pbo, 98), BL MRD positivity was balanced across arms and observed in 17 vs 19 pts in cemi vs pbo arms. Adj cemi showed a DFS benefit across all pts regardless of BL ctDNA MRD status (MRD positive: HR, 0.24; MRD negative: HR, 0.45).

Conclusions

Extended f/u (median, 43.8 mo) of this phase 3 study showed further improvement in the OS benefit of adj cemi vs pbo (HR, 0.63), along with a continued DFS benefit, in pts with high-risk CSCC. Data from this large prospective ctDNA-based analyses in high-risk CSCC pts showed that adj cemi led to a DFS benefit regardless of BL ctDNA MRD status.

Clinical trial identification

NCT03969004.

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Legal entity responsible for the study

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Disclosure

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