**Supplemental Methods**

**Search strategies and number of studies yielded from each database**

*PubMed*：1,118 results

(("Carcinoma, Non-Small-Cell Lung"[Mesh]) OR (((((((Carcinoma[Title/Abstract]) OR (Non Small Cell Lung[Title/Abstract])) OR (Lung Carcinoma[Title/Abstract])) OR (Non-Small-Cell[Title/Abstract])) OR (Non-Small-Cell Lung Carcinomas[Title/Abstract])) OR (Lung Neoplasms[Title/Abstract])) OR (Pulmonary Neoplasms[Title/Abstract]))) AND (("pembrolizumab" [Supplementary Concept]) OR ((((SCH-900475[Title/Abstract]) OR (Keytruda[Title/Abstract])) OR (MK-3475[Title/Abstract])) OR (lambrolizumab[Title/Abstract])))

*Embase*：7,155 results

('pembrolizumab'/exp OR 'sch-900475':ab,ti OR 'keytruda':ab,ti OR 'MK-3475':ab,ti OR 'lambrolizumab':ab,ti) AND ('non small cell lung cancer'/exp OR 'lung neoplasm':ab,ti OR 'non small cell lung carcinoma':ab,ti OR 'NSCLC':ab,ti OR 'lung carcinoma':ab,ti OR 'non-small-cell lung carcinomas':ab,ti OR 'pulmonary neoplasms':ab,ti)

*Cochrane*：640 results; 639 trials

#1 MeSH descriptor: [Carcinoma, Non-Small-Cell Lung] explode all trees

#2 "Non Small Cell Lung" OR "Non Small Cell Lung Carcinomas" OR "Non-Small-Cell" OR "Lung Neoplasms" OR "NSCLC"

#3 "pembrolizumab" OR "lambrolizumab" OR "Keytruda" OR "MK-3475"

#4 (#1 OR #2) AND #3

*Web of Science*：3,118 results

TS=((“Non small Cell Lung Cancer” OR “lung neoplasm” OR “Non Small Cell Lung Carcinoma” OR “NSCLC”) and (“Pembrolizumab” OR “Keytruda”))

Supplemental **TABLE S1** Bias risk evaluation of randomized controlled trials included in the meta-analysis.

| Reference | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias |
|---|---|---|---|---|---|---|---|
| D. Rodríguez-Abreu[2021] | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Unclear risk |
| Luis Paz-Ares [2018] | Low risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk |
| Mark M. Awad, MD[2020] | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Unclear risk |
| Oscar Arrieta, MD, MSc[2020] | Low risk | Low risk | Low risk | Unclear risk | High risk | Low risk | Unclear risk |
| Ying Cheng[2021] | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Unclear risk |
| Hidehito Horinouchi [2021] | Low risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk |
| Martin Reck [2016] | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Unclear risk |
| Tony S K Mok[2019] | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Unclear risk |
| R S Herbst [2021] | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Unclear risk |
| Zhou C [2020] | Low risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk |
| Yi-Long Wu[2021] | Low Risk | Unclear Risk | High Risk | Low Risk | Low Risk | Low risk | Unclear risk |

Supplemental **TABLE S2** Bias risk evaluation of the retrospective studies included in the meta-analysis.

