Comment on "Hemodynamic Influences of Remimazolam Versus Propofol During the Induction Period of General Anesthesia"

To the Editor:

We read with interest the recent systematic review and meta-analysis by Peng et al (1) comparing the hemodynamic effects of remimazolam versus propofol for the induction of general anesthesia. The authors found that remimazolam was associated with more stable hemodynamics and a lower risk of hypotension than propofol. This is an important topic because hemodynamic stability during anesthesia induction is crucial for patient safety. Identifying alternative induction agents with favorable hemodynamic profiles could reduce anesthesia-related complications.

Nevertheless, we would like to address three limitations in this meta-analysis (1). First, the included studies involved both cardiac and noncardiac surgeries in the meta-analysis (1). Patients undergoing cardiac surgery often have significant comorbidities, and subgroup analysis based on patient illness would provide a clearer understanding of the benefits of remimazolam in different patient populations. Second, although remimazolam was associated with smaller changes in blood pressure, the clinical significance of these differences remains unclear. The average change in blood pressure in the remimazolam group was only 5-6 mmHg less than that in the propofol group. Further studies should evaluate whether this leads to substantial differences in the clinical outcomes. Third, although the authors performed trial sequential analyses for all outcomes (1), we believe that the evidence for the incidence of total adverse events remains inconclusive. Considering that they did not provide methodological details regarding the analysis of total adverse events, we reanalyzed the raw data of the original meta-analysis (1). The control event rate was 29.2% in the original meta-analysis (101/346 patients in the control group) (1). The trial sequential analysis (TSA viewer version 0.9.5.10 Beta) was set at an α of 0.05, a power of 80%, and a hypothesized risk reduction of 20%. As shown in Fig. 1, the blue cumulative z curve does not cross the trial sequential monitoring boundary or reach the required information size, indicating inadequate evidence. Accordingly, more studies are required to determine the impact of remimazolam on the total adverse events compared to propofol.

In summary, additional randomized controlled trials are required to clarify the safety and efficacy of remimazolam as an induction agent. The evaluation of substantive clinical outcomes is warranted. Nevertheless, this article by Peng et al (1) provides early evidence that remimazolam may offer hemodynamic advantages over propofol during anesthesia induction.

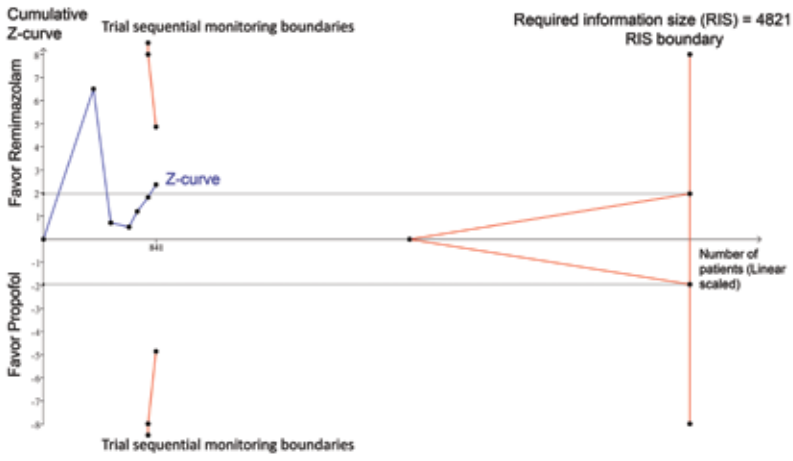

Fig. 1. *Trial sequential analysis (TSA) of total adverse events in patients receiving remimazolam versus propofol for anesthesia induction. The required information size to demonstrate a 20% relative risk reduction of total adverse events, with $\alpha = 0.05$ and $\beta = 0.20$, was calculated as 4821 events. The blue cumulative z curve does not cross the trial sequential monitoring boundary or reach the required information size, indicating insufficient evidence that remimazolam reduces total adverse events compared to propofol.*

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References

1. Peng X, Liu C, Zhu Y, et al. Hemodynamic influences of remimazolam versus propofol during the induction period of general anesthesia: A systematic review and meta-analysis of randomized controlled trials. *Pain Physician* 2023; 26:E761-E773.