Background Chemo-IO is generally known to have better efficacy than IO-only, despite a higher incidence of TRAEs. The incidence of treatment discontinuation related to TRAE is generally related to uncontrollable TRAE. However, differences in TRAE-related treatment discontinuation rates between the two treatments has not been well studied. In this study, we compared the discontinuation rates of the two treatments for first-line treatment of NSCLC and other cancer types.

Methods We searched PubMed, Embase, and the Web of Science databases for eligible articles that include prospective phase III randomized controlled trial data of first-line treatments using IO-only or chemo-IO. IO-only was defined as a single immunotherapy drug or a combination of immunotherapy drugs, and chemo-IO was defined as a combination of immunotherapy and other chemotherapy drugs. The analysis was performed separately for NSCLC and other cancer types because most of the first-line trials with immunotherapy were published in NSCLC. We found 19 and 22 trials encompassing 6,114 and 7,492 patients in NSCLC and other cancer types, respectively. The data for discontinuation rate due to TRAEs and their 95% confidence intervals (CIs) were extracted.

Results Although there was heterogeneity of specific drugs in both the IO-only and chemo-IO groups, overall, IO-only showed a significantly lower TRAE-related discontinuation rate than chemo-IO. For NSCLC, we found that IO-only had a lower TRAE-related discontinuation rate (8.13%, 95% CI 5.90-10.36) than chemo-IO (17.54%, 95% CI 13.75-21.34) (figure 1). IO-only also showed a lower TRAE-related discontinuation rate (9.32%, 95% CI 5.94-12.69) compared to chemo-IO (21.78%, 95% CI 16.56-26.98) in other cancer types (figure 2). Clinical trials of NSCLC patients showed that there were differences in TRAE-related discontinuation rates associated with specific drugs in both IO-only (p=0.02) and chemo-IO (p<0.001), as well as in other cancer types trials (IO-only : p=0.01, chemo-IO: p<0.001).

Conclusions Compared to IO-only, chemo-IO showed a higher treatment discontinuation rate due to TRAEs. Since TRAE-related discontinuation may lead to suboptimal treatment outcomes, further study to discover the novel biomarker that dictates who could achieve durable response from IO-only, without early treatment discontinuation should be warranted.