

Attached file 1: Table S1, S2 and S3: Search strategy for PubMed, Embase, and the Cochrane Library.

Attached file 2:Table S4 Reference list of all excluded studies.

Attached file 3: Figure S1 to Figure S3: Incidence of global irAEs (all grade and severe grade) associated with anti-PD-1, anti-PD-L1 or anti-CTLA-4 drugs; **Figure S4:** Incidence of global irAEs (all grade and severe grade) associated with anti-PD-1 and anti-PD-L1 drugs; **Figure S5 to Figure S32:** Incidence of organ-specific (i.e., disease of endocrinopathy, gastroenterology, hepatology, neurology, hematology, dermatology, pulmonology, nephrology, cardiology and rheumatic immunology) irAEs (all grade and severe grade) associated with anti-PD-1, anti-PD-L1, anti-CTLA-4, or anti-PD-1 and anti-PD-L1 drugs; **Figure S33:** Death related to irAEs.

Attached file 4: Table S5: General characteristics of patients receiving anti-PD-1/anti-PD-L1 antibodies, as described in case reports (n = 35); **Table S6:** Organ-specific immune-related adverse events.

Attached file 5: Figure S34 and S35: The Cochrane Collaboration's tool for assessing risk of bias in RCTs; **Figure S36:** The influence of a single study on the total merger effect.

Attached file 6: Figure S37: Galbraith Plot for Heterogeneity; **Figure S38:** Begg's funnel plot for publication bias; **Figure S39:** Egger's publication bias plot.

Attached file 1

Supplementary Table 1. Search strategy for PubMed

Query	Search term
#1	P (((Neoplasm, Stomach[Title/Abstract] OR Stomach oplasm[Title/Abstract] OR Neoplasms, Stomach[Title/Abstract] OR Gastric Neoplasms[Title/Abstract] OR Gastric Neoplasm[Title/Abstract] OR Neoplasm, Gastric[Title/Abstract] OR Neoplasms, Gastric[Title/Abstract] OR Cancer of Stomach[Title/Abstract] OR Stomach Cancers[Title/Abstract] OR Gastric Cancer[Title/Abstract] OR Cancer, Gastric[Title/Abstract] OR Cancers, Gastric[Title/Abstract] OR Gastric Cancers[Title/Abstract] OR Stomach Cancer[Title/Abstract] OR Cancer, Stomach[Title/Abstract] OR Cancers, Stomach[Title/Abstract] OR Cancer of the Stomach[Title/Abstract] OR Gastric Cancer, Familial Diffuse[Title/Abstract] OR gastroesophageal junction cancer[Title/Abstract] OR gastroesophageal junction adenocarcinoma[Title/Abstract] OR adenocarcinoma gastroesophageal junction[Title/Abstract] OR gastric gastroesophageal junction[Title/Abstract] OR gastroesophageal junction tumors[Title/Abstract] OR gastroesophageal junction tumor[Title/Abstract] OR gastric gastroesophageal junction cancer[Title/Abstract] OR gastroesophageal junction carcinoma[Title/Abstract] OR adenocarcinoma of gastroesophageal junction[Title/Abstract] OR gastric[Title/Abstract] AND gastroesophageal junction adenocarcinoma[Title/Abstract] OR immunotherapy for gastroesophageal cancer[Title/Abstract] OR advanced gastroesophageal cancer[Title/Abstract] OR gastroesophageal cancer her2[Title/Abstract] OR gastroesophageal junction cancer[Title/Abstract] OR gastroesophageal junction cancer gastric[Title/Abstract] OR gastroesophageal junction cancer

esophageal[Title/Abstract] OR gastroesophageal junction cancer chemotherapy[Title/Abstract] OR gastroesophageal junction cancer neoadjuvant[Title/Abstract] OR gastroesophageal junction cancer trastuzumab[Title/Abstract] OR gastroesophageal junction cancer trial[Title/Abstract] OR gastroesophageal junction cancer treated[Title/Abstract] OR gastroesophageal junction cancer patients with advanced[Title/Abstract] OR gastroesophageal junction cancer survival[Title/Abstract] OR gastroesophageal junction cancer staging[Title/Abstract] OR gastroesophageal junction cancer locally advanced[Title/Abstract] OR gastroesophageal junction cancer meta-analysis[Title/Abstract] OR gastroesophageal junction cancer pembrolizumab[Title/Abstract] OR gastroesophageal junction cancer gejc[Title/Abstract] OR gastroesophageal junction cancer gc[Title/Abstract] OR gastroesophageal junction cancer advanced gastric[Title/Abstract]) OR ("Stomach Neoplasms"[Mesh]))

#2 I ((Checkpoint Inhibitors, Immune[Title/Abstract] OR Immune Checkpoint Inhibitor[Title/Abstract] OR Checkpoint Inhibitor, Immune[Title/Abstract] OR Immune Checkpoint Blockers[Title/Abstract] OR Checkpoint Blockers, Immune[Title/Abstract] OR Immune Checkpoint Blockade[Title/Abstract] OR Checkpoint Blockade, Immune[Title/Abstract] OR Immune Checkpoint Inhibition[Title/Abstract] OR Checkpoint Inhibition, Immune[Title/Abstract] OR PD-L1 Inhibitors[Title/Abstract] OR PD L1 Inhibitors[Title/Abstract] OR PD-L1 Inhibitor[Title/Abstract] OR PD L1 Inhibitor[Title/Abstract] OR Programmed Death-Ligand 1 Inhibitors[Title/Abstract] OR Programmed Death Ligand 1 Inhibitors[Title/Abstract] OR CTLA-4 Inhibitors[Title/Abstract] OR CTLA 4 Inhibitors[Title/Abstract] OR CTLA-4 Inhibitor[Title/Abstract] OR CTLA 4 Inhibitor[Title/Abstract] OR Cytotoxic T-

Lymphocyte-Associated Protein 4 Inhibitors[Title/Abstract] OR Cytotoxic T Lymphocyte Associated Protein 4 Inhibitors[Title/Abstract] OR Cytotoxic T-Lymphocyte-Associated Protein 4 Inhibitor[Title/Abstract] OR Cytotoxic T Lymphocyte Associated Protein 4 Inhibitor[Title/Abstract] OR PD-1 Inhibitors[Title/Abstract] OR PD 1 Inhibitors[Title/Abstract] OR PD-1 Inhibitor[Title/Abstract] OR Inhibitor, PD-1[Title/Abstract] OR PD 1 Inhibitor[Title/Abstract] OR Programmed Cell Death Protein 1 Inhibitor[Title/Abstract] OR Programmed Cell Death Protein 1 Inhibitors[Title/Abstract] OR PD-1-PD-L1 Blockade[Title/Abstract] OR Blockade, PD-1-PD-L1[Title/Abstract] OR PD 1 PD L1 Blockade[Title/Abstract] OR ipilimumab[Title/Abstract] OR ticilimumab[Title/Abstract] OR nivolumab[Title/Abstract] OR pembrolizumab[Title/Abstract] OR pidilizumab[Title/Abstract] OR atezolizumab[Title/Abstract] OR durvalumab[Title/Abstract] OR avelumab[Title/Abstract]) OR ("Immune Checkpoint Inhibitors"[Mesh]))

#3 O (immune-related adverse events[Title/Abstract] OR immune related adverse events checkpoint inhibitors[Title/Abstract] OR immune related adverse events checkpoint blockade[Title/Abstract] OR management of immune related adverse events[Title/Abstract] OR immune related adverse events in patients[Title/Abstract] OR immune related adverse events systemic immunosuppression[Title/Abstract] OR immune related adverse events toxicity treatment[Title/Abstract] OR immune related adverse events anti-pd1 immunotherapy[Title/Abstract] OR related adverse events gastrointestinal cancer[Title/Abstract] OR adverse events on survival[Title/Abstract] OR adverse events of special interest[Title/Abstract] OR immune related adverse events promising predictors[Title/Abstract] OR immune

related adverse events anti-tumor efficacy[Title/Abstract] OR immune related adverse events comprehensive review[Title/Abstract] OR immune related adverse events treatment failure[Title/Abstract] OR immune related adverse events single centre[Title/Abstract] OR immune related adverse events drug administration[Title/Abstract] OR immune-related adverse events checkpoint[Title/Abstract] OR immune-related adverse events of checkpoint inhibitors[Title/Abstract] OR immune-related adverse events cancer[Title/Abstract] OR immune-related adverse events checkpoint inhibitors[Title/Abstract] OR management of immune-related adverse events in patients[Title/Abstract] OR checkpoint inhibitors immune-related adverse events[Title/Abstract] OR cutaneous immune-related adverse events[Title/Abstract] OR immune-related adverse events pneumonitis[Title/Abstract] OR rheumatic immune-related adverse events[Title/Abstract] OR multisystem immune-related adverse events[Title/Abstract] OR irAEs[Title/Abstract] OR trAEs[Title/Abstract] OR organ-specific adverse events[Title/Abstract] OR immune-related pneumonia[Title/Abstract] OR organ-specific AEs[Title/Abstract]))

