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CORRESPONDENCE

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Translational Therapeutics

Identifying optimal first-line treatment for advanced non-small cell lung carcinoma with high PD-L1 expression: a matter of debate

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Following the advent of several novel treatment options in treatment-naive patients, the challenge of choosing the best first-line treatment for advanced non-small cell lung cancer (NSCLC) with high PD-L1 expression has emerged [1]. Clinicians are now called to choose between immune checkpoint inhibitors (ICIs) monotherapy and chemoimmunotherapy in wild-type NSCLC [2]. Cross-trials comparisons, albeit being a commonly used tool in clinical practice, should be avoided for decision-making, since all trials assessing ICIs, alone or in combination with chemotherapy, present important differences—e.g., in terms of the patient population, primary endpoints, and length of median follow-up.

In the current systematic review and network meta-analysis (NMA) published by Wang et al., the authors pulled together 22 randomised controlled clinical trials encompassing a total of 4289 NSCLC patients [3]. According to the results of the NMA, Wang and colleagues suggested that chemoimmunotherapy was associated with a statistically significant improvement in overall response rate (ORR) and progression-free survival (PFS) when compared with immune checkpoint inhibitors, while no significant overall survival (OS) differences were observed [3].

Wang et al. performed Bayesian NMA to optimise data extrapolation and to compare different treatments when no direct comparative trial was available, and to obtain more precise effect estimated by jointly considering direct and indirect comparisons [4]. Herein, the authors used rigorous, well-accepted methods to assess evidence across clinical trials, also acknowledging important limitations.

However, we believe some methodological issues would deserve discussion.

Bayesian NMA—similarly to pairwise meta-analysis—may be associated with the inflation of type 1 (false positive) and type 2 (false negative) errors; since these specific errors have been suggested to play an important role validating true-positive as well as true-negative findings in meta-analyses, this issue should be carefully considered [5]. In our view, Wang et al. are to be commended for this interesting NMA aimed at evaluating a timely topic in NSCLC. A strength of this study is that the search was thorough and included the latest information on clinical trials; moreover, by assessing the quality of eligible studies, the authors highlighted that the studies included in their research were relatively well-controlled. At the same time, Bayesian NMA presents some limitations that should be carefully considered, and this analysis has not the statistical power to replace head-to-head clinical trials comparison. Thus, the interesting piece of work by Wang et al. further emphasises the need for large-scale, well-designed clinical trials aimed at comparing chemoimmunotherapy and ICIs monotherapy as first-line treatment for advanced NSCLC patients with high PD-L1 expression, which remains a matter of debate.

We invite the authors to share their views on these remarks.

Alessandro Rizzo [1]✉

[1]*Struttura Semplice Dipartimentale di Oncologia Medica per la Presa in Carico Globale del Paziente Oncologico "Don Tonino Bello", I.R.C.C.S. Istituto Tumori "Giovanni Paolo II,", Viale Orazio Flacco 65, Bari 70124, Italy.* ✉*email: rizzo.alessandro179@gmail.com*

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ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Alessandro Rizzo.