



P1.263: PD-(L)1 Monotherapy vs Chemo-Immunotherapy for NSCLC With PD-L1 1-49%: A Reconstructed Individual Patient Data Meta-Analysis

Alessandro Di Federico¹, Francesco Mantuano^{2,3}, Sara Stumpo^{2,3}, Linda Danielli^{2,3}, Samuele Compagno^{2,3}, Irene Zannini^{2,3}, Andrea De Giglio^{2,3},
Federica Pecci^{4,5}, Joao V. Alessi⁶, Xinan Wang⁷, Andrea Arfè⁸, Biagio Ricciuti⁴, Andrea Ardizzoni^{2,3}, Mark M. Awad¹

Affiliations: ¹ Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; ² Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy; ³ Medical Oncology, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; ⁴ Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; ⁵ Department of Medicine and Surgery, University of Parma, Parma, Italy; ⁶ Hospital S rio-Liban es, S o Paulo, Brazil; ⁷ Department of Biostatistics, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, USA; ⁸ Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA.



INTRODUCTION

PD-(L)1 inhibitor plus chemotherapy is the preferred first-line approach for patients with advanced non-small-cell lung cancer (NSCLC) and low-positive PD-L1 tumour proportion score (TPS 1–49%), as responses and durable benefit with PD-(L)1 inhibitor monotherapy are less frequent in this subgroup.¹ Despite this, the two strategies have never been compared in a prospective randomised trial, and the preference for PD-(L)1 inhibitor plus chemotherapy rests on indirect evidence. The most relevant comparative data derive from an FDA pooled analysis presented at the 2021 ASCO Annual Meeting, which reported improved outcomes with PD-(L)1 inhibitor plus chemotherapy in this population; however, these data have never been fully published.² Prior meta-analyses were further limited to comparing each strategy against chemotherapy rather than against each other, leaving the magnitude and durability of the differential benefit between the two immunotherapy-based approaches in this subgroup poorly characterised.

METHODS

PubMed, EMBASE, and major oncology conference proceedings were searched for phase 3 randomised clinical trials published through February 13, 2026, enrolling patients with treatment-na ve advanced NSCLC that compared PD-(L)1 inhibitor monotherapy or PD-(L)1 inhibitor plus chemotherapy versus chemotherapy and reported outcomes by PD-L1 expression. CTLA-4 inhibitor-containing regimens were excluded. Individual patient data (IPD) were extracted from published Kaplan-Meier curves using WebPlotDigitizer v5.2 and then reconstructed using validated methods (IPDfromKM and KMSubtraction).^{3,4} The primary outcome of the study was overall survival (OS), while the secondary outcome was progression-free survival (PFS).

REFERENCES & ACKNOWLEDGEMENTS

¹Di Federico A, *J Natl Cancer Inst*, 2023; ²Akinboro O, *J Clin Oncol* 2021; ³Liu N, *BMC Med Res Methodol*, 2021; ⁴Zhao JJ, *BMC Med Res Methodol*, 2022; ⁵Brahmer JR, *J Clin Oncol*, 2023; ⁶Jassem J, *J Thorac Oncol*, 2021; ⁷Reck M, *J Thorac Oncol*, 2024; ⁸de Castro G Jr, *J Clin Oncol*, 2023; ⁹Zhou C, *J Immunother Cancer*, 2024; ¹⁰Ren S, *J Thorac Oncol*, 2022; ¹¹Zhong J, *Signal Transduct Target Ther*, 2024; ¹²Zhou C, *Lancet Oncol*, 2025; ¹³Nishio M, *J Thorac Oncol*, 2021; ¹⁴Socinski MA, *J Thorac Oncol*, 2021; ¹⁵Garassino MC, *J Clin Oncol*, 2023; ¹⁶Novello S, *J Clin Oncol*, 2023; ¹⁷Yang Y, *J Thorac Oncol*, 2020; ¹⁸Garon EB, *Clin Lung Cancer*, 2024; ¹⁹Lu S, *ESMO Open*, 2024; ²⁰Wang J, *JAMA Oncol*, 2021

RESULTS

Table 1. Main characteristics of trials included, and treatment arm extracted and reconstructed in each trial.

Trial	Primary endpoint	Stage included	Arm included in reconstructed IPD analysis (n of patients)
PD-(L)1 inhibitor monotherapy group			
CheckMate 227 ⁵	OS	IV or recurrent	Nivolumab (182); CT (205)
IMpower 110 ⁶	OS	IV	Atezolizumab (170); CT (179)
JAVELIN Lung 100 ⁷	PFS and OS	IV	Avelumab QW (139); avelumab Q2W (148); CT vs the avelumab QW arm (138); CT vs the avelumab Q2W arm (222)
KEYNOTE-042 ⁸	OS	Locally advanced or IV	Pembrolizumab (338); CT (337)
PD-(L)1 inhibitor plus chemotherapy group			
CamelL ⁹	PFS	IIIB-IV	Camrelizumab + CT (108); CT (97)
Camel-Sq ¹⁰	PFS	IIIB-IV	Camrelizumab + CT (58); CT (49)
CHOICE-01 ¹¹	PFS	IIIB-IV	Toripalimab + CT (128); CT (75)
GEMSTONE-302 ¹²	PFS	IV	Sugemalimab + CT (92); CT (48)
IMpower 132 ¹³	PFS and OS	IV	Atezolizumab + CT (63); CT (73)
IMpower 150 ¹⁴	PFS and OS	IV or recurrent	Atezolizumab + CT (122); CT (100)
KEYNOTE-189 ¹⁵	PFS and OS	IV	Pembrolizumab + CT (128); CT (58)
KEYNOTE-407 ¹⁶	PFS and OS	IV	Pembrolizumab + CT (103); CT (104)
ORIENT-11 ¹⁷	PFS	IIIB-IV	Sintilimab + CT (74); CT (26)
POSEIDON ¹⁸	PFS and OS	IV	Durvalumab + CT (130); CT (110)
RATIONALE 304 ¹⁹	PFS	IIIB-IV	Tislelizumab + CT (53); CT (27)
RATIONALE 307 ²⁰	PFS	IIIB-IV	Tislelizumab + CT with paclitaxel (30) and nab-paclitaxel (30); CT (31)

PFS: progression-free survival; OS: overall survival; CT: chemotherapy; QW: weekly schedule; Q2W: every-two-week schedule.

DISCUSSION AND CONCLUSION

- In patients with treatment-na ve advanced NSCLC and low-positive PD-L1 expression (TPS 1-49%), PD-(L)1 inhibitor plus chemotherapy was associated with longer progression-free and overall survival over PD-(L)1 inhibitor monotherapy, supporting its preferred use in fit patients.
- PD-(L)1 inhibitor monotherapy remains a valid first-line option for those with contraindications to platinum-based chemotherapy, given overall survival comparable to chemotherapy alone and a more favourable toxicity profile.
- Prospective trials directly comparing these strategies, including the ongoing INSIGNA trial (NCT03793179), are needed to further define optimal treatment selection across PD-L1 expression levels.

