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ORIENT-12: Sintilimab plus gemcitabine and platinum (GP) as first-line (1L) treatment for locally advanced or metastatic squamous non-small-cell lung cancer (sqNSCLC)


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Background
Sintilimab, an anti-PD-1 antibody, plus GP showed promising efficacy and acceptable safety in 1L sqNSCLC in a phase Ib study. ORIENT-12, a randomized, double-blind, phase III study, compared the efficacy and safety of sintilimab plus GP with placebo plus GP as 1L treatment for patients with locally advanced or metastatic sqNSCLC (NCT03629925).

Methods
Patients with histologically/cytologically confirmed stage IIIB/C (ineligible for concurrent chemoradiation or surgery) and stage IV sqNSCLC were enrolled and randomized 1:1 to receive either sintilimab (S group) or placebo (P group) with GP every 3 weeks for 4 or 6 cycles, followed by sintilimab or placebo as maintenance therapy. Stratification factors included disease stage (IIIB/C vs IV), platinum (cisplatin vs. carboplatin), PD-L1 expression (TPS, ≥1% vs <1%). Conditional crossover was allowed. The primary endpoint was progression-free survival (PFS) assessed by Independent Radiographic Review Committee (IRRC) per RECIST v1.1.

Results
A total of 357 pts were enrolled and randomized to S group (n=179) and P group (n=178). At interim analysis (median follow-up 8.0 mon), mPFS (by IRRC) was 5.1 mo in S group vs 4.9 mo in P group (HR, 0.621; 95% CI 0.473 - 0.815; P=0.00056). mPFS benefit was also observed by investigator assessment (5.9 mo vs. 4.9 mo, HR, 0.575; 95%CI 0.435 - 0.761; P=0.00009). The mOS was not reached in both groups, but showed a nominally significant improvement favoring S group (HR, 0.567, 95%CI, 0.353 to 0.909, P=0.01701). The PFS benefit with sintilimab plus GP was observed in all PD-L1 subgroups. The incidence of grade ≥3 adverse events was similar between groups (86.6% vs 83.1%). No new safety signals were observed.

Conclusions
ORIENT-12 is the first study globally to demonstrate superiority of an anti-PD-1 antibody plus GP over GP in PFS and OS with acceptable safety profile as 1L treatment for locally advanced or metastatic sqNSCLC.

Clinical trial identification
NCT03629925.

Legal entity responsible for the study
Innovent Biologics, Inc.

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Disclosure

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