

# 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

- [Monica Khunger](#), MD<sup>1</sup>,
- [Prantesh Jain](#), MD<sup>2</sup>,
- [Sagar Rakshit](#), MD<sup>1</sup>,
- [Vinay Pasupuleti](#), MD, PhD<sup>3</sup>,
- [Adrian V. Hernandez](#), MD, MSc, PhD<sup>4</sup>,
- [James Stevenson](#), MD<sup>5</sup>,
- [Nathan A. Pennell](#), MD PhD<sup>5</sup>,
- [Vamsidhar Velcheti](#), MD, FACP<sup>5</sup>.

- <sup>1</sup> Department of Internal Medicine, Cleveland Clinic, Cleveland, Ohio
- <sup>2</sup> Department of Hospital Medicine, Cleveland Clinic, Cleveland, Ohio
- <sup>3</sup> ProEd Communications Inc., Cleveland, OH 44122, USA
- <sup>4</sup> University of Connecticut/Hartford Hospital Evidence-based Practice Center, Hartford, CT 06102; and School of Medicine, Universidad Peruana de Ciencias Aplicadas (UPC), Lima 9, Peru
- <sup>5</sup> Department of Hematology and Oncology, Tausig Cancer Institute, Cleveland Clinic, Cleveland, Ohio

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

## Show less

<https://doi.org/10.1016/j.clcc.2018.01.002>

[Get rights and content](#)

## 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  $I^2$  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