Safety and efficacy of PD-1/PD-L1 inhibitors in treatment naïve and chemotherapy refractory patients with Non-small cell lung cancer: a systematic review and meta-analysis

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Received 26 May 2017, Revised 20 December 2017, Accepted 1 January 2018, Available online 10 January 2018

Abstract

Introduction

PD-1/PD-L1 inhibitors show significant clinical activity in non-small cell lung carcinoma (NSCLC). However, there is relative lack of data on comparative efficacy of these drugs in front-line setting versus chemotherapy-treated patients. We compared the efficacy and toxicity of these drugs in these two distinct groups of patients.

Methods

Electronic databases (PubMed-Medline, EMBASE, Scopus) and major conference proceedings were systematically searched for all phase I-III clinical trials in NSCLC using PD-1/PD-L1 inhibitors. Objective response rate (ORR) and progression free survival (PFS) data were collected and combined using DerSimonian and Laird random effects model meta-analysis. The I² statistic was used to assess heterogeneity.

Results

Seventeen distinct trials (8 with treatment naïve patients [n = 937]; 14 with chemotherapy-treated patients [n = 3620]; 5 with separate treatment naïve and previously treated arms) were included. Treatment naïve patients had a statistically
significant higher objective response rate (ORR 30.2% (95% CI 22.70-38.2) than previously chemotherapy treated patients (ORR 20.1% (95%CI 17.5-22.9; p=0.02). No significant differences in PFS were observed between the two groups. Treatment naive patients had statistically significant higher rates of all grade pneumonitis as compared to previously treated patients (4.9%, 95%CI 3.4-6.7 vs 3.0%, 95% CI 2.0-4.1, p=0.04); however, no significant differences in any other immune related adverse events were observed.

Conclusions
PD-1/PD-L1 inhibitor therapy for advanced NSCLC has a significantly higher objective response rate (ORR) and a higher rate of immune mediated pneumonitis when used in front-line setting as compared to chemotherapy treated patients.

Keywords
- Non-small cell lung cancer;
- Meta-analysis;
- Immunotherapy;
- PD-1/PD-L1 inhibitors