| Reference | A clearly stated aim | Inclusion of consecutive patients | Prospective collection of data | Endpoints appropriate to the aim of the study | Unbiased assessment of the study endpoint | Follow-up period appropriate to the aim of the study | Loss to follow up less than 5% | Prospective calculation of the study size | Score |
|---|---|---|---|---|---|---|---|---|---|
| Muhammad Zubair Afzal[2018] | 2 | 2 | 0 | 1 | 0 | 1 | 2 | 2 | 18 |
| Jiatao Liao[2021] | 2 | 2 | 0 | 2 | 0 | 1 | 2 | 2 | 19 |
| Jie Zhang[2021] | 2 | 2 | 0 | 2 | 0 | 2 | 2 | 2 | 19 |
| Alex Friedlaender [2020] | 2 | 2 | 0 | 2 | 0 | 1 | 2 | 2 | 11 |
| Doran Ksienski [2019] | 2 | 2 | 0 | 1 | 0 | 1 | 2 | 2 | 10 |
| Karim Amrane [2019] | 2 | 2 | 0 | 2 | 0 | 1 | 2 | 2 | 11 |
| Alessio Cortellini [2020]-1 | 2 | 2 | 0 | 2 | 0 | 2 | 1 | 2 | 11 |
| Alessio Cortellini [2020]-2 | 1 | 2 | 0 | 2 | 0 | 2 | 1 | 2 | 10 |
| Francesco Facchinetti [2020] | 1 | 2 | 0 | 2 | 0 | 2 | 2 | 2 | 11 |
| EJ Aguilar [2019] | 2 | 2 | 0 | 2 | 0 | 2 | 2 | 2 | 12 |
| Giulio Metro[2020] | 2 | 2 | 0 | 2 | 0 | 1 | 2 | 2 | 11 |
| Joao V Alessi[2020] | 1 | 2 | 0 | 2 | 0 | 2 | 2 | 2 | 11 |
| Ryuya EdahiroI [2019] | 2 | 2 | 0 | 1 | 0 | 2 | 2 | 1 | 10 |
| Angel Qin[2017] | 2 | 2 | 0 | 1 | 0 | 1 | 2 | 1 | 9 |
| Tetsuya Sakai[2020] | 2 | 2 | 0 | 2 | 0 | 2 | 2 | 2 | 12 |
| Yuichi Tambo[2020] | 2 | 2 | 0 | 2 | 0 | 1 | 2 | 2 | 11 |
| Motohiro Tamiya [2019] | 2 | 2 | 0 | 2 | 0 | 1 | 2 | 2 | 11 |
| Hisao Imai[2020] | 2 | 2 | 0 | 2 | 0 | 1 | 2 | 2 | 11 |
| Kazushige Wakuda, MD[2020] | 2 | 2 | 0 | 2 | 0 | 1 | 2 | 2 | 11 |
| Ferréol Roborel de Climens [2021] | 2 | 2 | 0 | 2 | 0 | 1 | 2 | 2 | 11 |
| Nikolaj Frost-2021 | 2 | 2 | 0 | 2 | 0 | 2 | 2 | 2 | 12 |
| Rocío Jiménez Galán[2021] | 2 | 2 | 0 | 2 | 0 | 2 | 2 | 1 | 11 |
| Kazutaka Hosoya [2021] | 2 | 2 | 0 | 2 | 0 | 2 | 1 | 1 | 10 |
| Hisao Imai[2021] | 2 | 2 | 0 | 2 | 0 | 2 | 1 | 2 | 11 |
| Lova Sun[2020] | 2 | 2 | 0 | 2 | 0 | 2 | 2 | 1 | 11 |
| Velcheti [2021] | 2 | 2 | 0 | 2 | 0 | 2 | 2 | 1 | 11 |

Subgroup analysis of ORR in retrospective studies.

