Adjuvant Immunotherapy in High-Risk CSCC: Phase 3 Evidence

Adjuvant Immunotherapy in High-Risk CSCC

Patients with high-risk CSCC are at risk of recurrence despite surgery and radiation.[1]

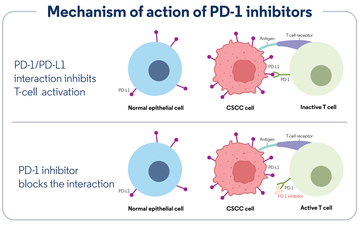
Adjuvant treatment after surgery and/or radiation aims to eliminate any remaining microscopic residual disease or micrometastatic disease.[2,3]

CSCCs are highly immunogenic[4]; therefore, they may respond well to adjuvant immunotherapy.

Some studies have found PD-L1 expression to be higher in CSCC compared to normal epithelial tissue or precancerous lesions.[5,6]

Tumor cells can exploit PD-L1 expression to suppress T cell activation through the PD-1/PD-L1 signaling axis.[7] **PD-1 inhibitors, such as pembrolizumab and cemiplimab, have the potential to block this inhibitory signal.**

Mechanism of action of PD-1 inhibitors



PD-1 Inhibitors: Phase 3 Trials in High-Risk CSCC

Randomized, double-blind, placebo-controlled, phase 3 studies evaluating PD-1 inhibitors as adjuvant therapy for high-risk CSCC

KEYNOTE-630

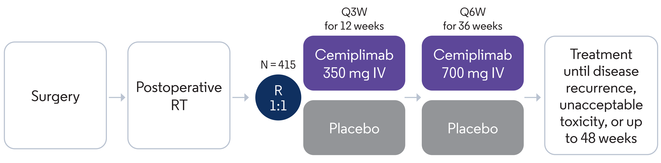
Pembrolizumab did not significantly affect recurrence-free survival, and the study was discontinued due to futility[8]

C-POST

Cemiplimab significantly improved disease-free survival compared to placebo[9]

C-POST: Trial Design

Study Design[9]



KEY ELIGIBILITY CRITERIA[9]

- Patients aged ≥18 years with local or regional CSCC
- Completed both curative-intent surgery (with macroscopic gross resection of all disease) and postoperative RT (or concurrent chemoradiotherapy) within 2 to 10 weeks before randomization
- High risk of recurrence due to nodal features and/or non-nodal features
- ECOG PS ≤1

KEY EXCLUSION CRITERIA[9]

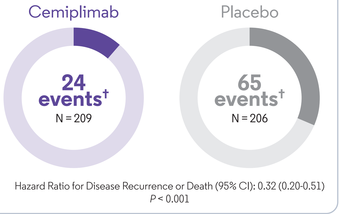
- Concurrent malignancy
- Autoimmune disease that required systemic therapy with immunosuppressant agents within 5 years
- History of solid organ transplant
- Prior allogeneic or autologous stem cell transplantation
- Uncontrolled HIV, hepatitis B or hepatitis C infection

Patient Characteristics at Baseline[9]

	Cemiplimab (N = 209)	Placebo (N = 206)
Median age (range) – year	71 (33-87)	70.5 (36-95)
Male sex – no. (%)	174 (83.3)	174 (84.5)
Race, White – no. (%)	189 (90.4)	189 (91.7)

C-POST: Efficacy and Safety Results

Primary endpoint: Disease-free survival*[9]



Hazard Ratio for Disease Recurrence or Death (95% CI): 0.32 (0.20-0.51)
P < 0.001

Secondary endpoints[9]

	Cemiplimab N = 209	Placebo N = 206	HR (95% CI)
Freedom From Locoregional Recurrence Locoregional recurrence events, n	9	40	0.20 (0.09-0.40)
Freedom From Distant Recurrence Distant recurrence events, n	10	26	0.35 (0.17-0.72)
Overall Survival Deaths, n	15	18	0.78 (0.39-1.56)

Safety Data[9]

	Any adverse event (AE)	Fatigue	Pruritus	Rash	Diarrhea	Immune-related AE
Cemiplimab (% of patients)	91.2	22.0	16.1	16.1	15.6	22.9
Placebo (% of patients)	89.2	21.6	12.3	8.8	18.6	6.4

The C-POST trial showed that adjuvant cemiplimab treatment resulted in **significant improvement in disease-free survival** as well as prolonged freedom from locoregional and distant recurrences compared to placebo.[9] Taken together, cemiplimab may be beneficial as an adjuvant treatment for high-risk CSCC.

Implications for Treatment of High-Risk CSCC

- Consider adjuvant cemiplimab after surgery and RT for appropriate patients with high-risk CSCC
- Initiate multidisciplinary conversations early to integrate adjuvant immunotherapy into treatment plans

THE dermatologist

*Disease-free survival is defined as time from randomization to the first documented occurrence of events.

†Events are defined as disease recurrence (locoregional or distant) or death due to any cause.

AE, adverse event; CI, confidence interval; CSCC, cutaneous squamous cell carcinoma; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HIV, human immunodeficiency virus; HR, hazard ratio; IV, intravenously; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomization; RT, radiation therapy.

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