#4 S ("randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR randomized[tiab] OR placebo[tiab] OR "drug therapy"[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR "randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR "clinical trials as topic"[mesh] OR "random allocation"[mesh] OR "double-blind method"[mesh] OR "single-blind method"[mesh] OR "clinical trial"[pt] OR "research design"[mesh:noexp] OR "comparative study"[pt] OR "evaluation studies"[pt] OR "follow-up studies"[mesh] OR "prospective studies"[mesh] OR "cross-over studies"[mesh] OR "clinical trial"[tw] OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw])) AND (mask*[tw] OR blind*[tw])) OR placebo*[tw] OR

random*[tw] OR "control"[tw] OR "controls"[tw] OR prospectiv*[tw] OR volunteer*[tw])

#5 #1 AND #2 AND #3 AND #4

Supplementary Table 2. Search strategy for Embase

Query	Search term
#1	P 'stomach cancer'/exp OR 'Neoplasm, Stomach' OR 'Stomach oplasm' OR 'Neoplasms, Stomach' OR 'Gastric Neoplasms' OR 'Gastric Neoplasm' OR 'Neoplasm, Gastric' OR 'Neoplasms, Gastric' OR 'Cancer of Stomach' OR 'Stomach Cancers' OR 'Gastric Cancer' OR 'Cancer, Gastric' OR 'Cancers, Gastric' OR 'Gastric Cancers' OR 'Stomach Cancer' OR 'Cancer, Stomach' OR 'Cancers,Stomach' OR 'Cancer of the Stomach' OR 'Gastric Cancer, Familial Diffuse' OR 'gastroesophageal junction cancer' OR 'gastroesophageal junction adenocarcinoma' OR 'adenocarcinoma gastroesophageal junction' OR 'gastric gastroesophageal junction' OR 'gastroesophageal junction tumors' OR 'gastroesophageal junction tumor' OR 'gastric gastroesophageal junction cancer' OR 'gastroesophageal junction carcinoma' OR 'adenocarcinoma of gastroesophageal junction' OR 'gastric and gastroesophageal junction adenocarcinoma' OR 'immunotherapy for gastroesophageal cancer' OR 'advanced gastroesophageal cancer' OR 'gastroesophageal cancer her2' OR 'gastroesophageal junction cancer' OR 'gastroesophageal junction cancer gastric' OR 'gastroesophageal junction cancer esophageal' OR 'gastroesophageal junction cancer chemotherapy' OR 'gastroesophageal junction cancer neoadjuvant' OR 'gastroesophageal junction cancer trastuzumab' OR 'gastroesophageal junction cancer trial' OR 'gastroesophageal junction cancer treated' OR

'gastroesophageal junction cancer patients with advanced' OR 'gastroesophageal junction cancer survival' OR 'gastroesophageal junction cancer staging' OR 'gastroesophageal junction cancer locally advanced' OR 'gastroesophageal junction cancer meta-analysis' OR 'gastroesophageal junction cancer pembrolizumab' OR 'gastroesophageal junction cancer gejc' OR 'gastroesophageal junction cancer gc' OR 'gastroesophageal junction cancer advanced gastric'

#2 I 'immune checkpoint inhibitor'/exp OR 'Immune checkpoint inhibitors' OR 'Checkpoint Inhibitors, Immune' OR 'Immune Checkpoint Inhibitor' OR 'Checkpoint Inhibitor, Immune' OR 'Immune Checkpoint Blockers' OR 'Checkpoint Blockers, Immune' OR 'Immune Checkpoint Blockade' OR 'Checkpoint Blockade, Immune' OR 'Immune Checkpoint Inhibition' OR 'Checkpoint Inhibition, Immune' OR 'PD-L1 Inhibitors' OR 'PD L1 Inhibitors' OR 'PD-L1 Inhibitor' OR 'PD L1 Inhibitor' OR 'Programmed Death-Ligand 1 Inhibitors' OR 'Programmed Death Ligand 1 Inhibitors' OR 'CTLA-4 Inhibitors' OR 'CTLA 4 Inhibitors' OR 'CTLA-4 Inhibitor' OR 'CTLA 4 Inhibitor' OR 'Cytotoxic T-Lymphocyte-Associated Protein 4 Inhibitors' OR 'Cytotoxic T Lymphocyte Associated Protein 4 Inhibitors' OR 'Cytotoxic T-Lymphocyte-Associated Protein 4 Inhibitor' OR 'Cytotoxic T Lymphocyte Associated Protein 4 Inhibitor' OR 'PD-1 Inhibitors' OR 'PD 1 Inhibitors' OR 'PD-1 Inhibitor' OR 'Inhibitor, PD-1' OR 'PD 1 Inhibitor' OR 'Programmed Cell Death Protein 1 Inhibitor' OR 'Programmed Cell Death Protein 1 Inhibitors' OR 'PD-1-PD-L1 Blockade' OR 'Blockade, PD-1-PD-L1' OR 'PD 1 PD L1 Blockade' OR 'ipilimumab' OR 'ticilimumab' OR 'nivolumab' OR 'pembrolizumab' OR 'pidilizumab' OR 'atezolizumab' OR 'durvalumab' OR 'avelumab'

#3 O 'immune-related adverse events' OR 'immune related adverse events checkpoint inhibitors' OR 'immune related

adverse events checkpoint blockade' OR 'management of immune related adverse events' OR 'immune related adverse events in patients' OR 'immune related adverse events systemic immunosuppression' OR 'immune related adverse events toxicity treatment' OR 'immune related adverse events anti-pd1 immunotherapy' OR 'related adverse events gastrointestinal cancer' OR 'adverse events on survival' OR 'adverse events of special interest' OR 'immune related adverse events promising predictors' OR 'immune related adverse events anti-tumor efficacy' OR 'immune related adverse events comprehensive review' OR 'immune related adverse events treatment failure' OR 'immune related adverse events single centre' OR 'immune related adverse events drug administration' OR 'immune-related adverse events checkpoint' OR 'immune-related adverse events of checkpoint inhibitors' OR 'immune-related adverse events cancer' OR 'immune-related adverse events checkpoint inhibitors' OR 'management of immune-related adverse events in patients' OR 'checkpoint inhibitors immune-related adverse events' OR 'cutaneous immune-related adverse events' OR 'immune-related adverse events pneumonitis' OR 'rheumatic immune-related adverse events' OR 'multisystem immune-related adverse events' OR 'irAEs' OR 'trAEs' OR 'organ-specific adverse events' OR 'immune-related pneumonia' OR 'organ-specific AEs'

#4 S 'randomized controlled trial'/exp OR 'controlled clinical trial'/exp OR randomized:ti,ab OR placebo:ti,ab OR 'drug therapy':lnk OR randomly:ti,ab OR trial:ti,ab OR groups:ti,ab