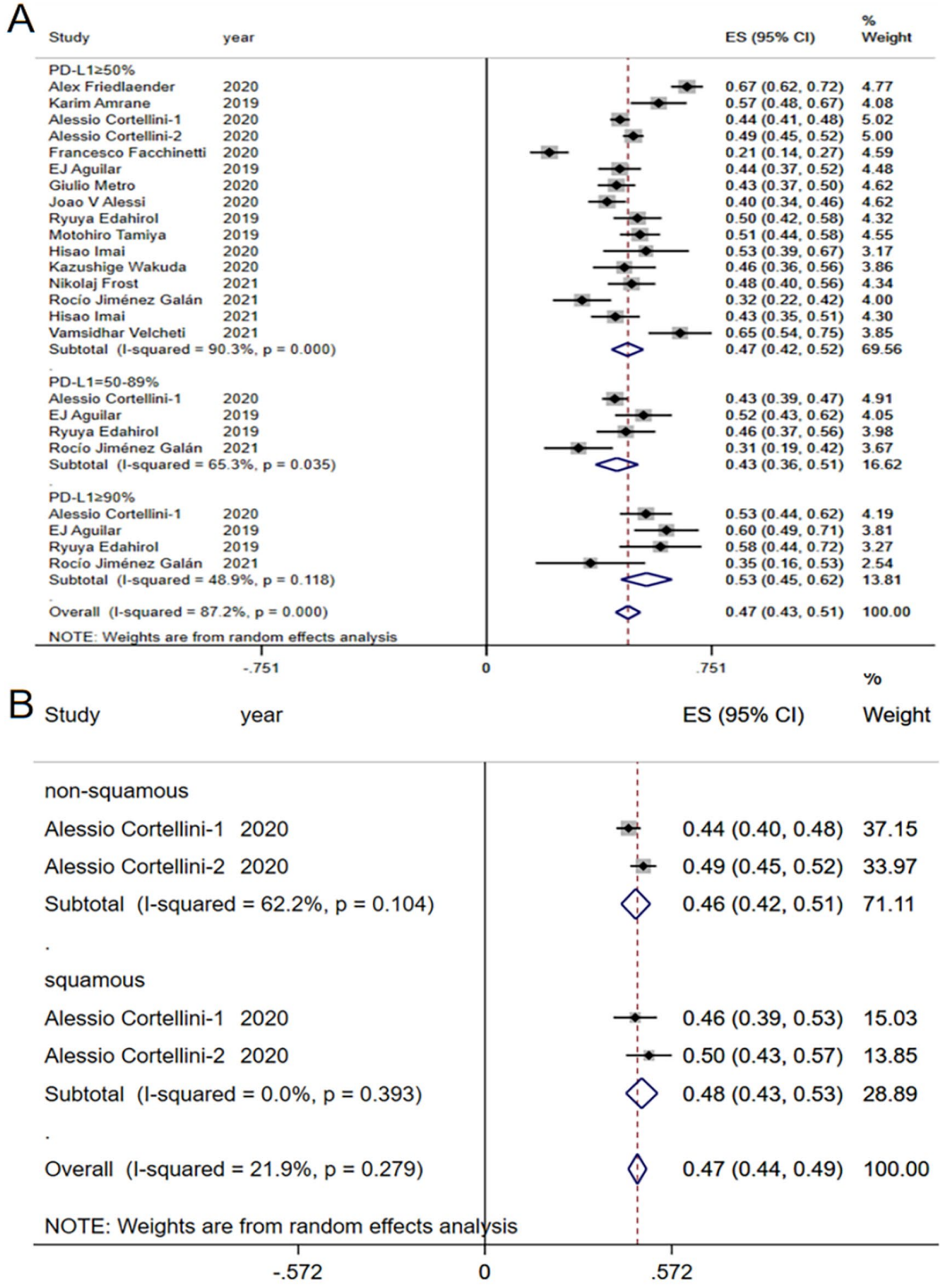


**FIGURE S1**

Forest plot of odds ratio(OR) of overall response rate (ORR) associated with Pembrolizumab in real-world studies (RWSs) with **A (**programmed death-ligand 1(PD-L1) subgroups), **B** (ECOG-PS subgroups), **C** (squamous or non-squamous subgroups), **D** (brain metastases or no-brain metastases subgroups), **E** (male or female subgroups).

