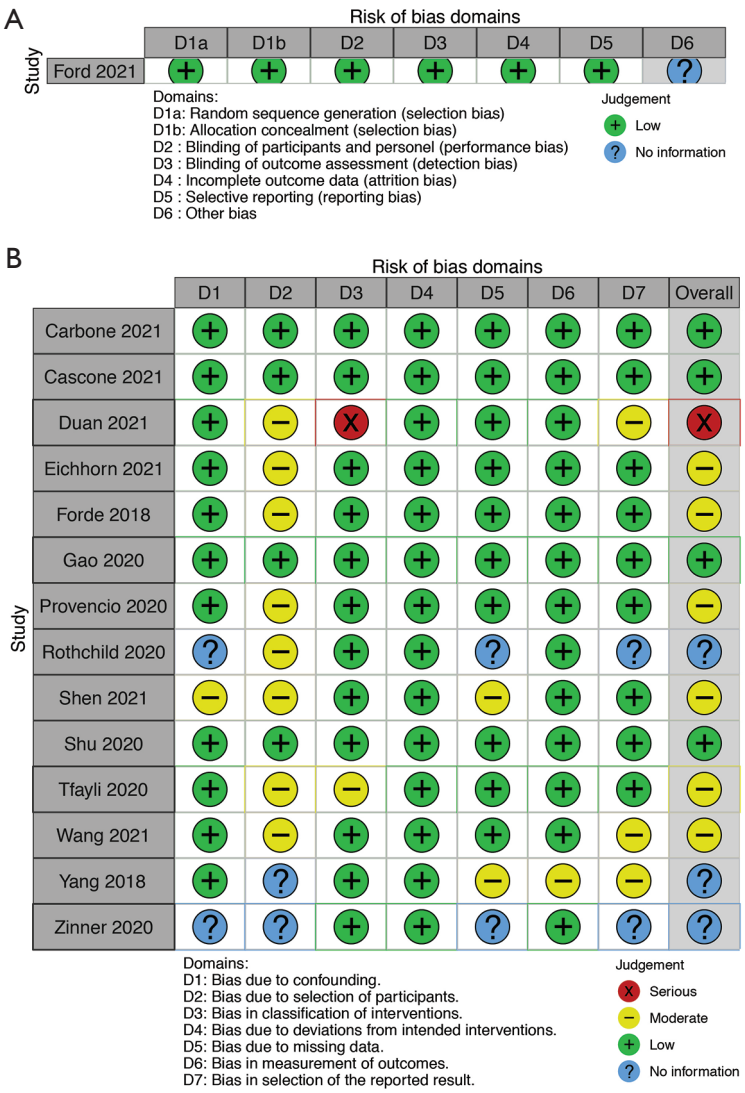

Figure S1 The risk of bias of the included studies. (A) Risk of bias of randomized trials; (B) Risk of bias of non-randomized trials.

