**Figure S1**. Pooled results of any-grade TRAEs (A), grade 3 or higher TRAEs (B), and severe TRAEs (C) in monotherapy trials, stratified by approved EZH2 inhibitors.

**Figure S2**. Pooled results of any-grade TRAEs (A), grade 3 or higher TRAEs (B), and severe TRAEs (C) in monotherapy trials at active dose (SHR2554: 350 mg, bid, po; Tazemetostat: 800 mg, bid, po; Valemetostat: 200 mg, qd, po), stratified by approved EZH2 inhibitors.

**Figure S3**. Pooled results of any-grade TRAEs by drug combinations subgroup (A) and by cancer types (B). Abbreviation: HM: Hematologic malignancies; ST: solid tumors. Weights and between-subgroup heterogeneity test are from random-effects model.

**Figure S4** Pooled results of grade 3 or higher TRAEs by drug combinations subgroup (A) and by cancer types (B). Abbreviation: HM: Hematologic malignancies; ST: solid tumors. Weights and between-subgroup heterogeneity test are from random-effects model

**Figure S5**. Pooled results of severe TRAEs by drug combinations subgroup (A) and by cancer types (B). Abbreviation: HM: Hematologic malignancies; ST: solid tumors. Weights and between-subgroup heterogeneity test are from random-effects model

**Figure S6**. Pooled results of TRAEs leading to dose reduction (A) and interruption (B). Weights and between-subgroup heterogeneity test are from random-effects model

**Figure S7**. Sensitivity analyses were conducted to evaluate the robustness of the pooled estimates for any-grade TRAEs (A), grade 3 or higher TRAEs (B), and TRAEs leading to discontinuation (C).

**Figure S8**. funnel plots were constructed for evaluate risk of bias of the pooled estimates for any-grade TRAEs (A), grade 3 or higher TRAEs (B), and TRAEs leading to discontinuation (C).

**Figure S9**. Pooled results of any-grade TRAEs (A), grade 3 or higher TRAEs (B), and severe TRAEs (C) stratified by cancer types after, excluding two studies that included both hematologic malignancies and solid tumors. Abbreviation: HM: Hematologic malignancies; ST: solid tumors. Weights and between-subgroup heterogeneity test are from random-effects model.