Subgroup analysis of ORR in RCT studies

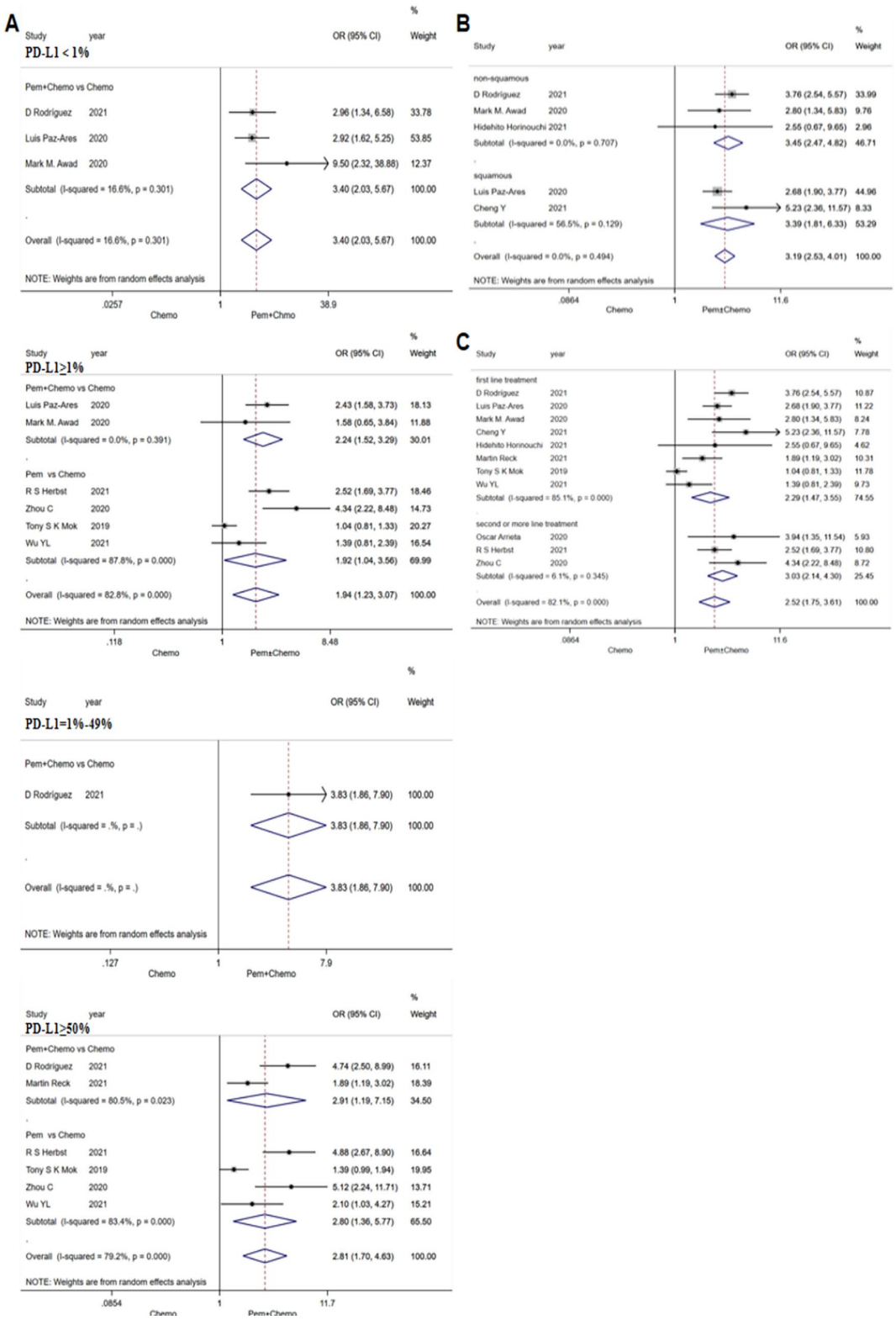


**FIGURE S2**

Forest plots of odds ratio(OR) of overall response rate (ORR) associated with Pem±Chemo vs Chemo in randomized clinical trials (RCTs) with **A**(programmed death-ligand 1(PD-L1) subgroups), **B**(squamous or non-squamous subgroups), **C**(first line treatment or second or more line treatment subgroups). Pem, pembrolizumab Chemo, chemotherapy.