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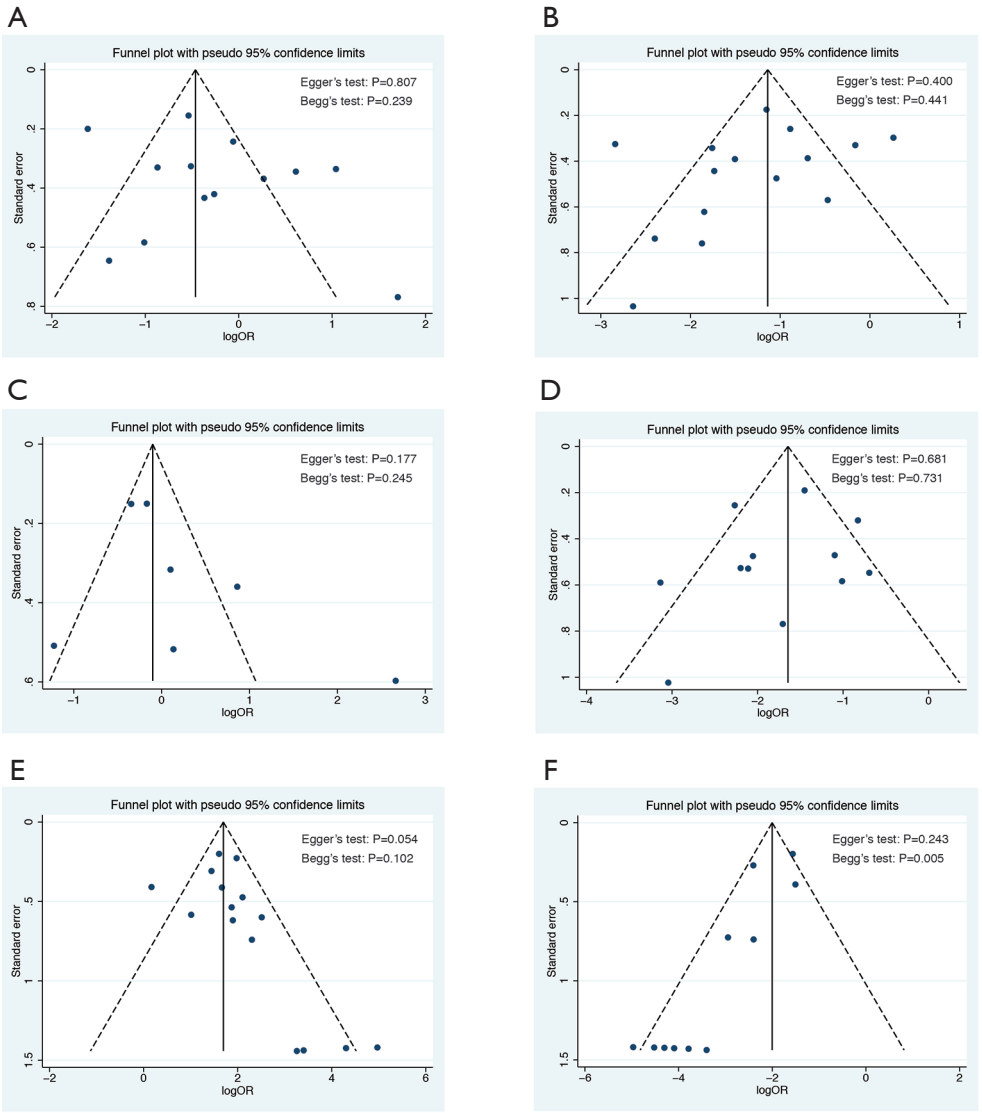

Figure S2 Publication bias of included studies. (A) Funnel plot for MPR; (B) Funnel plot for pCR; (C) Funnel plot for incidence of TRAE; (D) Funnel plot for incidence of SAE; (E) Funnel plot for resection rate; (F) Funnel plot for surgical delay rate.

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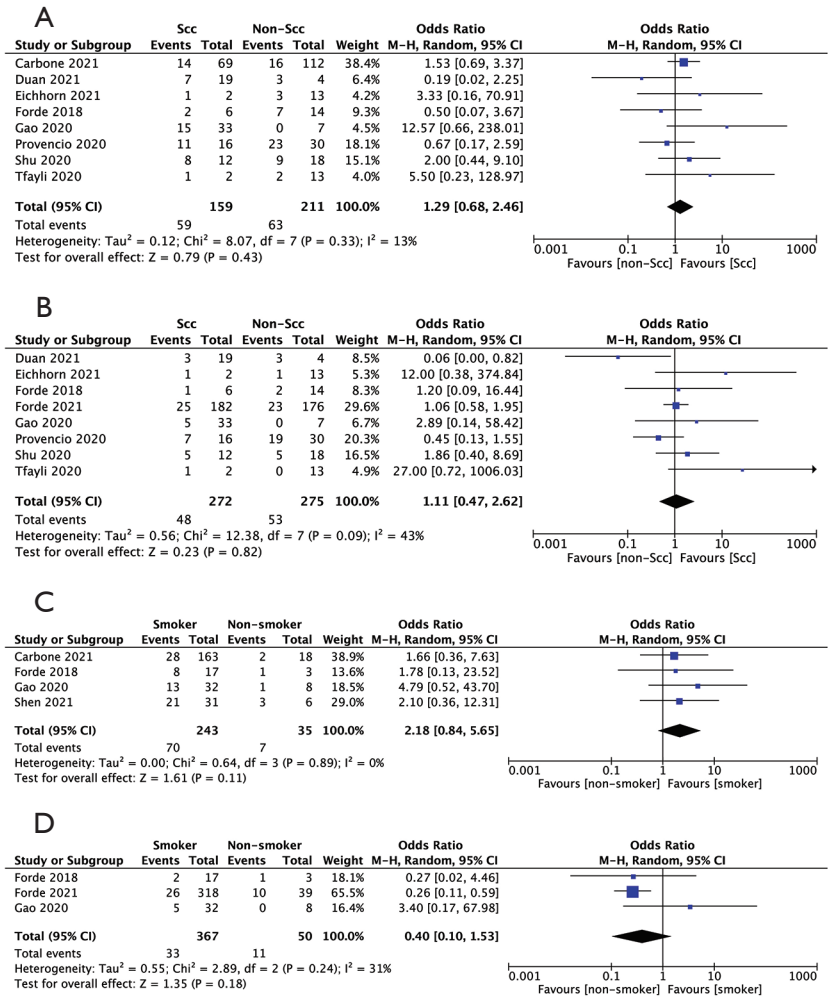