#5 #1 AND #2 AND #3 AND #4

Supplementary Table 3. Search strategy for Cochrane

Query	Search term
#1	<p>P MeSH descriptor: [Stomach Neoplasms] explode all trees OR Neoplasm, Stomach OR Stomach oplasm OR Neoplasms, Stomach OR Gastric Neoplasms OR Gastric Neoplasm OR Neoplasm, Gastric OR Neoplasms, Gastric OR Cancer of Stomach OR Stomach Cancers OR Gastric Cancer OR Cancer, Gastric OR Cancers, Gastric OR Gastric Cancers OR Stomach Cancer OR Cancer, Stomach OR Cancers, Stomach OR Cancer of the Stomach OR Gastric Cancer, Familial Diffuse OR gastroesophageal junction cancer OR gastroesophageal junction adenocarcinoma OR adenocarcinoma gastroesophageal junction OR gastric gastroesophageal junction OR gastroesophageal junction tumors OR gastroesophageal junction tumor OR gastric gastroesophageal junction cancer OR gastroesophageal junction carcinoma OR adenocarcinoma of gastroesophageal junction OR gastric and gastroesophageal junction adenocarcinoma OR immunotherapy for gastroesophageal cancer OR advanced gastroesophageal cancer OR gastroesophageal cancer her2 OR gastroesophageal junction cancer OR gastroesophageal junction cancer gastric OR gastroesophageal junction cancer esophageal OR gastroesophageal junction cancer chemotherapy OR gastroesophageal junction cancer neoadjuvant OR gastroesophageal junction cancer trastuzumab OR gastroesophageal junction cancer trial OR gastroesophageal junction cancer treated OR gastroesophageal junction cancer patients with advanced OR gastroesophageal junction cancer survival OR gastroesophageal junction cancer staging OR gastroesophageal junction cancer locally advanced OR gastroesophageal junction cancer meta-analysis OR gastroesophageal junction cancer pembrolizumab OR gastroesophageal junction cancer gejc OR gastroesophageal junction cancer gc OR gastroesophageal junction cancer advanced gastric</p>

- #2 I MeSH descriptor: [Immune Checkpoint Inhibitors] explode all trees OR Checkpoint Inhibitors, Immune OR Immune Checkpoint Inhibitor OR Checkpoint Inhibitor, Immune OR Immune Checkpoint Blockers OR Checkpoint Blockers, Immune OR Immune Checkpoint Blockade OR Checkpoint Blockade, Immune OR Immune Checkpoint Inhibition OR Checkpoint Inhibition, Immune OR PD-L1 Inhibitors OR PD L1 Inhibitors OR PD-L1 Inhibitor OR PD L1 Inhibitor OR Programmed Death-Ligand 1 Inhibitors OR Programmed Death Ligand 1 Inhibitors OR CTLA-4 Inhibitors OR CTLA 4 Inhibitors OR CTLA-4 Inhibitor OR CTLA 4 Inhibitor OR Cytotoxic T-Lymphocyte-Associated Protein 4 Inhibitors OR Cytotoxic T Lymphocyte Associated Protein 4 Inhibitors OR Cytotoxic T-Lymphocyte-Associated Protein 4 Inhibitor OR Cytotoxic T Lymphocyte Associated Protein 4 Inhibitor OR PD-1 Inhibitors OR PD 1 Inhibitors OR PD-1 Inhibitor OR Inhibitor, PD-1 OR PD 1 Inhibitor OR Programmed Cell Death Protein 1 Inhibitor OR Programmed Cell Death Protein 1 Inhibitors OR PD 1 PD L1 Blockade OR ipilimumab OR ticilimumab OR nivolumab OR pembrolizumab OR pidilizumab OR atezolizumab OR durvalumab OR avelumab
- #3 O immune-related adverse events OR immune related adverse events checkpoint inhibitors OR immune related adverse events checkpoint blockade OR management of immune related adverse events OR immune related adverse events in patients OR immune related adverse events systemic immunosuppression OR immune related adverse events toxicity treatment OR immune related adverse events anti-pd1 immunotherapy OR related adverse events gastrointestinal cancer OR adverse events on survival OR adverse events of special interest OR immune related adverse events promising predictors OR immune related adverse events anti-tumor efficacy OR immune related adverse events comprehensive

review OR immune related adverse events treatment failure OR immune related adverse events single centre OR immune related adverse events drug administration OR immune-related adverse events checkpoint OR immune-related adverse events of checkpoint inhibitors OR immune-related adverse events cancer OR immune-related adverse events checkpoint inhibitors OR management of immune-related adverse events in patients OR checkpoint inhibitors immune-related adverse events OR cutaneous immune-related adverse events OR immune-related adverse events pneumonitis OR rheumatic immune-related adverse events OR multisystem immune-related adverse events OR irAEs OR trAEs OR organ-specific adverse events OR immune-related pneumonia OR organ-specific AEs

#4 S ("randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR randomized[tiab] OR placebo[tiab] OR "drug therapy"[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR "randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR "clinical trials as topic"[mesh] OR "random allocation"[mesh] OR "double-blind method"[mesh] OR "single-blind method"[mesh] OR "clinical trial"[pt] OR "research design"[mesh:noexp] OR "comparative study"[pt] OR "evaluation studies"[pt] OR "follow-up studies"[mesh] OR "prospective studies"[mesh] OR "cross-over studies"[mesh] OR "clinical trial"[tw] OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw]) AND (mask*[tw] OR blind*[tw])) OR placebo*[tw] OR random*[tw] OR "control"[tw] OR "controls"[tw] OR prospectiv*[tw] OR volunteer*[tw])

#5 #1 AND #2 AND #3 AND #4

Supplementary Table 4- Reference list of all excluded studies

Studies excluded for duplications (n=62)

1. Aimonio, Y.; Kamoshida, T.; Kikuchi, S.; Kamata, E.; Abe, H.; Ogawa, T.; Suzuki, S.; Saitou, Y.; Aoyama, Y., Evaluation of risk factors for immune-related adverse events associated with treatment with immune check point inhibitors. *Japanese Journal of Cancer and Chemotherapy* 2021, 48 (1), 57-61.
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5. Bang, Y. J.; Ruiz, E. Y.; Van Cutsem, E.; Lee, K. W.; Wyrwicz, L.; Schenker, M.; Alsina, M.; Ryu, M. H.; Chung, H. C.; Evesque, L.; et al.,

Phase III, randomised trial of avelumab versus physician's choice of chemotherapy as third-line treatment of patients with advanced gastric or gastro-oesophageal junction cancer: primary analysis of JAVELIN Gastric 300. *Annals of oncology : official journal of the European Society for Medical Oncology* 2018, 29 (10), 2052 - 2060.

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Wyrwicz, L.; Kang, Y. K.; Lee, K. W.; Infante, J. R.; Lee, S. S.; Kemeny, M.; Keilholz, U.; Melichar, B.; Mita, A.; Plummer, R.; Smith, D.; Gelb, A. B.; Xiong, H.; Hong, J.; Chand, V.; Safran, H., Avelumab (anti-PD-L1) as first-line switch-maintenance or second-line therapy in patients with advanced gastric or gastroesophageal junction cancer: phase 1b results from the JAVELIN Solid Tumor trial. *Journal for immunotherapy of cancer* 2019, 7 (1), 30.

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23. Kelly, R. J.; Ajani, J. A.; Kuzdzal, J.; Zander, T.; Van Cutsem, E.; Piessen, G.; Mendez, G.; Feliciano, J.; Motoyama, S.; Lièvre, A.; et al.,

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Othertypes of tumors (n=1)

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Others (n=4)

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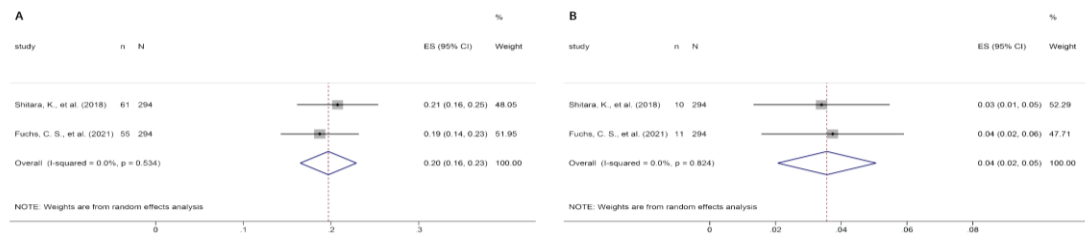
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Attached file 3