Subgroup analysis of PFS in RCT studies

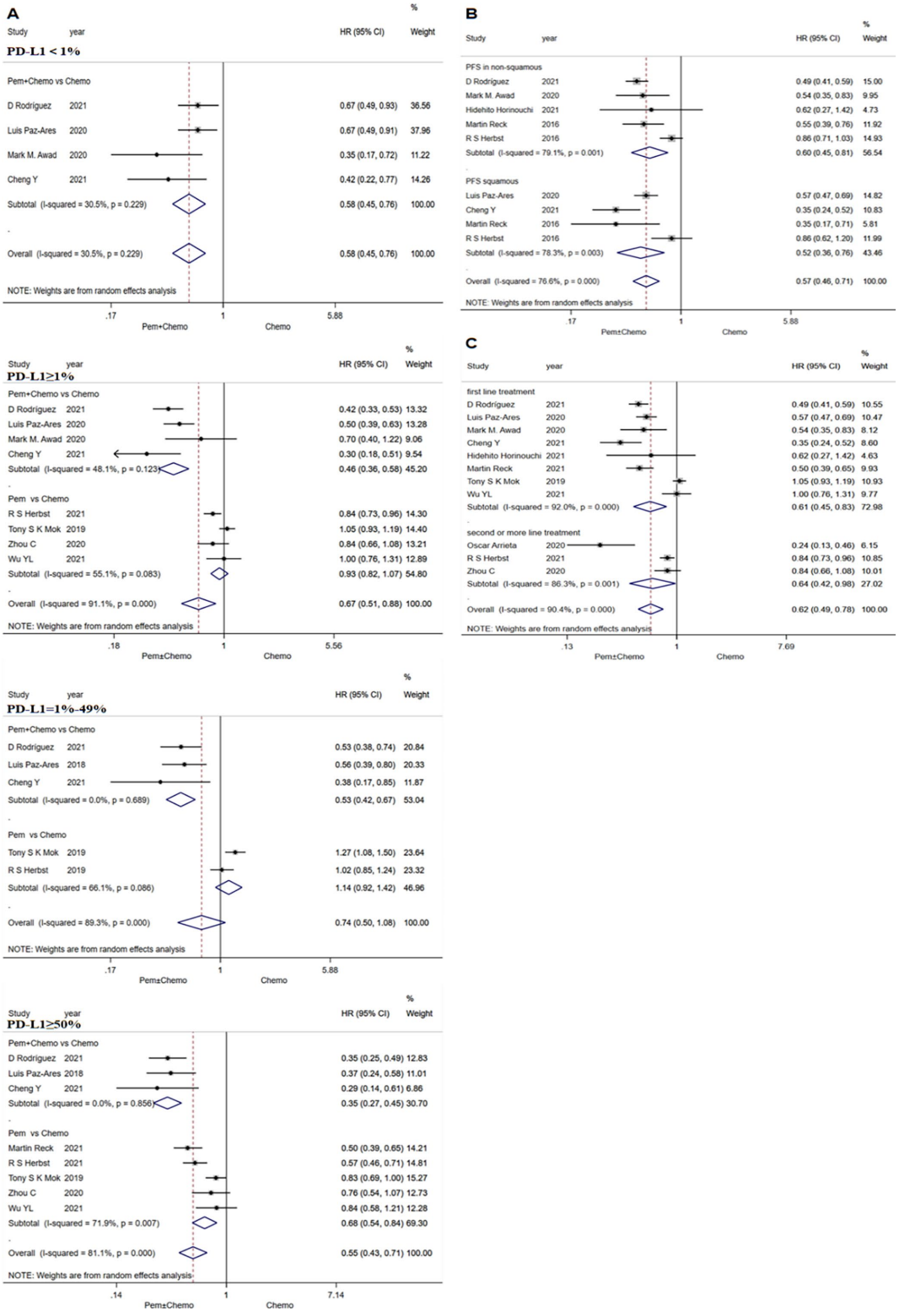


**FIGURE S3**

Forest plots of hazard ratio (HR) of progression-free survival (PFS) associated with Pem±Chemo vs Chemo in randomized clinical trials(RCTs) with **A** (programmed death-ligand 1(PD-L1) subgroups of PFS), **B** (squamous or non-squamous subgroups of PFS), **C** (first line treatment and second or more line treatment subgroups of PFS).

