**Supplementary Table 1: Checklist of items included when reporting a systematic review and meta- analysis**

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| --- | --- | --- | --- |
| **Section/topic**  | **Item No.** | **Checklist item** | **Reported on page No.** |
| Title |  |  |  |
| Title  | 1 | Identify the report as a systematic review, meta-analysis, or both | 1 |
| Abstract |  |  |  |
| Structured summary  | 2 | Provide a structured summary including, as applicable, background, objectives, data sources, study eligibility criteria, participants, interventions, study appraisal and synthesis methods, results, limitations, conclusions and implications of key findings, systematic review registration number | 2 |
| Introduction |  |  |  |
| Rationale  | 3 | Describe the rationale for the review in the context of what is already known | 2-3 |
| Objectives  | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS) | 4 |
| Methods |  |  |  |
| Protocol and registration  | 5 | Indicate if a review protocol exists, if and where it can be accessed (such as web address), and, if available, provide registration information including registration number |  |
| Eligibility criteria  | 6 | Specify study characteristics (such as PICOS, length of follow-up) and report characteristics (such as years considered, language, publication status) used as criteria for eligibility, giving rationale | 4 |
| Information sources  | 7 | Describe all information sources (such as databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched | 3-4 |
| Search  | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated | 3-4 |
| Study selection  | 9 | State the process for selecting studies (that is, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis) | 4 |
| Data collection process  | 10 | Describe method of data extraction from reports (such as piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators | 4 |
| Data items  | 11 | List and define all variables for which data were sought (such as PICOS, funding sources) and any assumptions and simplifications made | 4 |
| Risk of bias in individual studies  | 12 | Describe methods used for assessing risk of bias of individual studies(including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis | 4-5 |
| Summary measures  | 13 | State the principal summary measures (such as risk ratio, difference in means). | 4 |
| Synthesis of results  | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (such as I2 statistic) for each meta-analysis. | 4 |
| Risk of bias across studies  | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (such as publication bias, selective reporting within studies) | 4 |
| Additional analyses  | 16 | Describe methods of additional analyses (such as sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified | 4-5 |
| Results |  |  |  |
| Study selection  | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram | 5 |
| Study characteristics  | 18 | For each study, present characteristics for which data were extracted (such as study size, PICOS, follow-up period) and provide the citations | 5 |
| Risk of bias within studies  | 19 | Present data on risk of bias of each study and, if available, any outcome-level assessment (see item 12). | 8 |
| Results of individual studies  | 20 | For all outcomes considered (benefits or harms), present for each study (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot | 5-6 |
| Synthesis of results  | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency | 5-7 |
| Risk of bias across studies  | 22 | Present results of any assessment of risk of bias across studies (see item 15) | 8 |
| Additional analysis  | 23 | Give results of additional analyses, if done (such as sensitivity or subgroup analyses, meta-regression) (see item 16) | 6-8 |
| Discussion |  |  |  |
| Summary of evidence  | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (such as health care providers, users, and policy makers) | 8 |
| Limitations  | 25 | Discuss limitations at study and outcome level (such as risk of bias), and at review level (such as incomplete retrieval of identified research, reporting bias) | 11-12 |
| Conclusions  | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research | 12 |
| Funding |  |  |  |
| Funding  | 27 | Describe sources of funding for the systematic review and other support (such as supply of data) and role of funders for the systematic review | 12 |

**Supplementary Table 2. Search strategy for systematic review.**

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| --- |
| ***PubMed*** |
| #1 | (((((((((Neoplasms) OR Neoplasia) OR Neoplasias) OR Neoplasm) OR Tumors) OR Tumor) OR Malignancy) OR Malignancies) OR Cancer) OR Cancers | **5,217,382** |
| #2 | ("Programmed Cell Death 1 Receptor/antagonists and inhibitors"[Mesh] OR PD-1[tiab] OR PD1[tiab] OR PD-L1[tiab] OR CTLA4[tiab] OR CTLA-4[tiab] OR cytotoxic T-lymphocyte-associated protein 4[tiab] OR PDL1[tiab] OR Programmed Cell Death 1\*[tiab] OR Immune Checkpoint\*[tiab] OR nivolumab[tiab] OR pembrolizumab[tiab] OR atezolizumab[tiab] OR durvalumab[tiab] OR cemiplimab[tiab] OR avelumab[tiab] OR monoclonal antibodies [tiab] OR ipilimumab[tiab] OR tremelimumab[tiab]) | **162,392**  |
| #3 | (drug related side effects and adverse reactions [Mesh] OR adverse reactio\*[tiab] OR adverse even\*[tiab] OR side effec\*[tiab]) | **601,741** |
| #4 | (risk factor [Mesh] OR risk facto\*[tiab] OR predicto\*[tiab] OR exposur\*[tiab]) | **2,485,601** |
| #5 | #1 AND #2 AND #3 AND #4 | **Final research** **795** |
| ***EMBASE*** |
| #1 | 'tumor'/exp OR tumor OR tumor:ab,ti OR cancer:ab,ti OR neoplasm\*:ab,ti | **6,607,210** |
| #2 | 'pdl1 gene'/exp OR 'immune checkpoint inhibitor'/exp OR 'immunomodulating agent'/exp OR 'immunomodulating agent':ab,ti OR 'avelumab':ab,ti OR 'cemiplimab':ab,ti OR 'durvalumab':ab,ti OR 'atezolizumab':ab,ti OR 'pembrolizumab':ab,ti OR 'nivolumab':ab,ti OR 'pdl1':ab,ti OR 'pd1':ab,ti OR 'immune checkpoint inhibitor':ab,ti OR 'tremelimumab':ab,ti OR ' ipilimumab':ab,ti OR 'ctla4':ab,ti OR 'ctla-4':ab,ti OR 'cytotoxic T-lymphocyte-associated protein 4':ab,ti | **2,107,750** |
| #3 | 'side effect'/exp OR 'side effect':ab,ti OR 'adverse drug reaction'/exp OR 'adverse drug reaction':ab,ti OR 'adverse event'/exp OR 'adverse event':ab,ti  | **1,019,020** |
| #4 | 'risk factor'/exp OR 'risk factor':ab,ti OR 'exposure'/exp OR exposure:ab,ti OR predicto\*:ab,ti | **3,275,009** |
| #5 | #1 AND #2 AND #3 AND #4 | **Final research****12,776** |
| ***Web of science*** |
| #1 | TS= ("neoplasms" OR "cance\*" OR "neoplas\*") | **6,855,505** |
| #2 | TS= ("Immune Checkpoint Inhibit\*" OR "PD-1" OR "PD-L1" OR "PD1" OR "PDL1" OR "avelumab" OR "cemiplimab" OR "durvalumab" OR "atezolizumab" OR "pembrolizumab" OR "nivolumab" OR "CTLA-4" OR "CTLA4" OR "'tremelimumab" OR " ipilimumab" OR " cytotoxic T-lymphocyte-associated protein 4") | **72,299** |
| #3 | TS= ("drug related side effects" OR "adverse reactio\*" OR "adverse even\*" OR "side effec\*")  | **943,107** |
| #4 | TS= ("risk facto\*" OR "predicto\*" OR "exposur\*") | **4,361,695** |
| #5 | #1 AND #2 AND #3 AND #4 | **Final research****839** |

**Supplementary Figure 1. Forest plot of the incidence of grade III-V CIP in cancer patients treated with immune checkpoint inhibitors. Abbreviation: CIP,** **checkpoint inhibitor pneumonitis.**



**Supplementary Figure 2. Forest plot of the incidence of CIP in cancer patients treated with immune checkpoint inhibitors stratified by cancer types. Abbreviation: CIP, checkpoint inhibitor pneumonitis.**

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**Supplementary Figure 3. Forest plot of the incidence of CIP in cancer patients treated with immune checkpoint inhibitors stratified by regional distributions. Abbreviation: CIP, checkpoint inhibitor pneumonitis.**

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**Supplementary Figure 4. Forest plot of the incidence of CIP in cancer patients treated with immune checkpoint inhibitors stratified by treatment regimes. Abbreviation: CIP, checkpoint inhibitor pneumonitis.**

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**Supplementary Figure 5. Forest plot of the incidence of CIP in cancer patients treated with ICIs stratified by ICI types. Abbreviation: CIP, checkpoint inhibitor pneumonitis; ICI, immune checkpoint inhibitor.**

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**Supplementary Table 3. Classification of odds ratios assessing the risk factors for CIP in patients treated with ICIs.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Risk factor** | **Author/Year** | **OR** | **Lower CI** | **Upper CI** | **P value** | **Analysis** |
| Age (≥ 65 vs <65) | Chao, 2022 | 0.796 | 0.311 | 2.036 | 0.634 | Univariate |
|  | Chen,2021 | 0.51 | 0.21 | 1.25 | 0.142 | Univariate |
|  | Chu, 2020 | 1.417 | 0.789 | 2.746 | 0.225 | Multivariate |
|  | Jung.2021 | 0.593 | 0.234 | 1.499 | 0.269 | Univariate |
|  | Li,2020 | 2.20 | 1.06 | 4.58 | 0.035 | Multivariate |
|  | Lin, 2021 | 1.59 | 0.87 | 2.9 | 0.13 | Univariate |
|  | Jerzy.2021 | 0.95 | 0.86 | 1.05 | 0.3388 | Multivariate |
|  | Sugano, 2020 | 4.47 | 0.88 | 22.7 | 0.07 | Multivariate |
|  | Wang, 2022 | 0.769 | 0.279 | 2.121 | 0.612 | Univariate |
|  | Yamaguchi,2018 | 2.15 | 0.71 | 8.01 | 0.18 | Univariate |
|  | Yamaguchi,2021 | 1.53 | 0.44 | 6.11 | 0.51 | Multivariate |
|  | Yamaguchi,2022 | 2.40 | 0.56 | 10.27 | 0.24 | Multivariate |
| Age | Fukihara,2019 | 0.980 | 0.939 | 1.023 | 0.347 | Univariate |
|  | Nakanishi,2019 | 1.003 | 0.949 | 1.068 | 0.919 | Univariate |
|  | Shimoji, 2020 | 1.25 | 0.08 | 18.80 | 0.86 | Multivariate |
|  | Sukari, 2019 | 0.99 | 0.96 | 1.03 | 0.665 | Multivariate |
|  | Suresh, 2018  | 1 | 0.96 | 1.04 | 0.69 | Univariate |
|  | Suzuki,2020 | 0.983 | 0.939 | 1.029 | 0.47 | Univariate |
| Age (per 10-y increase) | William,2021 | 0.90 | 0.62 | 1.3 |  | Univariate |
| Age (≥60) | Asada, 2021  | 1.70 | 1.61 | 1.80 | <0.001 | Univariate |
| Age (≥70) | Hata,2020 | 1.945 | 0.624 | 6.523 | 0.304 | Univariate |
|  | Suzuki,2020 | 0.522 | 0.201 | 1.353 | 0.18 | Univariate |
| Age (≥75) | Isono, 2021 | 0.251 | 0.059 | 1.058 | 0.060 | Univariate |
|  | Tamiya, 2017 | 2.01 | 0.95 | 4.23 | / | Univariate |
| Sex (female) | Asada, 2021 | 1.04 | 0.93 | 1.17 | 0.47 | Multivariate |
|  | Chao, 2022 | 1.315 | 0.403 | 4.293 | 0.650 | Univariate |
|  | Chen,2021 | 1.33 | 0.52 | 3.45 | 0.547 | Univariate |
|  | Chu, 2020 | 0.499 | 0.197 | 1.263 | 0.142 | Multivariate |
|  | Fukihara,2019 | 0.967 | 0.379 | 2.469 | 0.944 | Univariate |
|  | Hata,2020 | 0.982 | 0.245 | 3.378 | 1.000 | Univariate |
|  | Isono, 2021 | 0.589 | 0.204 | 1.704 | 0.329 | Univariate |
|  | Jung.2021 | 0.510 | 0.167 | 1.558 | 0.237 | Univariate |
|  | Li,2020 | 0.662 | 0.311 | 1.408 | 0.291 | Univariate |
|  | Lin, 2021 | 1.67 | 0.78 | 3.5 | 0.19 | Univariate |
|  | Jerzy.2021 | 0.870 | 0.787 | 0.962 | 0.0051 | Multivariate |
|  | Nakahama,2018 | 0.505 | 0.141 | 1.818 | 0.296 | Multivariate |
|  | Nakanishi,2019 | 0.914 | 0.230 | 3.086 | 0.889 | Univariate |
|  | Shimoji, 2020 | 0.556 | 0.156 | 2 | 0.36 | Multivariate |
|  | Sugano, 2020 | 3.06 | 0.69 | 13.6 | 0.14 | Multivariate |
|  | Suresh, 2018 | 1.09 | 0.54 | 2.20 | 0.81 | Univariate |
|  | Suzuki,2020 | 0.215 | 0.028 | 1.638 | 0.15 | Univariate |
|  | Wang, 2022 | 2.778 | 0.666 | 11.627 | 0.161 | Univariate |
|  | William,2021 | 0.55 | 0.25 | 1.20 |  | Univariate |
|  | Yamaguchi,2018 | 0.58 | 0.079 | 2.98 | 0.53 | Multivariate |
|  | Yamaguchi,2021 | 0.179 | 0.048 | 0.99 | 0.049 | Multivariate |
|  | Yamaguchi,2022 | 0.69 | 0.14 | 3.31 | 0.64 | Multivariate |
|  | Yamamoto,2022 | 0.971 | 0.694 | 1.351 |  | Multivariate |
| Smoking history (ever smoker) | Chao, 2022 | 1.217 | 0.458 | 3.234 | 0.694 | Univariate |
|  | Chu, 2020 | 1.438 | 0.794 | 2.607 | 0.231 | Univariate |
|  | Hata,2020 | 0.660 | 0.139 | 4.267 | 0.691 | Univariate |
|  | Isono, 2021 | 2.549 | 0.604 | 10.770 | 0.203 | Univariate |
|  | Jung.2021 | 2.178 | 0.604 | 7.859 | 0.234 | Multivariate |
|  | Li,2020 | 1.54 | 0.72 | 3.29 | 0.267 | Univariate |
|  | Lin, 2021 | 1.15 | 0.63 | 2.1 | 0.65 | Univariate |
|  | Nakahama,2018 | 1.24 | 0.27 | 5.69 | 0.778 | Multivariate |
|  | Nakanishi,2019 | 3.925 | 0.696 | 73.997 | 0.136 | Univariate |
|  | Shimoji, 2020 | 0.32 | 0.09 | 1.10 | 0.07 | Multivariate |
|  | Sugano, 2020 | 1.62 | 0.23 | 11.6 | 0.63 | Multivariate |
|  | Suresh, 2018 | 1.36 | 0.53 | 3.53 | 0.52 | Univariate |
|  | Wang, 2022 | 2.314 | 0.679 | 7.881 | 0.180 | Multivariate |
|  | William,2021 | 3.03 | 0.4 | 23.17 | 0.28 | Univariate |
|  | Yamaguchi,2018 | 2.63 | 0.69 | 17.35 | 0.17 | Univariate |
|  | Yamaguchi,2021 | 1.52 | 0.53 | 5.50 | 0.45 | Univariate |
|  | Yamaguchi,2022 | 2.33 | 0.63 | 8.64 | 0.205 | Univariate |
|  | Yamamoto,2022 | 1.47 | 1.01 | 2.15 |  | Multivariate |
| Smoking history (<40 pack-year) | Chen,2021 | 3.18 | 1.22 | 8.30 | 0.018 | Univariate |
| Smoking (pack-years) | Fukihara,2019 | 0.994 | 0.981 | 1.007 | 0.362 | Univariate |
| Smoking history (≥50 pack-year) | Okada,2020 | 3.01 | 1.04 | 8.72 | 0.042 | Multivariate |
|  | Owen, 2018 | 0.98 | 0.32 | 3.03 | 0.97 | Univariate |
| Race (African vs. Caucasian) | Jerzy.2021 | 0.94 | 0.79 | 1.11 | 0.4602 | Multivariate |
|  | Suresh, 2018 | 1.08 | 0.43 | 2.69 | 0.87 | Univariate |
|  | William,2021 | 1.40 | 0.57 | 3.43 |  | Univariate |
| Race (Asian vs. Caucasian) | Jerzy.2021 | 1.26 | 0.88 | 1.81 | 0.2114 | Multivariate |
|  | Suresh, 2018 | 1.44 | 0.28 | 7.43 | 0.66 | Univariate |
| History of thoracic radiotherapy | Barrón, 2020 | 6.04 | 2.03 | 18.0 | < 0.001 | Univariate |
|  | Cui.2018 | 3.34 | 1.51 | 7.39 | / | Multivariate |
|  | Fukihara,2019 | 0.888 | 0.362 | 2.178 | 0.795 | Univariate |
|  | Isono, 2021 | 1.369 | 0.543 | 3.448 | 0.506 | Univariate |
|  | Jung.2021 | 2.08 | 0.87 | 4.95 | 0.10 | Univariate |
|  | Mamesaya,2019 | 1.95 | 1.13 | 3.34 | / | Multivariate |
|  | Lin, 2021 | 1.95 | 0.75 | 5.02 | 0.19 | Multivariate |
|  | Jerzy.2021 | 1.33 | 1.19 | 1.49 | <0.0001 | Multivariate |
|  | Nakahama,2018 | 3.96 | 1.35 | 11.60 | 0.012 | Multivariate |
|  | Nakanishi,2019 | 0.622 | 0.158 | 2.069 | 0.449 | Univariate |
|  | Owen, 2018 | 0.99 | 0.32 | 3.08 | 0.98 | Univariate |
|  | Stahlbaum,2021 | 9.14 | 1.15 | 408.78 | 0.018 | Multivariate |
|  | Sugano, 2020 | 1.26 | 0.33 | 4.82 | 0.73 | Multivariate |
|  | William,2021 | 2.03 | 0.94 | 4.38 |  | Univariate |
| Concurrent thoracic radiation therapy | William,2021 | 4 | 0.74 | 21.6 |  | Univariate |
| Chemotherapy prior to ICI | Jung.2021 | 0.619 | 0.260 | 1.478 | 0.280 | Univariate |
|  | Li,2020 | 1.21 | 0.56 | 2.62 | 0.636 | Univariate |
|  | Suresh, 2018 | 0.66 | 0.31 | 1.39 | 0.27 | Univariate |
| Tumors proximal to the subsegmental branch | Moda, 2019 | 8.27 | 6.63 | 14.4 | <0.01 | - |
| Imaging findings of airway obstruction adjacent to lung tumors | Nakahama,2018 | 6.59 | 1.82 | 23.90 | 0.004 | Multivariate |
| Radiation dose prior to ICI (cGy≥6,000) | Jung.2021 | 2.642 | 0.932 | 7.490 | 0.068 | Multivariate |
| ECOG (PS=0) | Chen,2021 | 1.54 | 0.53 | 4.48 | 0.423 | Univariate |
| ECOG (PS=1) | Hata,2020 | 1.592 | 0.504 | 4.982 | 0.432 | Univariate |
| ECOG (PS≥1) | Wang, 2022 | 0.512 | 0.031 | 8.575 | 0.641 | Univariate |
| ECOG (PS≥2) | Chao, 2022 | 1.343 | 0.275 | 6.555 | 0.715 | Univariate |
|  | Chen,2021 | 1.04 | 0.06 | 17.18 | 0.98 | Univariate |
|  | Chu, 2020 | 0.412 | 0.094 | 1.813 | 0.241 | Univariate |
|  | Fukihara,2019 | 1.757 | 0.923 | 4.878 | 0.280 | Univariate |
|  | Isono, 2021 | 1.787 | 0.537 | 5.945 | 0.344 | Univariate |
|  | Jung.2021 | 1.091 | 0.461 | 2.578 | 0.843 | Univariate |
|  | Lin, 2021 | 0.38 | 0.12 | 1.17 | 0.09 | Multivariate |
|  | Nakahama,2018 | 0.63 | 0.18 | 2.21 | 0.471 | Multivariate |
|  | Nakanishi,2019 | 0.983 | 0.140 | 4.367 | 0.984 | Univariate |
|  | Okada,2020 | 3.44 | 1.01 | 11.80 | 0.048 | Multivariate |
|  | Shimoji, 2020 | 0.64 | 0.229 | 1.818 | 0.39 | Univariate |
|  | Sugano, 2020 | 0.77 | 0.2 | 2.92 | 0.70 | Multivariate |
|  | Yamaguchi,2018 | 0.38 | 0.020 | 2.11 | 0.31 | Univariate |
|  | Yamaguchi,2021 | 0.75 | 0.17 | 2.38 | 0.64 | Univariate |
|  | Yamaguchi,2022 | 1.57 | 0.40 | 6.19 | 0.52 | Univariate |
|  | Zhang, 2020 | 6.53 | 1.74 | 24.46 | 0.005 | Multivariate |
| Stage I | Suresh, 2018  | 0.33 | 0.01 | 1.83 | 0.3 | Univariate |
| Stage II | Suresh, 2018  | 1.24 | 0.26 | 4.39 | 0.74 | Univariate |
| Stage III | Chen,2021 | 0.68 | 0.22 | 2.14 | 0.509 | Univariate |
|  | Suresh, 2018  | 1.44 | 0.62 | 3.26 | 0.38 | Univariate |
| Stage IV | Chen,2021 | 0.68 | 0.22 | 2.14 | 0.51 | Univariate |
|  | Isono, 2021 | 1.007 | 0.406 | 2.496 | 0.988 | Univariate |
|  | Jung.2021 | 0.682 | 0.217 | 2.148 | 0.513 | Multivariate |
|  | Suresh, 2018 | 0.8 | 0.4 | 1.61 | 0.54 | Univariate |
|  | Suzuki,2020 | 0.940 | 0.362 | 2.439 | 0.90 | Univariate |
| Stage III/IV | Wang, 2022 | 1.781 | 0.502 | 6.317 | 0.371 | Univariate |
| Cancer type Lung cancer | Li,2020 | 2.29 | 1.05 | 5.00 | 0.038 | Multivariate |
| Cancer type (NSCLC) | Sukari, 2019 | 1.00 | 0.35 | 2.80 | 0.999 | Multivariate |
|  | Yamaguchi,2021 | 1.79 | 0.73 | 4.70 | 0.21 | Univariate |
| Pulmonary metastasis | Nakahama,2018 | 0.89 | 0.33 | 2.41 | 0.821 | Multivariate |
|  | Shimoji, 2020 | 0.42 | 0.14 | 1.23 | 0.11 | Univariate |
| Brain metastasis | Wang, 2022 | 1.500 | 0.306 | 7.358 | 0.617 | Univariate |
| Liver metastasis | Wang, 2022 | 2 | 0.263 | 15.209 | 0.503 | Univariate |
| Bone metastasis | Wang, 2022 | 1.125 | 0.398 | 3.178 | 0.824 | Univariate |
| Squamous cell carcinoma | Chao, 2022 | 1.551 | 0.561 | 4.291 | 0.398 | Univariate |
|  | Chen,2021 | 1.06 | 0.41 | 2.77 | 0.901 | Univariate |
|  | Fukihara,2019 | 0.760 | 0.311 | 1.857 | 0.547 | Univariate |
|  | Hata,2020 | 1.10 | 0.39 | 3.13 | 0.86 | Univariate |
|  | Isono, 2021 | 1.051 | 0.424 | 2.605 | 0.915 | Univariate |
|  | Lin, 2021 | 3.02 | 1.41 | 6.43 | 0.004 | Multivariate |
|  | Jerzy.2021 | 1.32 | 1.18 | 1.47 | <0.0001 | Multivariate |
|  | Nakahama,2018 | 1.28 | 0.44 | 3.78 | 0.648 | Multivariate |
|  | Nakanishi,2019 | 1.609 | 0.323 | 6.327 | 0.529 | Univariate |
|  | Sugano, 2020 | 0.81 | 0.23 | 2.85 | 0.75 | Multivariate |
|  | Suresh, 2018 | 2.12 | 1.02 | 4.40 | 0.04 | Univariate |
|  | William,2021 | 1.40 | 0.61 | 3.24 |  | Univariate |
|  | Yamaguchi,2018 | 2.00 | 0.63 | 5.81 | 0.23 | Univariate |
|  | Yamaguchi,2022 | 0.36 | 0.044 | 2.90 | 0.34 | Univariate |
| Adenocarcinoma | Hata,2020 | 1.010 | 0.297 | 3.206 | 1.000 | Univariate |
|  | Isono, 2021 | 1.289 | 0.495 | 3.356 | 0.603 | Univariate |
|  | Suresh, 2018 | 0.28 | 0.19 | 0.8 | 0.01 | Univariate |
|  | Suzuki,2020 | 3.000 | 0.993 | 9.005 | 0.052 | Multivariate |
|  | Wang, 2022 | 2.047 | 0.732 | 5.722 | 0.172 | Univariate |
| Small cell | Chen,2021 | 0.81 | 0.30 | 2.19 | 0.682 | Univariate |
|  | William,2021 | 0.94 | 0.30 | 2.96 |  | Univariate |
| History of autoimmune disease | William,2021 | 1.06 | 0.13 | 8.65 |  | Univariate |
| Pre-existing respiratory disease | Chu, 2020 | 0.902 | 0.329 | 2.474 | 0.841 | Univariate |
|  | Cui，2018 | 2.86 | 1.45 | 5.64 | / | Multivariate |
|  | Isono, 2021 | 1.36 | 1.11 | 1.66 | 0.003 | Multivariate |
|  | Jerzy.2021 | 2.91 | 2.6 | 3.25 | <0.0001 | Multivariate |
|  | Komiya, 2018 | 15.33 | 3.02 | 77.96 | 0.001 | Univariate |
|  | Stahlbaum,2021 | 5.4 | 1.02 | 53.2 | 0.026 | Multivariate |
|  | William,2021 | 2.79 | 1.07 | 7.29 |  | Multivariate |
| Pre-existing Abnormal CT findings | Fukihara,2019 | 1.530 | 0.669 | 3.500 | 0.313 | Univariate |
|  | Nakanishi,2019 | 0.725 | 0.225 | 2.334 | 0.585 | Univariate |
|  | Shimoji, 2020 | 1.83 | 0.40 | 8.35 | 0.43 | Univariate |
|  | Yamamoto,2022 | 1.36 | 1.02 | 1.81 |  | Multivariate |
| Pleural effusion  | Nakahama,2018 | 0.77 | 0.30 | 1.98 | 0.587 | Multivariate |
| Pre-existing ILD | Chen,2021 | 2.8 | 0.52 | 15.19 | 0.233 | Univariate |
|  | Hata,2020 | 4.626 | 1.289 | 16.686 | 0.008 | Univariate |
|  | Isono, 2021 | 4.350 | 1.225 | 15.440 | 0.023 | Multivariate |
|  | Komiya, 2018 | 15.33 | 3.02 | 77.96 | 0.001 | Univariate |
|  | Nakanishi,2019 | 6.643 | 1.782 | 24.761 | 0.005 | Univariate |
|  | Okada,2020 | 0.78 | 0.14 | 4.24 | 0.77 | Multivariate |
|  | Shimoji, 2020 | 6.42 | 1.96 | 21.03 | 0.002 | Multivariate |
|  | Sugano, 2020 | 14.7 | 2.16 | 99.6 | 0.006 | Multivariate |
|  | William,2021 | 15.7 | 2.52 | 98.2 |  | Univariate |
|  | Yamaguchi,2018 | 9.53 | 2.47 | 44.79 | 0.0008 | Multivariate |
|  | Yamaguchi,2021 | 5.92 | 2.07 | 18.54 | 0.0008 | Multivariate |
|  | Yamaguchi,2022 | 19.07 | 4.24 | 85.67 | 0.0001 | Multivariate |
|  | Yamamoto,2022 | 2.62 | 1.85 | 3.7 |  | Multivariate |
|  | Zhang, 2020 | 20.13 | 3.64 | 111.44 | 0.001 | Multivariate |
| Pre-existing Ground glass attenuation | Nakanishi,2019 | 44.040 | 5.830 | 997.528 | <0.001 | Multivariate |
|  | Shimoji, 2020 | 4.05 | 1.29 | 12.71 | 0.01 | Multivariate |
|  | William,2021 | 2.18 | 0.98 | 4.85 |  | Univariate |
| Pre-existing Honeycombing | Nakanishi,2019 | 1.932 | 0.037 | 83.463 | 0.729 | Multivariate |
|  | William,2021 | 6.61 | 2.48 | 17.7 |  | Multivariate |
| Pre-existing Reticular shadow | Nakanishi,2019 | 2.863 | 0.543 | 12.699 | 0.198 | Univariate |
|  | Shimoji, 2020 | 2.28 | 0.63 | 8.21 | 0.20 | Multivariate |
| Pre-existing radiation-induced pulmonary fibrosis | Isono, 2021 | 3.096 | 0.735 | 13.040 | 0.124 | Multivariate |
|  | Nakahama,2018 | 3.96 | 1.35 | 11.60 | 0.012 | Multivariate |
|  | Nakanishi,2019 | 0.331 | 0.017 | 1.907 | 0.246 | Univariate |
|  | Shimoji, 2020 | 1.94 | 0.21 | 17.56 | 0.55 | Univariate |
| Pre-existing COPD | Chao, 2022 | 7.194 | 1.130 | 45.798 | 0.037 | Multivariate |
|  | Li,2020 | 1.67 | 0.72 | 3.90 | 0.234 | Univariate |
|  | William,2021 | 2.42 | 1.12 | 5.22 |  | Univariate |
|  | Yamamoto,2022 | 1.33 | 0.98 | 1.80 |  | Multivariate |
| Pre-existing pulmonary emphysema | Chen,2021 | 5.67 | 1.66 | 19.37 | 0.006 | Multivariate |
|  | Isono, 2021 | 2.088 | 0.645 | 6.760 | 0.219 | Multivariate |
|  | Nakanishi,2019 | 0.977 | 0.275 | 3.161 | 0.971 | Univariate |
|  | Shimoji, 2020 | 0.36 | 0.08 | 1.63 | 0.18 | Univariate |
|  | Stahlbaum,2021 | 7.28 | 1.37 | 71.32 | 0.007 | Multivariate |
|  | William,2021 | 1.39 | 0.65 | 2.99 |  | Univariate |
|  | Yamaguchi,2018 | 0.68 | 0.16 | 2.73 | 0.58 | Multivariate |
| Pre-existing pulmonary mass(es) | William,2021 | 0.80 | 0.36 | 1.76 |  | Univariate |
| ICI types (PD-1) | Chen,2021 | 1.29 | 0.36 | 4.54 | 0.694 | Univariate |
|  | Jung.2021 | 0.94 | 0.11 | 7.79 | 0.96 | Univariate |
| ICI types (PD-L1) | Jung.2021 | 1.909 | 0.213 | 17.084 | 0.563 | Univariate |
| Corticosteroid use | Chu, 2020 | 0.729 | 0.362 | 1.467 | 0.375 | Univariate |
|  | Sukari, 2019 | 4.14 | 1.51 | 13.29 | 0.009 | Multivariate |
| Inhaled corticosteroids | Li,2020 | 3.09 | 1.32 | 7.24 | 0.009 | Multivariate |
| ICI Monotherapy | Chao, 2022 | 0.95 | 0.36 | 2.54 | 0.92 | Univariate |
|  | Lin, 2021 | 6.56 | 1.79 | 23.98 | 0.004 | Multivariate |
|  | Jerzy.2021 | 1.64 | 0.89 | 3.02 | 0.1104 | Multivariate |
| Combination therapy | Cui，2018 | 2.73 | 1.40 | 5.31 | / | Multivariate |
|  | Chao, 2022 | 1.050 | 0.394 | 2.796 | 0.923 | Univariate |
|  | Jerzy.2021 | 1.06 | 0.78 | 1.44 | 0.6984 | Multivariate |
|  | Suresh, 2018 | 0.66 | 0.31 | 1.39 | 0.27 | Univariate |
|  | Wang, 2022 | 0.771 | 0.276 | 2.153 | 0.620 | Univariate |
| Combined chemotherapy | Chao, 2022 | 1.050 | 0.394 | 2.796 | 0.923 | Univariate |
|  | Suresh, 2018 | 0.66 | 0.31 | 1.39 | 0.27 | Univariate |
| Combined chemotherapy (pemetrexed vs. paclitaxel) | Yamaguchi,2022 | 5.67 | 1.28 | 25.11 | 0.022 | Multivariate |
| Combination ICI | Suresh, 2018 | 1.72 | 0.8 | 3.67 | 0.16 | Univariate |
| Pembrolizumab | Fukihara,2019 | 3.259 | 1.361 | 7.807 | 0.008 | Multivariate |
|  | Isono, 2021 | 1.129 | 0.522 | 2.442 | 0.758 | Univariate |
|  | Li, 2020 | 3.63 | 0.96 | 13.70 |  | Univariate |
|  | Suresh, 2018 | 0.37 | 0.08 | 1.66 | 0.20 | Univariate |
|  | William,2021 | 2.57 | 1.08 | 6.11 |  | Multivariate |
| Nivolumab | Isono, 2021 | 0.91 | 0.39 | 2.12 | 0.83 | Univariate |
|  | Li, 2020 | 2.63 | 0.76 | 9.17 | / | Univariate |
|  | Suresh, 2018 | 4.06 | 1.19 | 13.89 | 0.03 | Univariate |
| Atezolizumab | Isono, 2021 | 0.603 | 0.079 | 4.589 | 0.626 | Univariate |
|  | Yamaguchi,2022 | 0.70 | 0.21 | 2.31 | 0.56 | Univariate |
| Ipilimumab + Nivolumab | Li, 2020 | 2.79 | 0.56 | 13.81 | / | Univariate |
|  | William,2021 | 3.48 | 0.36 | 33.2 |  | Multivariate |
| Bevacizumab | Yamaguchi,2022 | 0.68 | 0.18 | 2.54 | 0.56 | Univariate |
| Treatment line（=1） | Chao, 2022 | 0.88 | 0.34 | 2.29 | 0.80 | Univariate |
|  | Chen,2021 | 0.52 | 0.22 | 1.21 | 0.128 | Univariate |
|  | Isono, 2021 | 1.256 | 0.447 | 3.535 | 0.665 | Univariate |
| Treatment line (≥1) | Wang, 2022 | 1.905 | 0.655 | 5.543 | 0.237 | Univariate |
| Treatment line（=2） | Chao, 2022 | 1.020 | 0.311 | 3.346 | 0.974 | Univariate |
|  | Li,2020 | 0.48 | 0.19 | 1.23 | / | Univariate |
| Treatment line（=3） | Chao, 2022 | 1.233 | 0.416 | 3.651 | 0.705 | Univariate |
|  | Li,2020 | 0.62 | 0.26 | 1.45 | 0.244 | Univariate |
| Treatment line (≥2) | Chao, 2022 | 1.13 | 0.44 | 2.94 | 0.80 | Univariate |
|  | Chen,2021 | 1.92 | 0.83 | 4.55 | 0.128 | Univariate |
|  | Chu, 2020 | 1.277 | 0.673 | 2.421 | 0.455 | Univariate |
|  | Fukihara,2019 | 0.455 | 0.178 | 1.164 | 0.100 | Univariate |
|  | Isono, 2021 | 0.75 | 0.28 | 2.03 | 0.57 | Univariate |
|  | Lin, 2021 | 1.66 | 0.82 | 3.36 | 0.16 | Univariate |
|  | Shimoji, 2020 | 0.75 | 0.233 | 2.439 | 0.53 | Univariate |
|  | Yamaguchi,2018 | 0.775 | 0.244 | 2.941 | 0.68 | Univariate |
|  | Yamamoto,2022 | 1.12 | 0.88 | 1.43 |  | Multivariate |
| Driver mutation positive | Nakanishi,2019 | 0.454 | 0.024 | 2.699 | 0.430 | Univariate |
| EGFR positive | Jerzy.2021 | 0.82 | 0.69 | 0.98 | 0.0273 | Multivariate |
| PD-L1≥1% | Jerzy.2021 | 1.16 | 0.8 | 1.69 | 0.441 | Multivariate |
|  | Wang, 2022 | 1.422 | 0.340 | 5.941 | 0.629 | Univariate |
|  | Nakanishi,2019 | 0.686 | 0.065 | 7.235 | 0.754 | Univariate |
|  | Suzuki,2020 | 1.470 | 0.567 | 3.812 | 0.43 | Univariate |
|  | William,2021 | 1.44 | 0.36 | 5.67 |  | Univariate |
|  | Isono, 2021 | 0.257 | 0.06 | 1.098 | 0.067 | Multivariate |
|  | Yamaguchi,2022 | 2.06 | 0.55 | 7.70 | 0.28 | Univariate |
| PD-L1≥50% | Chao, 2022 | 7.184 | 1.154 | 44.721 | 0.035 | Multivariate |
|  | Isono, 2021 | 2.488 | 0.660 | 9.38 | 0.178 | Multivariate |
|  | Yamaguchi,2022 | 1.38 | 0.48 | 3.95 | 0.55 | Univariate |
| WBC (103/mm3) | Fukihara,2019 | 1.090 | 1.000 | 1.188 | 0.051 | Univariate |
|  | Nakanishi,2019 | 1.00005 | 0.99999 | 1.0002 | 0.062 | Univariate |
| WBC (/μL) ≥9000 | Isono, 2021 | 1.263 | 0.492 | 3.243 | 0.627 | Multivariate |
| NLR | Fukihara,2019 | 1.060 | 0.993 | 1.131 | 0.080 | Univariate |
|  | Lin, 2021 | 1.28 | 0.25 | 6.70 | 0.77 | Multivariate |
|  | Nakanishi,2019 | 1.03783 | 0.99754 | 1.1014 | 0.066 | Univariate |
| NLR≥ 5 | Isono, 2021 | 1.394 | 0.626 | 3.108 | 0.416 | Univariate |
|  | Owen, 2018 | 1.00 | 0.32 | 3.09 | 1.00 | Univariate |
|  | Yamaguchi,2021 | 0.68 | 0.21 | 1.82 | 0.45 | Univariate |
| NLR≥ 2.5 | Yamaguchi,2021 | 0.87 | 0.35 | 2.22 | 0.76 | Univariate |
| lymphocyte-to-monocyte ratio < 3 | Isono, 2021 | 2.256 | 0.985 | 5.166 | 0.054 | Univariate |
| platelet-to-lymphocyte ratio | Lin, 2021 | 1.76 | 0.36 | 8.60 | 0.48 | Multivariate |
| platelet-to-lymphocyte ratio ≥ 300 | Isono, 2021 | 1.843 | 0.828 | 4.106 | 0.135 | Univariate |
| platelet-to-lymphocyte ratio ≥237  | Owen, 2018 | 0.93 | 0.24 | 3.70 | 0.92 | Univariate |
| Neutrophils (/μL) ≥ 6000 | Isono, 2021 | 1.593 | 0.714 | 3.553 | 0.255 | Univariate |
|  | Nakanishi,2019 | 1.00003 | 0.99999 | 1.0001 | 0.125 | Univariate |
| Lymphocytes (/μL) ≥ 1500 | Isono, 2021 | 1.686 | 0.789 | 3.604 | 0.178 | Univariate |
|  | Nakanishi,2019 | 0.99933 | 0.99834 | 1.0003 | 0.170 | Univariate |
| absolute lymphocyte count (≥1.15 vs. <1.15) | Lin, 2021 | 0.19 | 0.03 | 1.08 | 0.06 | Multivariate |
| LDH  | Lin, 2021 | 1.83 | 0.73 | 4.58 | 0.19 | Univariate |
|  | Nakanishi,2019 | 0.99987 | 0.99908 | 1.0007 | 0.659 | Univariate |
| LDH (U/L) ≥ 230 | Isono, 2021 | 1.066 | 0.488 | 2.331 | 0.872 | Univariate |
| LDH >240 vs. ≤240 IU/L | Nakahama,2018 | 2.10 | 0.81 | 5.38 | 0.126 | Multivariate |
|  | Yamaguchi,2018 | 0.45 | 0.12 | 1.34 | 0.16 | Univariate |
|  | Yamaguchi,2021 | 1.52 | 0.59 | 3.74 | 0.37 | Univariate |
| Platelets (/μL) ≥ 300000 | Isono, 2021 | 1.142 | 0.513 | 2.543 | 0.745 | Univariate |
| CRP (mg/dL) | Nakanishi,2019 | 1.06826 | 0.96172 | 1.1866 | 0.236 | Univariate |
|  | Fukihara,2019 | 1.090 | 0.993 | 1.197 | 0.071 | Univariate |
| CRP (mg/dL) ≥1 | Isono, 2021 | 1.711 | 0.645 | 4.537 | 0.281 | Multivariate |
|  | Yamaguchi,2018 | 0.67 | 0.23 | 1.85 | 0.44 | Univariate |
|  | Yamaguchi,2021 | 0.71 | 0.27 | 1.75 | 0.46 | Univariate |
| CRP >0.3 vs. ≤0.3 mg/dl | Nakahama,2018 | 0.95 | 0.30 | 2.95 | 0.925 | Multivariate |
| KL-6 (U/mL) | Nakanishi,2019 | 0.99975 | 0.99860 | 1.0001 | 0.297 | Univariate |
| AST (U/L) | Fukihara,2019 | 0.987 | 0.949 | 1.028 | 0.538 | Univariate |
| ALT (U/L) | Fukihara,2019 | 1.017 | 0.992 | 1.041 | 0.185 | Univariate |
| Creatinine (mg/dL) | Fukihara,2019 | 1.356 | 0.414 | 4.445 | 0.615 | Univariate |
| Peak eosinophilia | Husain, 2021 | 0.56 | 0.139 | 2.226 | / | Multivariate |
| Absolute eosinophil count (≥ 0.125 vs. < 0.125) | Chu, 2020 | 3.518 | 1.851 | 6.686 | 0.001 | Multivariate |
| Eosinophils (/μL) ≥500 | Isono, 2021 | 1.853 | 0.705 | 4.873 | 0.211 | Multivariate |
| Albumin (g/dL) | Fukihara,2019 | 0.381 | 0.179 | 0.808 | 0.012 | Multivariate |
|  | Lin, 2021 | 0.16 | 0.04 | 0.64 | 0.009 | Multivariate |
| Albumin (g/dL) <4 | Isono, 2021 | 2.090 | 0.588 | 7.420 | 0.254 | Multivariate |
| Monocytes (/μL) ≥600 | Isono, 2021 | 2.080 | 0.875 | 4.941 | 0.097 | Multivariate |
| IL-8 (pg/mL) | Chao, 2022 | 0.758 | 0.587 | 0.978 | 0.033 | Multivariate |
| TNF (pg/mL) | Chao, 2022 | 1.021 | 0.931 | 1.120 | 0.657 | Univariate |
| IL-1β (pg/mL) | Chao, 2022 | 0.838 | 0.470 | 1.496 | 0.551 | Univariate |
| IL-2R (U/mL) | Chao, 2022 | 1.000 | 0.999 | 1.001 | 0.776 | Univariate |
| IL-6 (pg/mL) | Chao, 2022 | 1.006 | 0.977 | 1.035 | 0.691 | Univariate |
| IL-6 (≥11.81 vs. <11.81) | Lin, 2021 | 5.23 | 1.15 | 23.86 | 0.033 | Multivariate |
| IL-10 (pg/mL) | Chao, 2022 | 1.095 | 0.989 | 1.213 | 0.082 | Univariate |
| IL-10 (≥3.79 vs. <3.79) | Lin, 2021 | 1.85 | 0.45 | 7.63 | 0.39 | Multivariate |
| IL-10 (≥0.704 vs.＜0.704) | Wang, 2022 | 9.969 | 1.144 | 86.843 | 0.037 | Multivariate |
| Baseline IL-12 | Wang, 2022 | 3.461 | 0.961 | 12.461 | 0.058 | Multivariate |
| FVC, % pred. | Suzuki,2020 | 0.734 | 0.891 | 0.979 | 0.0044 | Multivariate |
| FEV1, % pred. | Suzuki,2020 | 1.026 | 0.994 | 1.059 | 0.110 | Multivariate |
| FVC, % pred., ≤ 77.6% | Suzuki,2020 | 1.838 | 0.446 | 7.571 | 0.400 | Multivariate |
| FEV1, % pred., ≤75.6% | Suzuki,2020 | 3.077 | 0.676 | 14.00 | 0.150 | Multivariate |
| TLC, % pred. | Suzuki,2020 | 0.961 | 0.938 | 0.984 | 0.00093 | Univariate |
| FRC, % pred. (functional residual capacity) | Suzuki,2020 | 0.967 | 0.943 | 0.992 | 0.0093 | Univariate |
| FVC, % pred., ≤77.6%, and FEV, % pred., ≤75.6% | Suzuki,2020 | 2.408 | 1.370 | 4.232 | 0.0023 | Univariate |
| Grade 2-5 CIP |
| Age | Sukari, 2019 | 1.00 | 0.96 | 1.04 | 0.879 | Multivariate |
| Pre-existing Lung disease | Sukari, 2019 | 0.65 | 0.20 | 2.41 | 0.487 | Multivariate |
| Steroid use | Sukari, 2019 | 4.19 | 1.53 | 13.50 | 0.009 | Multivariate |
| Grade 3-5 CIP |
| IL-6 (≥11.81 vs. <11.81) | Lin, 2021 | 5.23 | 1.15 | 23.86 | 0.033 | Multivariate |
| IL-10 (≥3.79 vs. <3.79) | Lin, 2021 | 1.85 | 0.45 | 7.63 | 0.39 | Multivariate |
| absolute lymphocyte count (≥1.15 vs. <1.15) | Lin, 2021 | 0.19 | 0.03 | 1.08 | 0.06 | Multivariate |
| neutrophil to lymphocyte ratio | Lin, 2021 | 1.28 | 0.25 | 6.70 | 0.77 | Multivariate |
| platelet-to-lymphocyte ratio | Lin, 2021 | 1.76 | 0.36 | 8.60 | 0.48 | Multivariate |
| albumin | Lin, 2021 | 0.16 | 0.04 | 0.64 | 0.009 | Multivariate |
| LDH  | Lin, 2021 | 1.83 | 0.73 | 4.58 | 0.19 | Univariate |
| ECOG (PS≥2) | Okada,2020 | 4.36 | 1.02 | 18.71 | 0.048 | Multivariate |
| Smoking history (≥50 pack-year) | Okada,2020 | 3.65 | 0.85 | 15.57 | 0.084 | Multivariate |
|  | Yamamoto,2022 | 1.6 | 1.04 | 2.46 | 0.03 | Univariate |
| Pre-existing ILD | Okada,2020 | 0.72 | 0.075 | 6.88 | 0.77 | Multivariate |
|  | Yamamoto,2022 | 3.4 | 2.14 | 5.39 | ＜0.001 | Univariate |
| Abnormal CT finding other than lung cancer | Yamamoto,2022 | 2.43 | 1.71 | 3.44 | ＜0.001 | Univariate |
| Development of CIP at 1 Year |
| Adenocarcinoma | Suresh, 2018 | 0.38 | 0.17 | 0.82 | 0.01 | Univariate |
| Sex(female) | Suresh, 2018 | 1.12 | 0.53 | 2.35 | 0.75 | Univariate |
| Smoking history (ever smoker) | Suresh, 2018 | 0.86 | 0.41 | 1.82 | 0.70 | Univariate |
| Age | Suresh, 2018 | 1 | 0.96 | 1.04 | 0.69 | Univariate |
| Race (Asian vs. Caucasian) | Suresh, 2018 | 2.09 | 0.28 | 10.2 | 0.39 | Univariate |
| Race (African vs. Caucasian) | Suresh, 2018 | 1.08 | 0.37 | 2.72 | 0.87 | Univariate |
| Stage I | Suresh, 2018 | 0.33 | 0.01 | 1.83 | 0.3 | Univariate |
| Stage II | Suresh, 2018 | 1.24 | 0.26 | 4.39 | 0.74 | Univariate |
| Stage III | Suresh, 2018 | 1.44 | 0.62 | 3.26 | 0.38 | Univariate |
| Prior chemotherapy | Suresh, 2018 | 0.86 | 0.38 | 2 | 0.72 | Univariate |
| Pembrolizumab | Suresh, 2018 | 0.39 | 0.06 | 1.44 | 0.22 | Univariate |
| Combination ICI | Suresh, 2018 | 1.72 | 0.8 | 3.67 | 0.16 | Univariate |

Abbreviation: ALT, Alanine transaminase; AST, Aspartate transaminase; CI, confidence interval; CIP, checkpoint inhibitor pneumonitis; CRP, c-reactive protein; COPD, Chronic obstructive pulmonary disease; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; ICI, immune checkpoint inhibitor; ILD, Interstitial lung disease; LDH, lactate dehydrogenase; NLR, neutrophil to lymphocyte ratio; NSCLC, non-small cell lung cancer; OR, odd ratio; PD-L1, programmed death-ligand 1; PS, performance status.

**Supplementary Table 4. Pooled crude and adjusted odds ratios assessing the risk factors for CIP in patients treated with ICIs.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk factors** | **Pooled OR** | **Lower CI** | **Upper CI** | **I2** | **P value** | **Number of studies** | **Number of participants** |
| Age (years) | 0.99  | 0.97 | 1.01 | 0% | 0.30 | 6 | 963 |
| Age (≥ 65 vs < 65) | 1.08 | 0.93 | 1.25 | 38% | 0.33 | 12 | 84,074 |
| Age (≥70 vs < 70) | 0.97 | 0.27 | 3.51 | 67% | 0.96 | 2 | 232 |
| Age (≥75 vs < 75) | 0.78  | 0.10 | 5.95 | 84% | 0.81 | 2 | 381 |
| Sex (male vs female) | 2.39 | 0.98 | 5.82 | 0% | 0.06 | 23 | 14,0426 |
| Smoking history (ever smoker vs never smoker) | 1.39  | 1.14 | 1.71 | 0% | 0.001 | 18 | 7,228 |
| Smoking history (≥50 vs < 50 packs/year) | 1.74  | 0.58 | 5.23 | 51% | 0.32 | 2 | 193 |
| Race (African vs. Caucasian) | 1.00 | 0.88 | 1.13 | 0% | 0.94 | 3 | 82,148 |
| Race (Asian vs. Caucasian) | 1.12  | 0.86 | 1.47 | 0% | 0.40 | 2 | 81,833 |
| Previous thoracic radiotherapy vs no radiotherapy | 1.57  | 1.29 | 1.92 | 49% | <0.001 | 14 | 84,209 |
| Previous chemotherapy vs no chemotherapy | 0.82 | 0.55 | 1.22 | 0% | 0.32 | 3 | 1284 |
| ECOG (PS≥2 vs <2) | 1.14  | 0.78 | 1.67 | 27% | 0.49 | 16 | 2,571 |
| Stage III  | 1.09  | 0.54 | 2.22 | 8% | 0.81 | 2 | 301 |
| Stage IV | 0.83  | 0.55 | 1.25 | 0% | 0.37 | 5 | 861 |
| Cancer type (NSCLC) | 1.40 | 0.71 | 2.77 | 0% | 0.33 | 2 | 356 |
| Squamous cell carcinoma | 1.28 | 1.18 | 1.40 | 0% | <0.001 | 14 | 83,688 |
| Adenocarcinoma | 0.95  | 0.44 | 2.02 | 70% | 0.89 | 5 | 684 |
| Small cell | 0.86  | 0.41 | 1.83 | 0% | 0.70 | 2 | 411 |
| Pulmonary metastasis | 0.64 | 0.30 | 1.33 | 0% | 0.23 | 2 | 400 |
| Pre-existing respiratory disease | 2.51 | 1.90 | 3.32 | 86% | <0.001 | 7 | 82,710 |
| Pre-existing abnormal CT findings | 1.35 | 1.04 | 1.75 | 0% | 0.03 | 4 | 4,053 |
| Pre-existing ILD | 5.66  | 3.48 | 9.21 | 50% | <0.001 | 13 | 5,330 |
| Pre-existing ground glass attenuation | 5.49 | 1.39 | 21.65 | 73% | 0.01 | 3 | 597 |
| Pre-existing honeycombing | 6.11  | 2.37 | 15.79 | 0% | <0.001 | 2 | 398 |
| Pre-existing reticular shadow | 2.48 | 0.90 | 6.87 | 0% | 0.08 | 2 | 282 |
| Pre-existing radiation-induced pneumonitis | 1.91 | 0.65 | 5.63 | 49% | 0.24 | 4 | 663 |
| Pre-existing COPD | 1.77  | 1.11 | 2.81 | 39% | 0.02 | 4 | 4,917 |
| Pre-existing pulmonary emphysema | 1.60  | 0.80 | 3.22 | 55% | 0.18 | 7 | 1,056 |
| ICI types (PD-1 vs other ICIs) | 1.19  | 0.40 | 3.56 | 0% | 0.76 | 2 | 338 |
| Pembrolizumab vs other ICIs | 1.56  | 0.79 | 3.09 | 57% | 0.20 | 5 | 1,707 |
| Nivolumab vs other ICIs | 1.95  | 0.76 | 5.02 | 56% | 0.17 | 3 | 1,222 |
| Atezolizumab vs other ICIs | 0.67 | 0.24 | 1.90 | 0% | 0.45 | 2 | 305 |
| Ipilimumab + Nivolumab vs other ICIs | 3.00 | 0.81 | 11.14 | 0% | 0.10 | 2 | 1,152 |
| ICI monotherapy | 1.94  | 0.79 | 4.75 | 64% | 0.15 | 3 | 81,966 |
| Combined therapy vs ICI monotherapy | 1.27 | 0.92 | 1.74 | 48% | 0.15 | 5 | 82,229 |
| Combined chemotherapy vs ICI monotherapy | 1.36  | 0.34 | 5.46 | 87% | 0.67 | 2 | 369 |
| Treatment line (=1) | 0.79 | 0.46 | 1.35 | 0% | 0.39 | 3 | 440 |
| Treatment line (=2) | 0.64  | 0.31 | 1.33 | 0% | 0.23 | 2 | 1,001 |
| Treatment line (=3) | 0.81 | 0.41 | 1.60 | 0% | 0.54 | 2 | 1,001 |
| Treatment line (≥2) | 1.12 | 0.92 | 1.35 | 0% | 0.26 | 9 | 5,007 |
| Baseline corticosteroid therapy | 2.02 | 0.66 | 6.20 | 81% | 0.22 | 3 | 1,305 |
| PD-L1≥1%vs < 1% | 1.02 | 0.80 | 1.30 | 0% | 0.85 | 7 | 82,536 |
| PD-L1 ≥50%vs < 50% | 2.30  | 0.99 | 5.32 | 16% | 0.05 | 3 | 469 |
| WBC (/μL) | 1.03 | 0.95 | 1.12 | 74% | 0.44 | 2 | 253 |
| NLR | 1.04  | 1.01 | 1.08 | 0% | 0.01 | 3 | 427 |
| NLR (≥ 5 vs < 5) | 1.08  | 0.61 | 1.92 | 0% | 0.79 | 3 | 459 |
| Lymphocytes (/μL) ≥ 1500 vs <1500 | 1.12  | 0.73 | 1.73 | 45% | 0.59 | 2 | 263 |
| LDH (U/L) | 1.13  | 0.70 | 1.81 | 40% | 0.62 | 2 | 257 |
| LDH (>240 vs ≤240 IU/L) | 1.26  | 0.56 | 2.84 | 44% | 0.58 | 3 | 512 |
| CRP (mg/dL) | 1.08 | 1.01 | 1.16 | 0% | 0.03 | 2 | 253 |
| CRP (mg/dL) ≥1 vs <1 | 0.95 | 0.52 | 1.73 | 7% | 0.86 | 3 | 491 |
| Albumin (g/dL) | 0.30  | 0.14 | 0.64 | 14% | 0.002 | 2 | 344 |

Abbreviation: CI, confidence interval; CIP, checkpoint inhibitor pneumonitis; CRP, c-reactive protein; COPD, Chronic obstructive pulmonary disease; ECOG, Eastern Cooperative Oncology Group; ICI, immune checkpoint inhibitor; ILD, interstitial lung disease; LDH, lactate dehydrogenase; NLR, neutrophil to lymphocyte ratio; NSCLC, non-small cell lung cancer; OR, odd ratio; PD-L1, programmed death-ligand 1; PS, performance status.

**Supplementary Table 5. Subgroup analysis. Pooled odd ratios assessing the risk factors for grade III-V CIP in patients treated with ICIs.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk factors** | **Pooled OR** | **Lower CI** | **Upper CI** | **I2** | **P value** | **Number of studies** | **Number of participants** |
| