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Abstract CT011: Penpulimab versus placebo in combination with chemotherapy as first-line treatment for recurrent or metastatic nasopharyngeal carcinoma: A global, multicenter, randomized, double-blind, phase 3 trial (AK105-304) FREE

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+ Author & Article Information

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Abstract

Background:

Studies have shown that the combination of PD-1 inhibitors with chemotherapy exhibits promising efficacy as a first-line treatment for Asian patients with recurrent or metastatic nasopharyngeal carcinoma (R/M NPC). This presentation reports the results of a global phase 3 clinical trial with ethnically diverse patients treated with penpulimab plus chemotherapy vs. placebo plus chemotherapy as the first-line therapy for R/M NPC (NCT04974398).

Methods:

AK105-304 trial was conducted across 46 sites worldwide. Participants aged 18-75 years with previously non-systemically treated R/M NPC, stratified by disease stages (de novo metastases vs. recurrent), ECOG (0 vs. 1), liver metastasis (present vs. absent), were randomized (1:1) to receive penpulimab or placebo (200mg, Day1) in combination with gemcitabine (1000mg/m^2, Day 1 and 8) and cisplatin (80mg/m^2, Day1) or carboplatin (AUC5, Day1) every 3 weeks (Q3W) for up to 6 cycles, followed by maintenance therapy with penpulimab or placebo (200mg, Q3W). Placebo-arm patients were allowed to crossover to receive penpulimab monotherapy (200 mg, Q3W) upon confirmed disease progression by blinded independent center review (BICR).

Primary endpoint was PFS assessed by BICR, and key secondary endpoint was OS. Other secondary endpoints included ORR, DoR and safety.

Results:

291 patients were randomized to penpulimab arm (n=144) or placebo arm (n=147). Baseline characteristics were generally balanced between treatment arms. By April 29, 2024, median follow-up time was 19.1 months. Per BICR assessment, median PFS was 9.6 months (95% CI: 7.1, 12.5) and 7.0 months (95% CI: 6.9, 7.3), respectively, for penpulimab+chemo and placebo+chemo (HR=0.45, 95% CI: 0.33, 0.62, two-sided P < 0.0001). Confirmed ORR was 68.1% vs. 63.9%, and median DoR was 9.8 months (95% CI: 7.0, 17.5) vs. 5.7 months (95% CI: 5.5, 6.7) (HR=0.4, 95%CI: 0.27, 0.59). OS was not mature, with 48 deaths in penpulimab arm and 49 in placebo arm (HR=0.94, 95% CI: 0.63, 1.40). After adjusting for crossover of patients from placebo to penpulimab upon PD, OS benefit became more evident, with HR of 0.62 (0.41, 0.94) by Rank Preserving Structural Failure Time (RPSFT) model, 0.75 (0.43, 1.30) by Inverse Probability of Censoring Weighting (IPCW) method, and 0.78 (0.52, 1.17) by two-stage Accelerated Failure Time (AFT) model. The incidence of Grade ≥3 TRAEs was 89.0% vs. 85.9%; SAEs was 50.7% vs. 48.6%; irAEs was 30.8% vs. 8.5%; Grade ≥3 irAEs was 4.1% vs. 0.

Conclusions:

Penpulimab combined with gemcitabine and cisplatin or carboplatin demonstrated statistically significant and clinically meaningful benefit with a manageable safety profile, and provides a new beneficial treatment option in the first-line treatment for R/M NPC patients globally.

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