PD-(L)1 inhibitors for treatment of locally advanced or metastatic NSCLC in Asian and non-Asian patients: a meta-analysis

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ABSTRACT

Introduction: Non-small cell lung cancer (NSCLC) is the leading cause of cancer mortality worldwide, with higher death rates in Asia than in Europe and North America. Programmed cell death protein-(ligand) 1 (PD-[L]1) inhibitors are effective in NSCLC treatment, but their comparative effectiveness in Asian vs non-Asian populations is unclear.

Methods: A meta-analysis was conducted to assess the efficacy of PD-(L)1 inhibitor monotherapy or combination therapy (with platinum-based chemotherapy or cytotoxic T-lymphocyte–associated protein-4 [CTLA-4] inhibitors) in Asian and non-Asian patients with locally advanced or metastatic NSCLC, and to monitor safety and treatment patterns in the two cohorts using randomized controlled studies. Analyses were based on randomized controlled studies and by first- and second-line (1L, 2L/2L+) therapy. Overall survival (OS) and progression-free survival (PFS) hazard ratios (HRs) were extracted using random effects models. Safety outcomes were described if reported.

Results: Overall, 1431 records were screened, and 1L (n=21) and 2L/2L+ (n=10) studies that had enrolled a total of 10,233 patients with locally advanced or metastatic squamous/non-squamous NSCLC were identified. OS favoured 1L PD-(L)1 inhibitor monotherapy or combination therapy in both Asian (HR=0.70; 95% CI: 0.64, 0.76) and non-Asian (HR=0.71; 95% CI: 0.65, 0.77) patients (Table). Similar findings were observed with PFS in Asian (HR=0.53; 95% CI: 0.47, 0.59) and non-Asian

(HR=0.58; 95% CI: 0.53, 0.64) patients. 1L PD-(L)1 inhibitor plus platinum-based chemotherapy and/or CTLA-4 inhibitors and 2L/2L+ PD-(L)1 inhibitor monotherapy were equally effective in Asian and non-Asian populations, but there was a greater magnitude of effect on PFS with 2L/2L+ PD-(L)1 inhibitor monotherapy in Asian (HR=0.57; 95% CI: 0.49, 0.67) than non-Asian (HR=0.73; 95% CI: 0.56, 0.95) patients; this may be related to differences in treatment patterns or prior surgery. Most studies showed low risk of bias using the Cochrane Risk of Bias 2 tool and rank-based Begg test. Safety data were obtained from eight 1L and two 2L/2L+ PD-(L)1 inhibitor studies. There was a higher incidence of treatment-related and immune-related adverse events (AEs) and discontinuations in some Asian populations. This may be linked to regional differences in AE resolution and differences in study periods.

Conclusion: These data demonstrate general consistency of outcomes with PD-(L)1 inhibitors for both Asian and non-Asian patients with 1L or 2L/2L+ locally advanced or metastatic NSCLC. More real-world evidence at the regional level will further confirm long-term clinical benefits and tolerability in specific patient populations.

Table: Survival Outcomes in Asian and Non-Asian Populations With Locally Advanced or Metastatic NSCLC (100 words)

Outcome	**Asian HR [95% CI]**	**Non-Asian HR [95% CI]**	**RE Model I^2 (*P* value)**
Overall survival			
PD-(L)1 inhibitor 1L monotherapy or combination therapy	0.70 [0.64, 0.76]	0.71 [0.65, 0.77]	25% (.08)
PD-(L)1 inhibitor 1L combination therapy	0.70 [0.63, 0.76]	0.70 [0.62, 0.79]	32% (.06)
PD-(L)1 inhibitor 1L monotherapy or combination therapy (PD-L1 expression ≥50%)	0.50 [0.39, 0.64]	0.64 [0.55, 0.76]	0% (.53)
PD-(L)1 inhibitor as 2L/2L+ monotherapy or combination therapy	0.73 [0.64, 0.83]	0.71 [0.64, 0.78]	0% (.54)
Progression-free survival			
PD-(L)1 inhibitor 1L monotherapy or combination therapy	0.53 [0.47, 0.59]	0.58 [0.53, 0.64]	48% (.003)
PD-(L)1 inhibitor 1L combination therapy	0.53 [0.47, 0.60]	0.60 [0.53, 0.68]	55% (.001)
PD-(L)1 inhibitor 1L monotherapy or combination therapy (PD-L1 expression ≥50%)	0.38 [0.32, 0.44]	0.46 [0.37, 0.56]	4.6% (.40)
PD-(L)1 inhibitor as 2L/2L+ monotherapy or combination therapy	0.57 [0.49, 0.67]	0.73 [0.56, 0.95]	74% (.005)
Abbreviations: 1L, first-line; 2L/2L+, second-line/second-line-plus; CI, confidence interval; HR, hazard ratio; NSCLC, non-small cell lung cancer; PD-(L)1, programmed cell death protein-(ligand) 1; RE, random effects.			