Subgroup analysis of OS in RCT studies

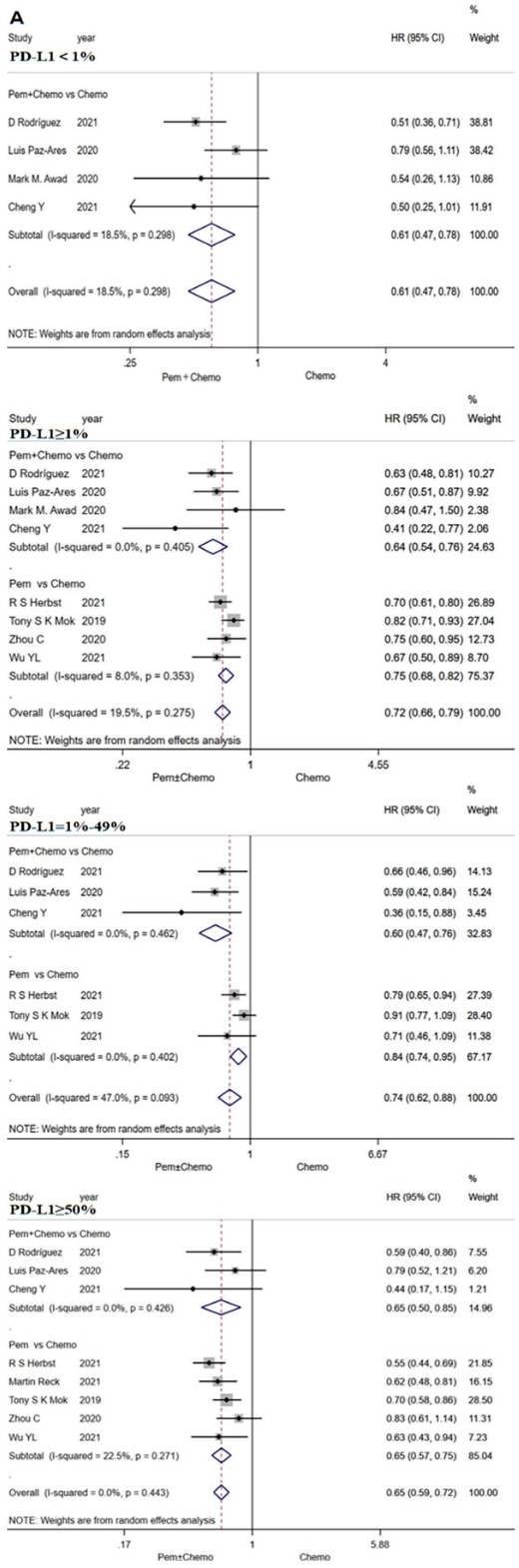


**FIGURE S4**

Forest plots of hazard ratio (HR) of overall survival (OS) associated with Pem±Chemo vs Chemo in randomized clinical trials(RCTs) with **A** (programmed death-ligand 1(PD-L1) subgroups of OS), **B** (squamous or non-squamous subgroups of OS), **C** (first line treatment and second or more line treatment subgroups of OS). Pem, pembrolizumab; Chemo, chemotherapy.

Sensitivity analysis of ORR for Pembrolizumab monotherapy or plus chemotherapy

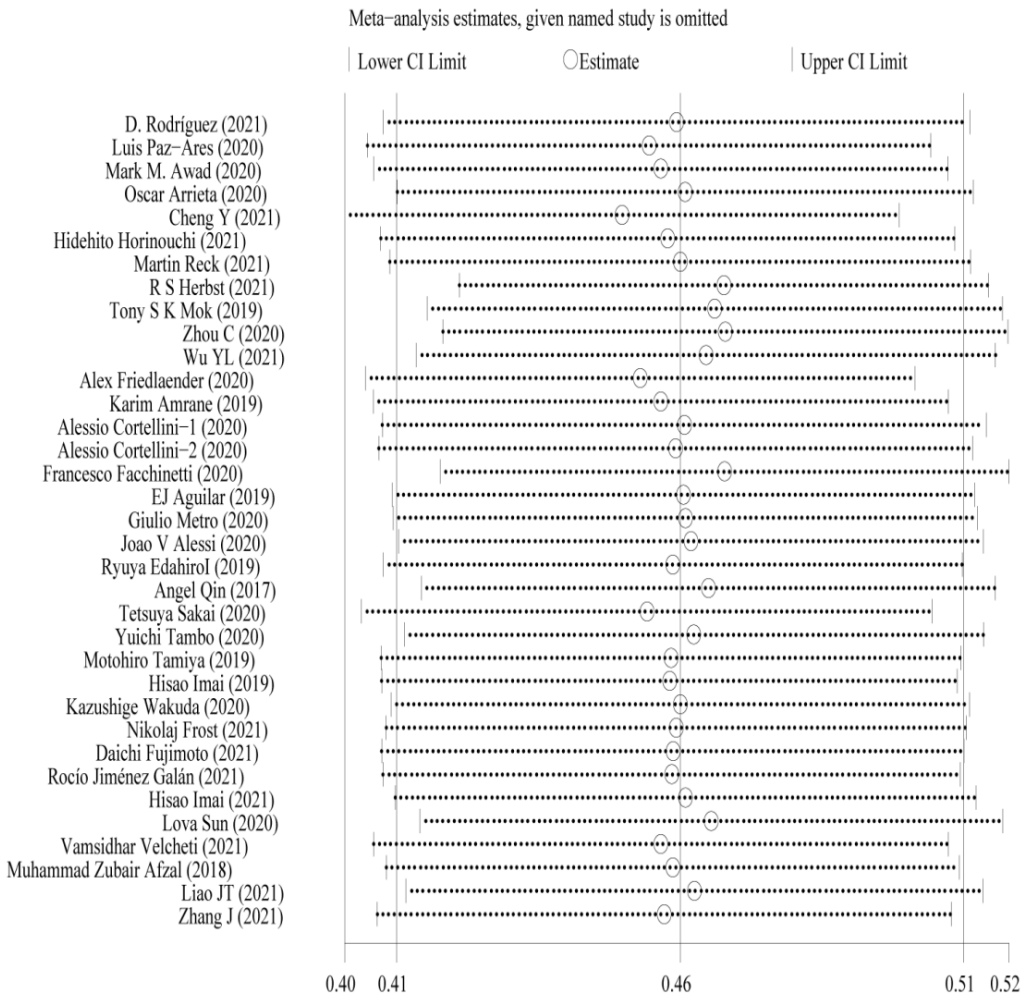


**FIGURE S5**

Sensitivity analysis of ORR for Pembrolizumab monotherapy or plus chemotherapy.

