authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

*Naoya Murakami, Noriyuki Okonogi, Yasuhisa Terao, Naoto Shikama
n.murakami.zi@juntendo.ac.jp

Juntendo University, Tokyo 113-0033, Japan (NM, NO, YT, NS)

1 Lorusso D, Xiang Y, Hasegawa K, et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial. *Lancet* 2024; **403:** 1341–50.
2 Pötter R, Tanderup K, Schmid MP, et al. MRI-guided adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-I): a multicentre prospective cohort study. *Lancet Oncol* 2021; **22:** 538–47.

We commend Domenica Lorusso and colleagues for their Article[1] reporting a phase 3 clinical trial that analysed the comparison between pembrolizumab or placebo combined with chemoradiotherapy in the treatment of newly diagnosed, high-risk, locally advanced cervical cancer. However, the strength of evidence in this study could be enhanced by further discussion of some issues.

First, on the basis of previous evidence,[2] pembrolizumab was approved by the US Food and Drug Administration for first-line or second-line treatment in patients with PD-L1-positive (combined positive score ≥1) cervical cancer. The study's conclusions would be more easily understood if the authors could provide the rationale for the inclusion of participants with PD-L1-negative (combined positive score <1) tumours. Previous studies[3,4] found that patients with PD-L1-negative status also benefited from pembrolizumab treatment in terms of progression-free survival and overall survival, although prognosis seemed to be better among patients with PD-L1-positive status. In this study,[1] participants were also categorised by PD-L1 combined positive scores (≥1 and <1). Furthermore, Lorusso and colleagues indicated that the key secondary endpoints included progression-free survival and overall survival by PD-L1 status. However, figure 2 of their Article does not provide an analysis of progression-free survival for these two stratified groups. We recommend the inclusion of detailed information on progression-free survival and overall survival for participants with varying levels of PD-L1 expression.

Second, in the comparison of adverse events between the two treatment methods, we suggest the inclusion of the p value for the difference between the two groups. This recommendation stems from the incidence rates in table 2 of their Article, which seem to indicate higher occurrences of both treatment-related adverse events and immune-mediated adverse events in the pembrolizumab–chemoradiotherapy group, with a greater difference in the incidence of immune-mediated adverse events, in particular.

Third, participants in this study included individuals with squamous cell carcinoma, adenocarcinoma, and adenosquamous carcinoma, but specific case numbers were not provided. There is evidence that PD-L1 is expressed by most cervical squamous cell carcinomas but not necessarily by other histological types of cervical cancer (such as adenocarcinoma).[2,5] Moreover, a previous study showed a statistically significant difference in response rates to pembrolizumab treatment between patients with PD-L1-positive cervical cancer and those with PD-L1-negative cervical cancer.[2]

Fourth, in figure 3 of their Article, only overall survival for the two treatments is displayed, and the hazard ratios for comparisons of overall survival of various subgroups are not provided. Differences in overall survival have been shown among protocol-specified subgroups for the treatment of persistent, recurrent, or metastatic cervical cancer using pembrolizumab combined with chemotherapy or placebo combined with chemotherapy.[4] We recommend the reporting of these results.

We declare no competing interests.

*Binhua Dong, Yong Lu, Yue Wang, Pengming Sun, *Huachun Zou
zouhuachun@fudan.edu.cn

Fujian Maternity and Child Health Hospital, College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, Fujian 350001, China (BD, YW, PS, HZ); School of Public Health, the Key Laboratory of Environmental Pollution Monitoring and Disease Control, Ministry of Education, Guizhou Medical University, Guiyang, China (YL); School of Public Health, Fudan University, Shanghai, China (HZ)

1 Lorusso D, Xiang Y, Hasegawa K, et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial. *Lancet* 2024; **403:** 1341–50.
2 Chung HC, Ros W, Delord JP, et al. Efficacy and safety of pembrolizumab in previously treated advanced cervical cancer: results from the phase II KEYNOTE-158 study. *J Clin Oncol* 2019; **37:** 1470–78.
3 Colombo N, Dubot C, Lorusso D, et al. KEYNOTE-826 Investigators. Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. *N Engl J Med* 2021; **385:** 1856–67.
4 Monk BJ, Colombo N, Tewari KS, et al. First-line pembrolizumab + chemotherapy versus placebo + chemotherapy for persistent, recurrent, or metastatic cervical cancer: final overall survival results of KEYNOTE-826. *J Clin Oncol* 2023; **41:** 5505–11.
5 Li C, Cang W, Gu Y, Chen L, Xiang Y. The anti-PD-1 era of cervical cancer: achievement, opportunity, and challenge. *Front Immunol* 2023; **14:** 1195476.

Regarding the Article by Domenica Lorusso and colleagues on ENGOT-cx11/GOG-3047/KEYNOTE-A18,[1] this trial finally shows the long-awaited progress in patients with high-risk locally advanced cervical cancer: addition of pembrolizumab to chemoradiation statistically significantly improved progression-free survival at 24 months. We do not want to question the results of a randomised controlled trial or the potential role of pembrolizumab, but we would like to focus attention on the central treatment component, which is chemoradiotherapy, including brachytherapy.