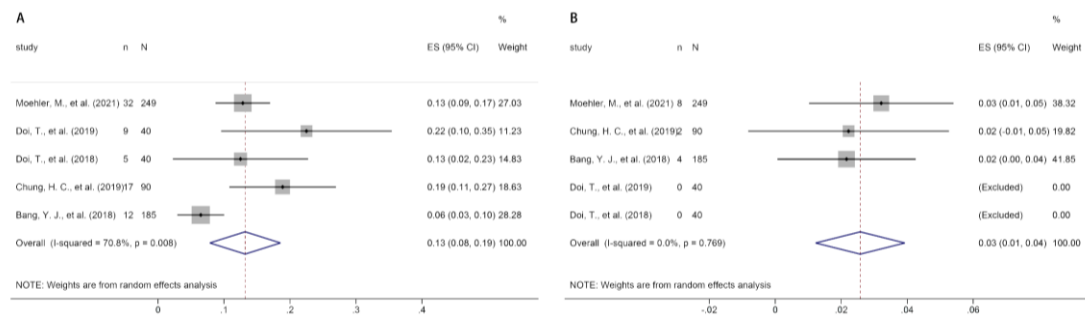
Results

Meta-analysis

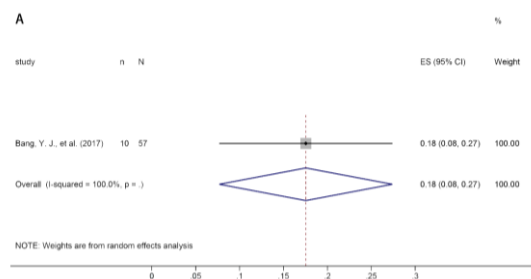
All immune related adverse events



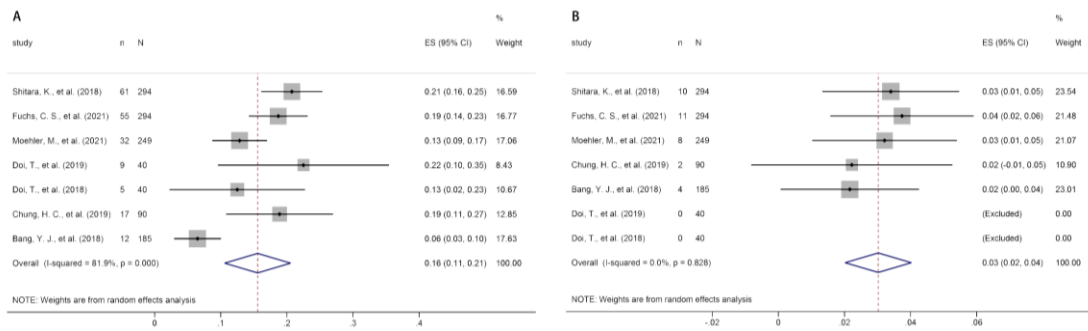
Supplementary fig. 1 - Incidence of global irAEs with anti-PD-1 all dosage, all-grade (A) and severe grade (B).



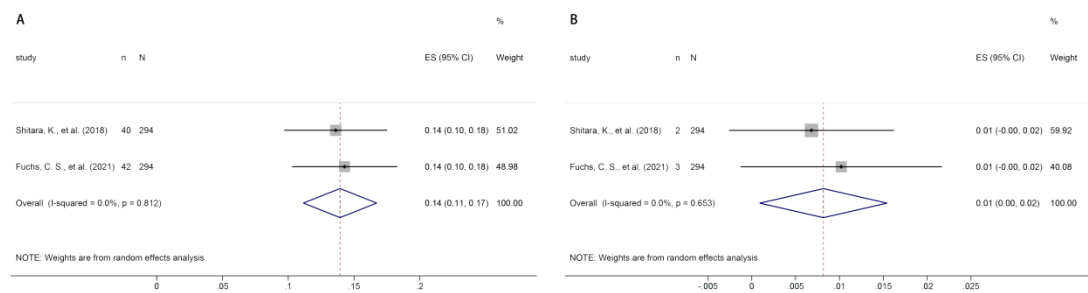
Supplementary fig. 2 - Incidence of global irAEs with anti-PD-L1 all dosage, all-grade (A) and severe grade (B).



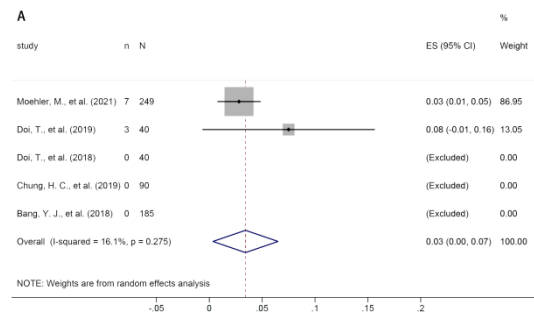
Supplementary fig. 3 - Incidence of global irAEs with anti-CTLA-4 all dosage, all-grade (A) and severe grade (B).



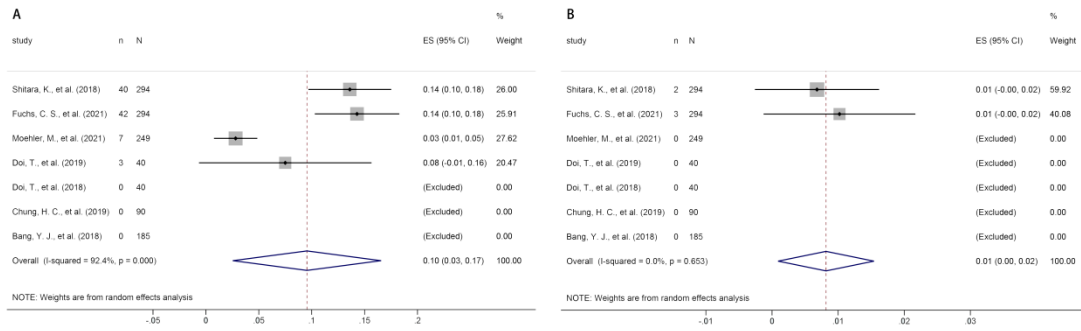
Supplementary fig. 4 - Incidence of global irAEs with anti-PD-1 and anti-PD-L1 all dosage, all-grade (A) and severe grade (B).



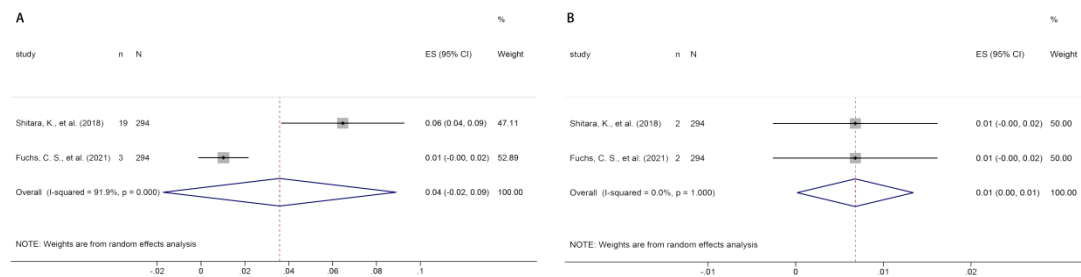
Supplementary fig. 5 - Incidence of endocrinologic irAEs with anti-PD-1 all dosage, all-grade (A) and severe grade (B).



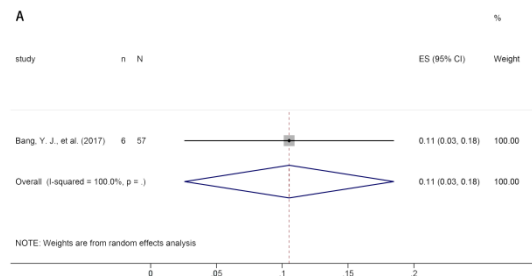
Supplementary fig. 6 - Incidence of endocrinologic irAEs with anti-PD-L1 all dosage, all-grade (A) and severe grade (B).