Figure S3 Forest plot of the pathological response of subgroup analysis based on histology subtypes and smoking status. (A) MPR among patients who are diagnosed with squamous cell carcinoma or non-squamous cell carcinoma; (B) pCR among patients diagnosed with squamous cell carcinoma or non-squamous cell carcinoma; (C) MPR among patients who are smokers or non-smokers; (D) pCR among patients who are smokers or non-smokers. Smokers, including current and former smokers; MPR, major pathological response; pCR, complete pathological response; M-H, Mantel-Haenszel; CI, confidence interval.

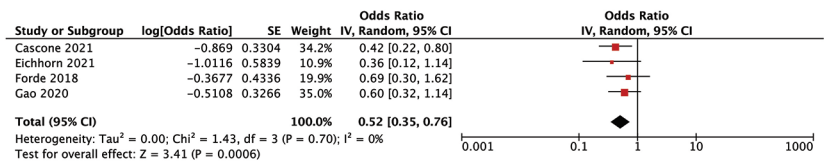

Figure S4 Forest plot of the MPR rate of the mono-ICI subgroup after removal of the Carbone 2021 study in the sensitivity analysis. MPR, major pathological response; ICI, immune checkpoint inhibitor.

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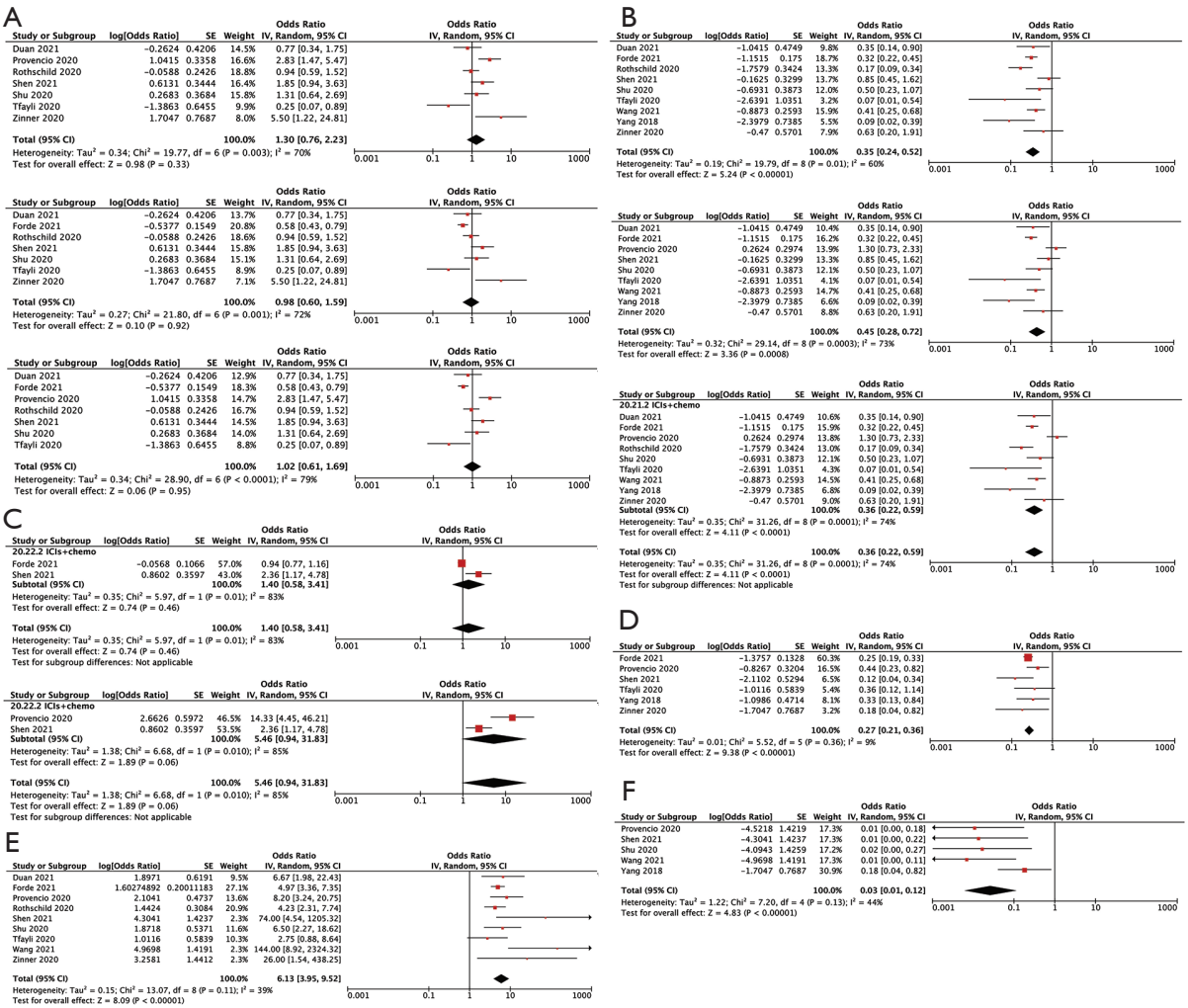

Figure S5 Forest plot of the efficacy and safety of the ICI + chemo subgroup in the sensitivity analysis. (A) MPR rate; (B) pCR rate; (C) Incidence of TRAEs; (D) incidence of SAEs; (E) resection rate; (F) surgical delay rate. MPR, major pathological response; pCR, complete pathological response; TRAE, treatment-related adverse event; SAE, severe adverse event; SE, standard error; IV, inverse variance; CI, confidence interval.

