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Primary results of the phase III KEYNOTE-412 study: Pembrolizumab (pembro) with chemoradiation therapy (CRT) vs placebo plus CRT for locally advanced (LA) head and neck squamous cell carcinoma (HNSCC)

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Background

Pembro is approved as monotherapy or in combination with chemotherapy for recurrent/metastatic HNSCC. The randomized, double-blind, phase 3 KEYNOTE-412 (NCT03040999) study investigated the efficacy and safety of pembro + CRT vs placebo + CRT in patients (pts) with LA-HNSCC.

Methods

Pts with newly diagnosed, pathologically proven, treatment-naive LA-HNSCC (T3–T4 [N0–N3] or any N2a–3 [T1–T4] larynx/hypopharynx/oral cavity/p16-negative oropharynx cancers and T4 or N3 p16-positive oropharynx cancer) who were eligible for definitive CRT were randomized (1:1) to pembro 200 mg Q3W + CRT (70Gy/35F + cisplatin 100 mg/m^2 Q3W) followed by pembro or placebo Q3W + CRT followed by placebo. A pembro/placebo priming dose was given 1 wk before CRT, followed by 2 doses during CRT and 14 doses of maintenance therapy after CRT, for a total of 17 doses. Primary endpoint was EFS (Efficacy boundary, one-sided P=0.0242). OS and safety/tolerability were secondary endpoints.

Results

804 pts were randomized (402 pts in each arm). Overall, baseline characteristics were well balanced between arms. At data cutoff (May 31, 2022) for the final analysis, median time from randomization to data cutoff was 47.7 (range, 37.0-61.4) mo. There was a favorable trend toward improved EFS with adding pembro vs placebo to CRT (HR 0.83, P=0.0429; Table), but the difference did not achieve statistical significance. AEs were grade ≥3 in 92.2% of pts in the pembro arm vs 88.4% in the placebo arm and led to discontinuation of cisplatin, RT, and/or pembro/placebo in 41.2% vs 33.2%; treatment-related AEs led to death in 1.0% vs 1.5%.Table: 000LBA5

		Pembro + CRT (N=402)	Placebo + CRT (N=402)
EFS	Median (95% CI), mo	NR (44.7-NR)	46.6 (27.5-NR)
	HR (95% CI), P	0.83 (0.68-1.03), P=0.0429	
	EFS rate at 24 mo, % (95% CI)	63.2 (58.2-67.8)	56.2 (51.1-61.0)
OS*	Median (95% CI), mo	NR (NR-NR)	NR (NR-NR)
	HR (95% CI)	0.90 (0.71-1.15)	
	OS rate at 24 mo, % (95% CI)	77.9 (73.5-81.7)	76.8 (72.4-80.7)
EFS by PD-L1 expression level	CPS≥1 (n=685)	CPS<1 (n=82)	
HR (95% CI)	0.80 (0.64-1.00)	1.09 (0.56-2.11)	

	Pembro + CRT (N=402)	Placebo + CRT (N=402)

*Per the statistical analysis plan, the OS difference would be tested only if there was a significant difference in EFS.

Conclusions

Pembro + CRT was associated with a favorable trend toward improved EFS vs placebo + CRT in patients with LA-HNSCC, but the difference did not reach statistical significance. No new safety signals were seen.

Clinical trial identification

NCT03040999.

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Legal entity responsible for the study

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Disclosure

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