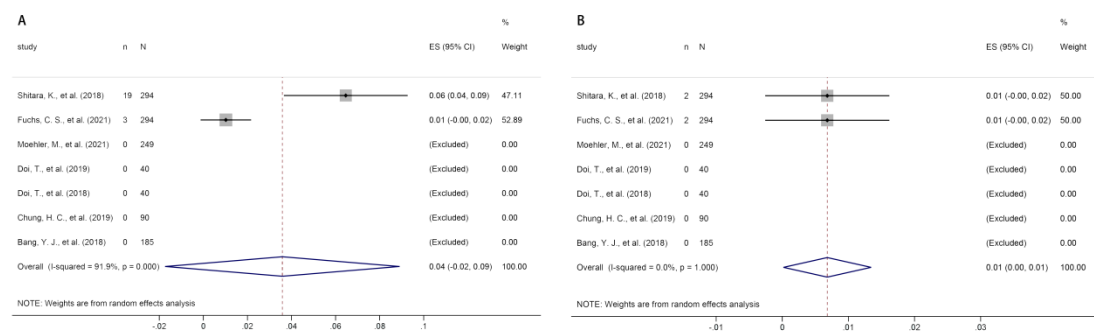
Supplementary fig. 7 - Incidence of endocrinologic irAEs with anti-PD-1 and anti-PD-L1, all-grade (A) and severe grade (B).



Supplementary fig. 8 - Incidence of gastro intestinal irAEs with anti-PD-1 all dosage, all-grade (A) and severe grade (B).

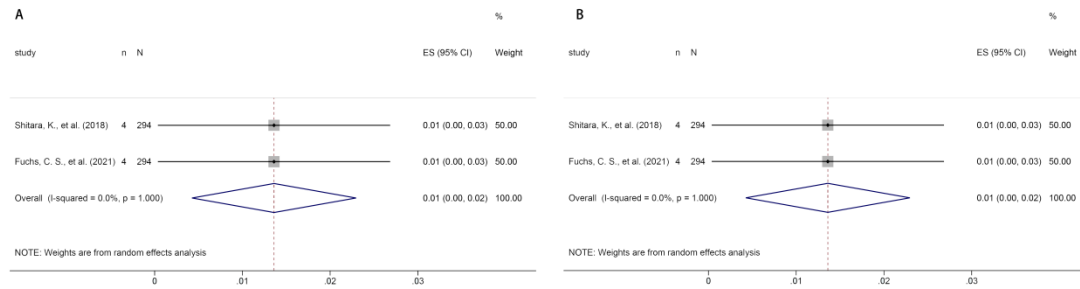


Supplementary fig. 9 - Incidence of gastro intestinal irAEs with anti-CTLA-4 all dosage, all-grade (A) and severe grade (B).

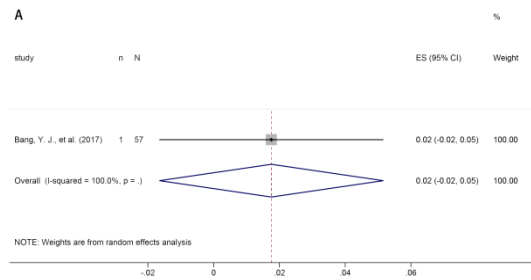


Supplementary fig. 10 - Incidence of gastro intestinal irAEs with anti-PD-1

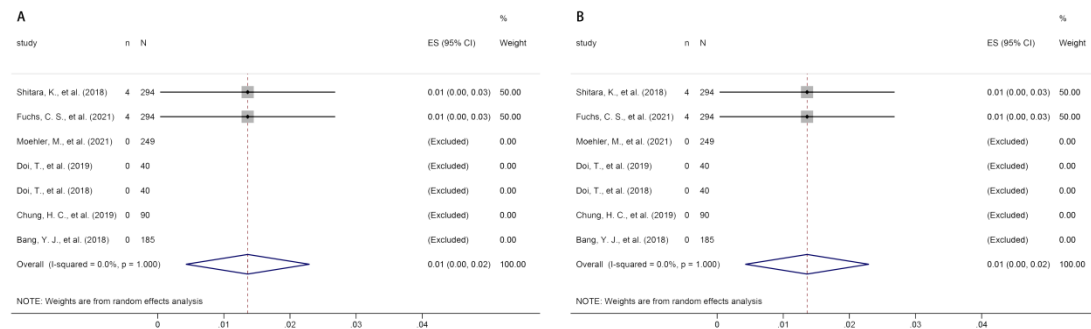
and anti-PD-L1 all dosage, all-grade (A) and severe grade (B).



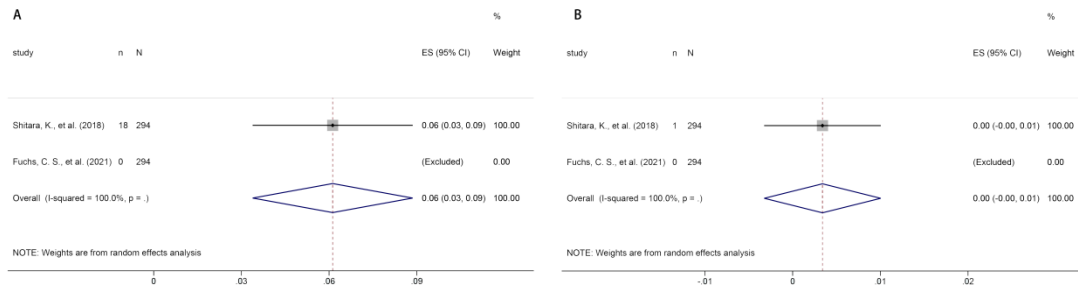
Supplementary fig. 11 - Incidence of hepatic irAEs with anti-PD-1 all dosage, all-grade (A) and severe grade (B).



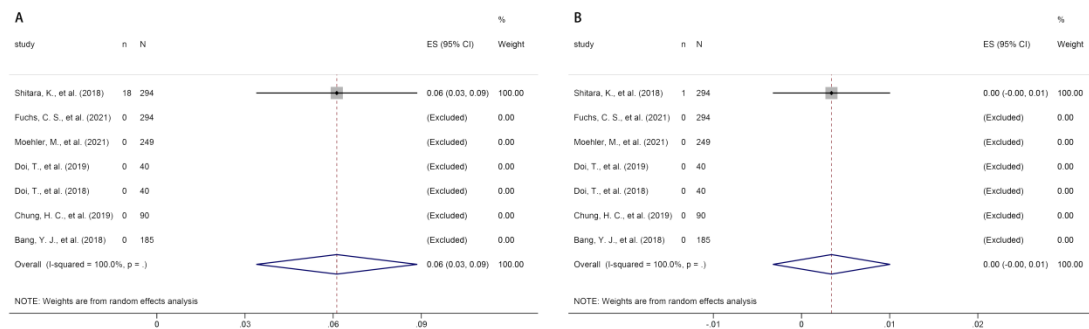
Supplementary fig. 12 - Incidence of hepatic irAEs with anti-CTLA-4 all dosage, all-grade (A) and severe grade (B).



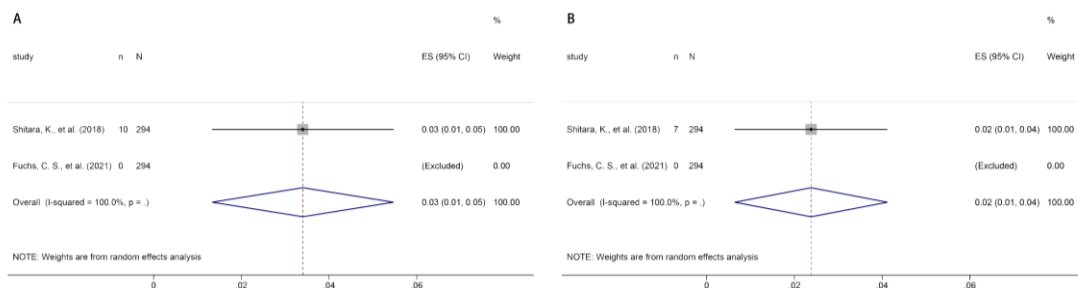
Supplementary fig. 13 - Incidence of hepatic irAEs with anti-PD-1 and anti-PD-L1, all-grade (A) and severe grade (B).



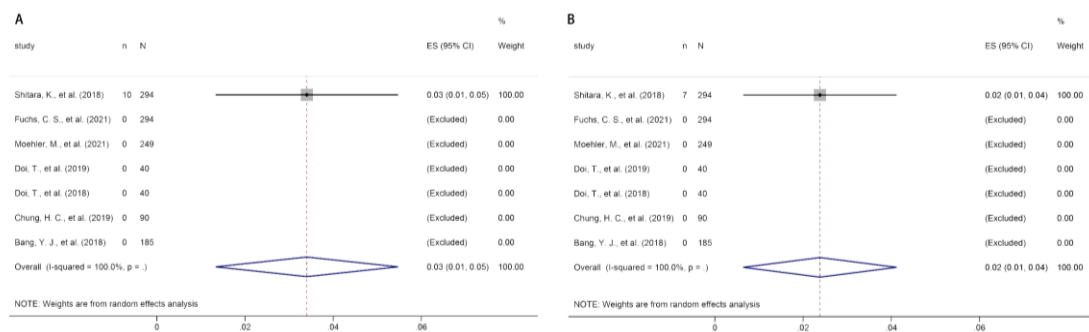
Supplementary fig. 14 - Incidence of neurological irAEs with anti-PD-1 all dosage, all-grade (A) and severe grade (B).



Supplementary fig. 15 - Incidence of neurological irAEs with anti-PD-1 and anti-PD-L1 all dosage, all-grade (A) and severe grade (B).

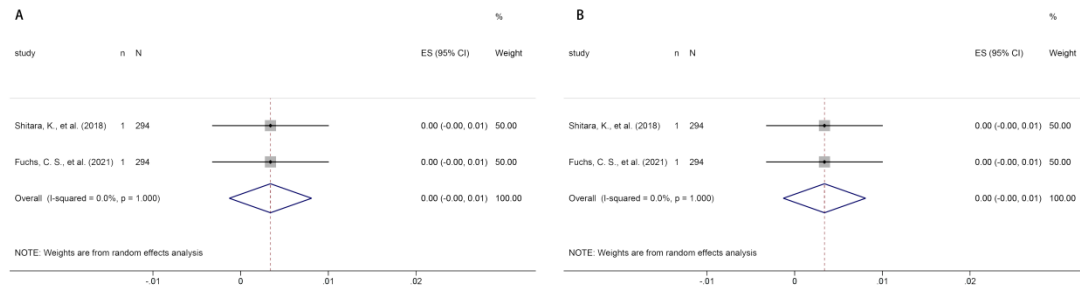


Supplementary fig. 16 - Incidence of hematological irAEs with anti-PD-1 all dosage, all-grade (A) and severe grade (B).

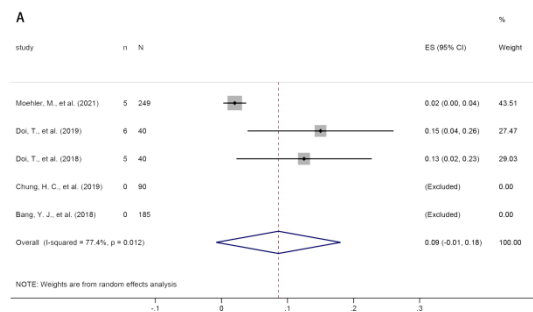


Supplementary fig. 17 - Incidence of hematological irAEs with anti-PD-1 and anti-PD-L1 all dosage, all-grade (A) and severe grade (B).

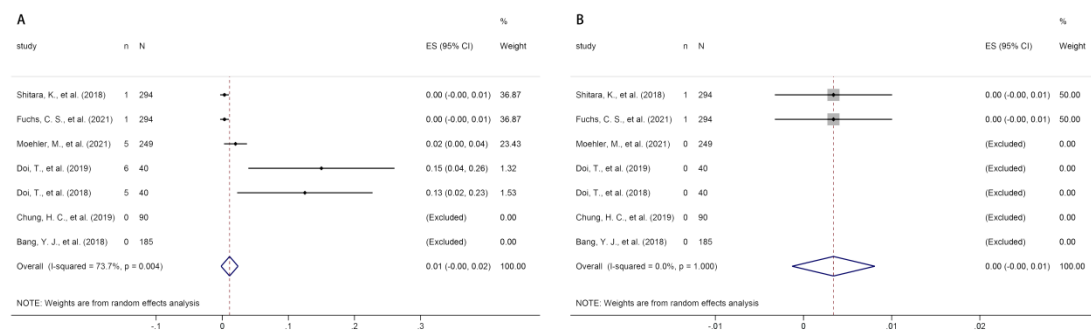
anti-PD-L1, all-grade (A) and severe grade (B).



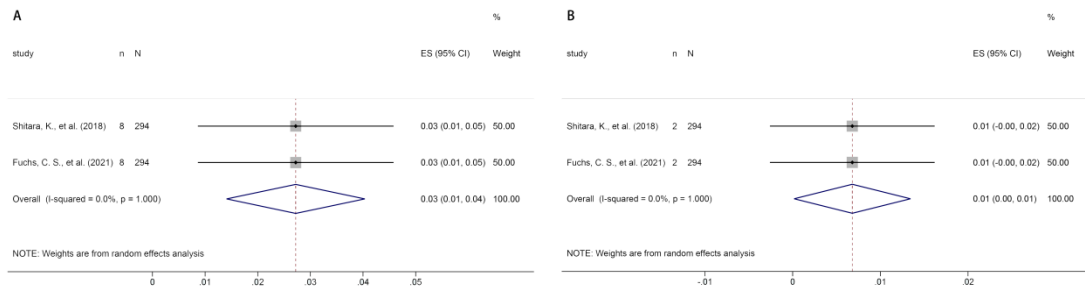
Supplementary fig. 18 - Incidence of cutaneous irAEs with anti-PD-1 all dosage, all-grade (A) and severe grade (B).



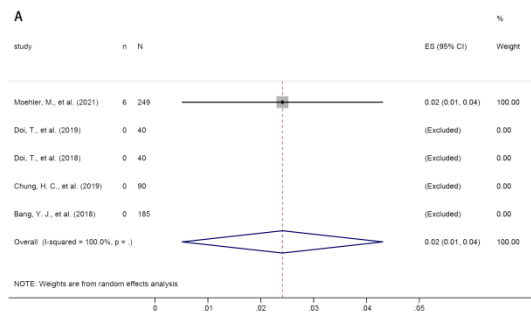
Supplementary fig. 19 - Incidence of cutaneous irAEs with anti-PD-L1 all dosage, all-grade (A) and severe grade (B).



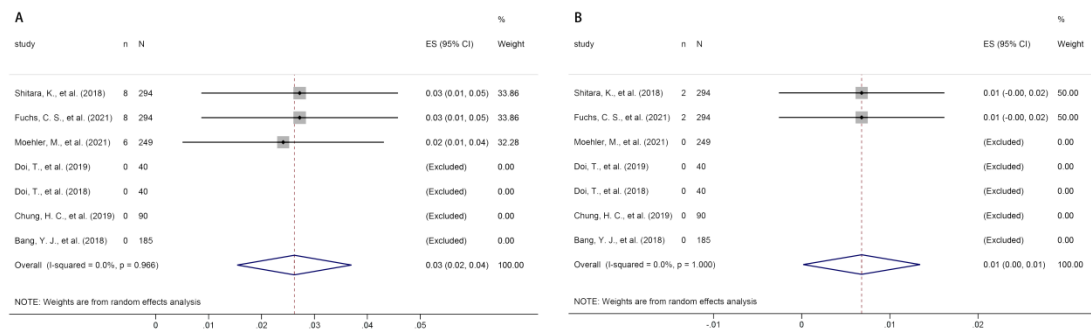
Supplementary fig. 20 - Incidence of cutaneous irAEs with anti-PD-1 and anti-PD-L1 all dosage, all-grade (A) and severe grade (B).



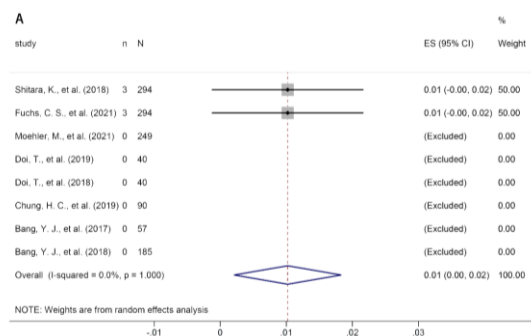
Supplementary fig. 21 - Incidence of pulmonary irAEs with anti-PD-1 all dosage, all-grade (A) and severe grade (B).



Supplementary fig. 22 - Incidence of pulmonary irAEs with anti-PD-L1 all dosage, all-grade (A) and severe grade (B).



Supplementary fig. 23 - Incidence of pulmonary irAEs with anti-PD-1 and anti-PD-L1, all-grade (A) and severe grade (B).



Supplementary fig. 24 - Incidence of death related to irAEs (A).

Attached file 4**Supplementary table 5** General characteristics of patients receiving anti-PD-1 treatment, as described in case report (n=14)

Age (y), mean±SD	69.7±4.5
Male sex, n (%)	11 (79)
Oncologic treatment, n (%)	
History of chemotherapy	13 (93)
Unknown	1(7)
PD-1 treatment	14 (100)
Nivolumab treatment	13 (93)
Pembrolizumab treatment	1(7)
IRAEs	
Endocrinopathy	4 (29)
Gastroenterology and hepatology	1 (7)
Neurology	2 (14)
Hematology	2 (14)
Nephrology	2 (14)
Dermatology	1 (7)
Cardiology	1 (7)
Pulmonology	2 (14)
Rheumatic immunology	2 (14)
No. of cycles, median (interquartile range)	14.6 (5.5–17.5)
Onset of irAE (wk), median (interquartile range)	8.2 (3.0–6.0)
Continued treatment (anti-PD-1/anti-PD-L1)	4 (29)
Evolution, n (%)	
Cancer	
Progressive disease	5 (36)
Oncologic response	3 (21)
irAEs	

Healing	6 (43)
Persistence	5 (36)
Death	1 (7)
Unknown	2 (14)

AI, auto-immune; irAEs, immune-related adverse events; PD-1, programmed cell death receptor-1; SD, standard deviation

Supplementary table 6 Organ-specific immune-related adverse events

Endocrinopathy (n=5)

Hyperthyroidism	1 (7)
Thyroiditis	2 (14)
ACTH deficiency	2 (14)
Diabetes	1 (7)
Treatment	
Steroids	3 (21)

Neurology (n=1)

Dizziness	1 (7)
nausea	1 (7)
truncal ataxia	1 (7)
Treatment	
Steroids	1 (7)

Gastroenterology and Hepatology (n=1)

chronic intestinal pseudo-obstruction	1 (7)
nivolumab-related cholangitis	1 (7)
Treatment	
Steroids	1 (7)

Hematology (n=2)

eosinophilia	1 (7)
cervical lymphadenopathy	1 (7)
Treatment	
Steroids	1 (7)
Evolution	
Healing of irAE	1 (7)

Nephrology (n=2)

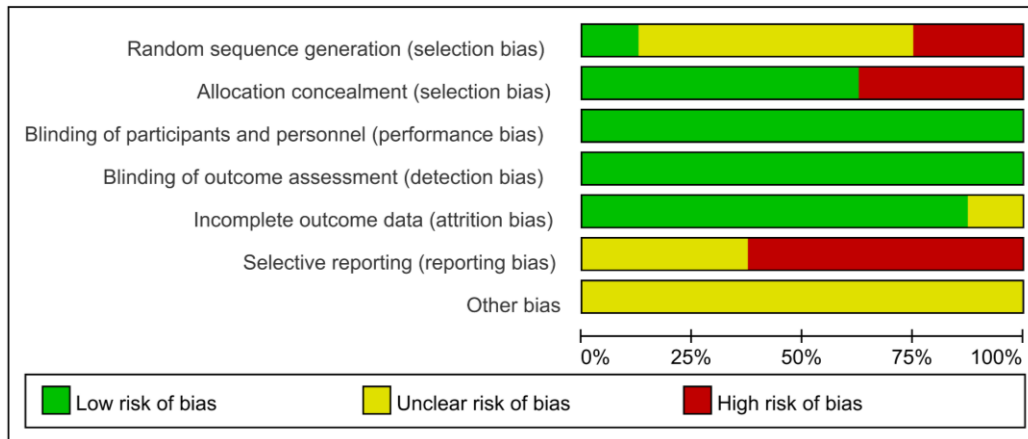
Acute interstitial nephritis	1 (7)
IgA nephropathy	1 (7)

Treatment	
Steroids	1 (7)
Evolution	
Healing of irAE	1 (7)
Dermatology (n=1)	
Rash	1 (7)
sequential herpes zoster virus activation	1 (7)
Cardiology (n=2)	
Mvocarditis	1 (7)
Pericardial effusion	1 (7)
Treatment	
Steroids	1 (7)
Evolution	
Healing of irAE	1 (7)
Pulmonology (n=2)	
Interstitial pneumonia	2 (14)
Treatment	
Steroids	1 (7)
Rheumatic immunology (n=2)	
Stevens-Johnson svndrome	2 (14)
Treatment	
Steroids	1 (7)

AI, auto-immune; irAE, immune-related adverse event; SD,

standard deviation. All values are n (%) unless otherwise noted.

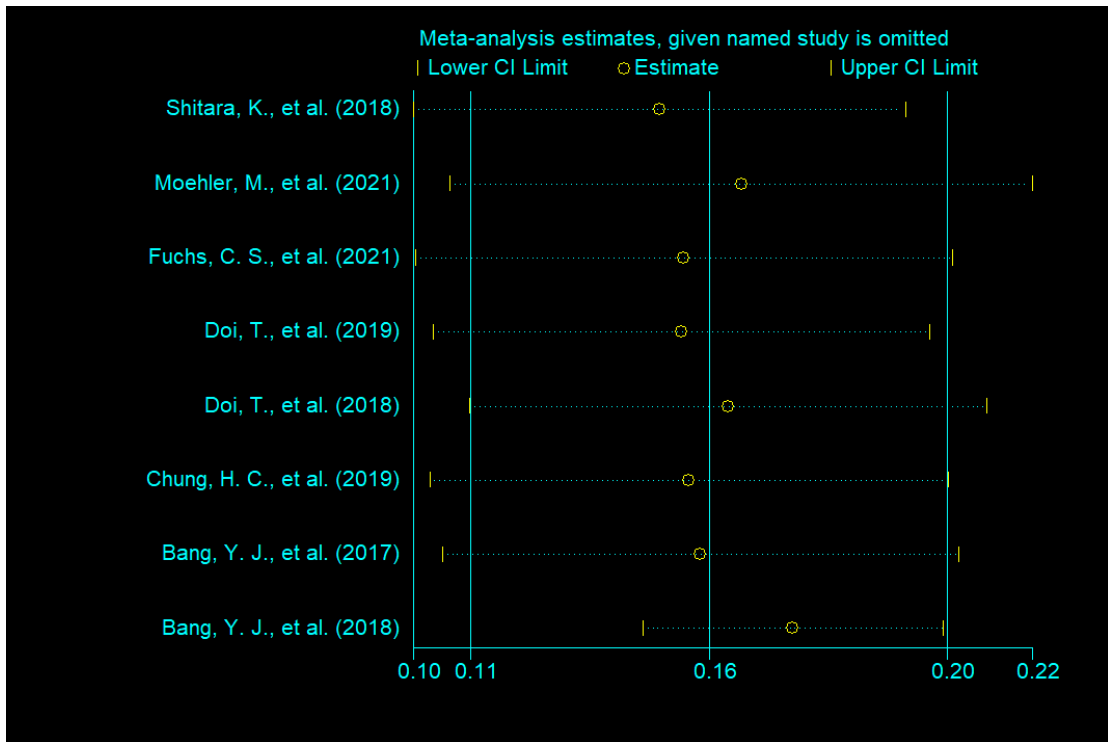
Attached file 5



Supplementary fig. 25 - Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

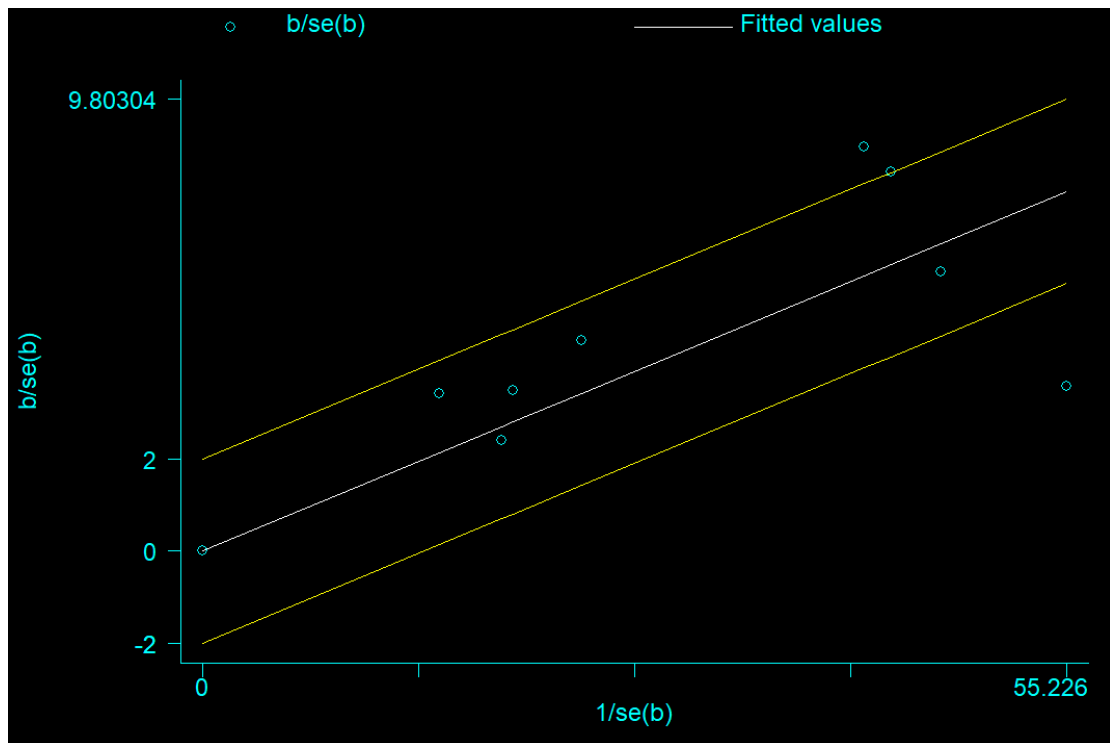
Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bang, Y. J., et al. (2017)	?	+	+	+	+	-	?
Bang, Y. J., et al. (2018)	?	+	+	+	+	-	?
Chung, H. C., et al. (2019)	-	-	+	+	+	?	?
Doi, T., et al. (2018)	?	-	+	+	?	?	?
Doi, T., et al. (2019)	-	-	+	+	+	-	?
Fuchs, C. S., et al. (2021)	?	+	+	+	+	?	?
Moehler, M., et al. (2021)	?	+	+	+	+	-	?
Shitara, K., et al. (2018)	+	+	+	+	+	-	?

Supplementary fig. 26 - Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

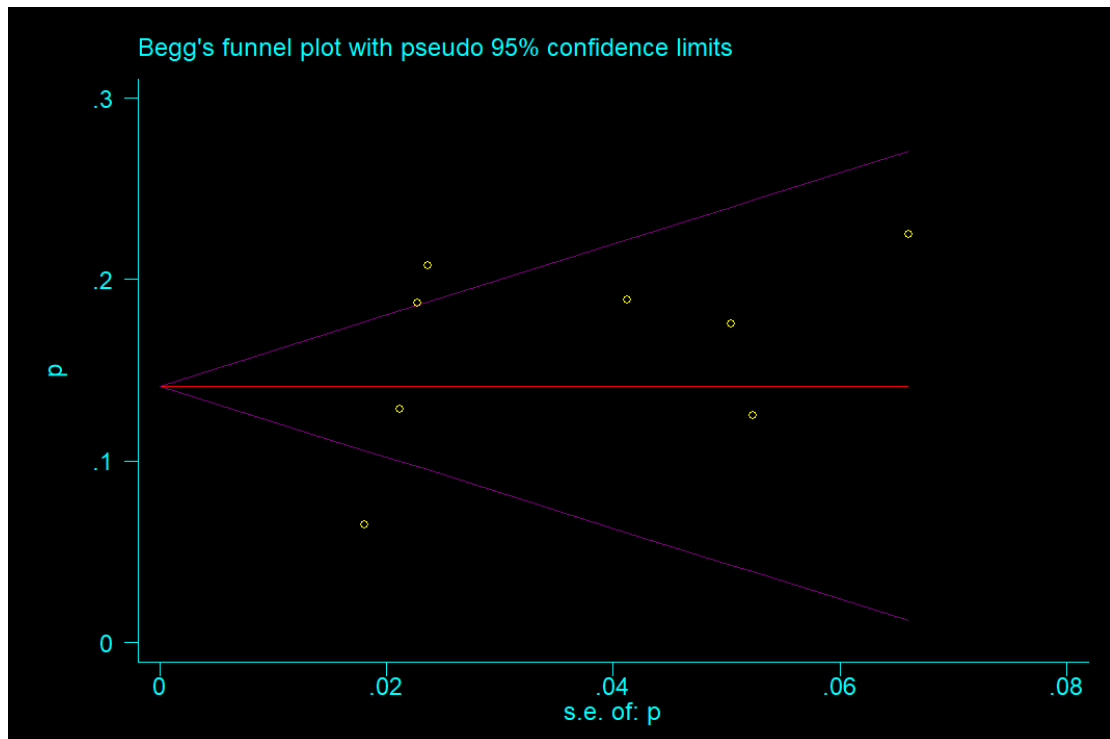


Supplementary fig. 27 - Sensitivity analysis: the influence of single study on the total merger effect.

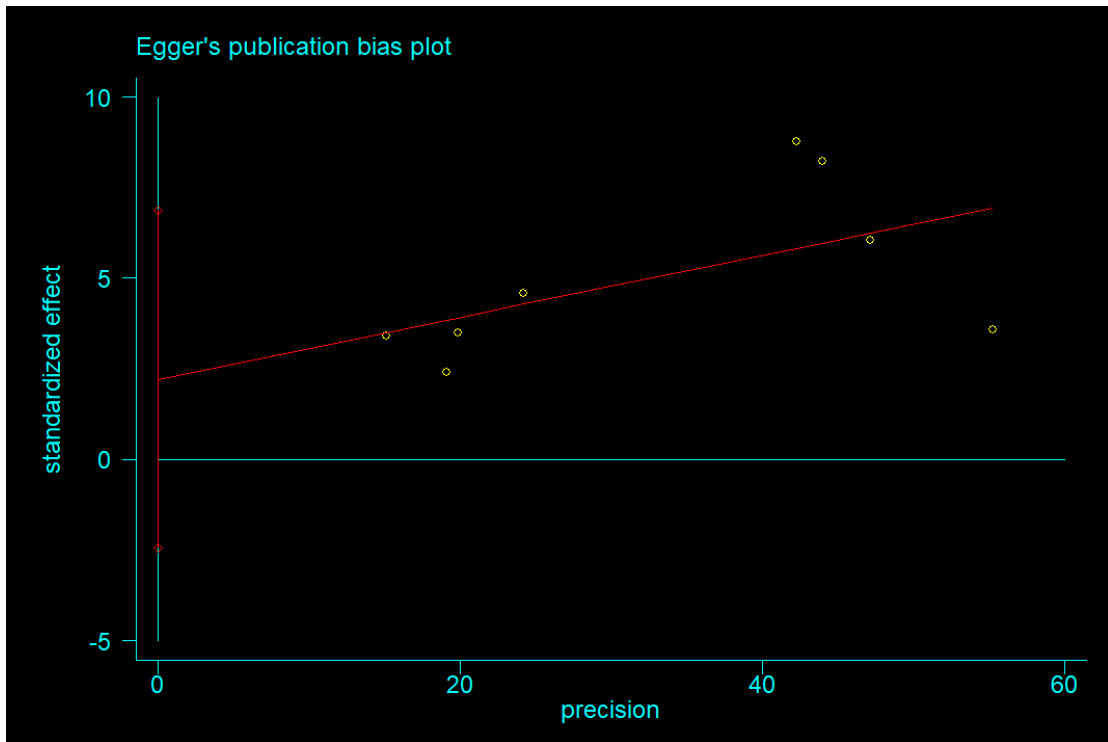
Attached file 6



Supplementary fig. 28 - Heterogeneity test for all included clinical trials.



Supplementary fig. 29 - Begg's funnel plot for publication bias in all included clinical trials.



Supplementary fig. 30 - Egger's Publication bias plot in all included clinical trials.