Table S1 Sensitivity analysis of efficacy- and safety-related endpoints

Subgroup	Endpoints	Ratio (95% CI)
Mono-ICI	MPR rate	34.2 (25.9–43.2)
ICI + chemo	MPR rate	56.5 (43.2–69.0)[a]; 49.5 (37.5–61.4)[b]; 50.5 (37.9–62.8)[c]
ICI + chemo	pCR rate	25.9 (19.4–34.2)[d]; 31.0 (21.9–41.9)[e]; 26.5 (18.0–37.1)[f]
ICI + chemo	Incidence of TRAEs	58.3 (36.7–77.3)[g]; 84.5 (48.5–97.0)[h]
ICI + chemo	Incidence of SAEs	21.3 (17.4–26.5)
ICI + chemo	Resection rate	86.0 (79.8–90.5)
ICI + chemo	Surgical delay rate	2.9 (1.0–10.7)

[a, b, c] refer to the pooled MPR rate of the ICI + chemo subgroup after removal of the Forde 2021 study, Provencio 2020 study, or Zinner 2020 study, respectively; [d, e, f] refer to the pooled pCR rate of the ICI + chemo subgroup after removal of the Provencio 2020 study, Rothschild 2021 study, or Shen 2021 study, respectively; [g, h] refer to the pooled incidence of TRAEs of the ICI + chemo subgroup after removal of the Provencio 2020 study and Forde 2021 study, respectively. ICI, immune checkpoint inhibitor; chemo, chemotherapy; mono-ICI, single-agent immune checkpoint inhibitor; MPR, major pathological response; pCR, complete pathological response; TRAE, treatment-related adverse event; SAE, severe adverse event; CI, confidence interval.

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