Begg’s and Egger linear regression test of ORR for Pembrolizumab monotherapy or plus chemotherapy

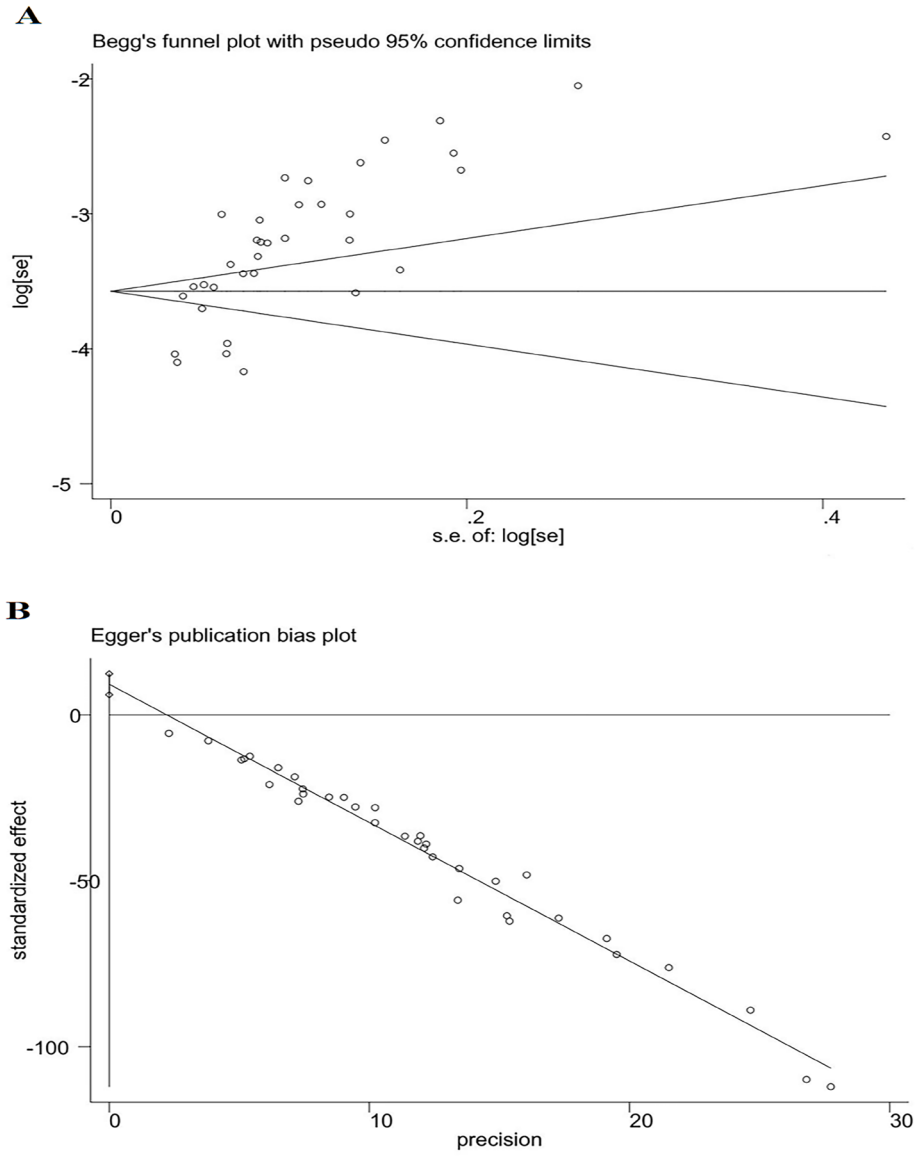


**FIGURE S6**

(**A**) Begg’s test of ORR for Pembrolizumab monotherapy or plus chemotherapy, (**B**) Egger’s linear regression test of ORR for Pembrolizumab monotherapy or plus chemotherapy.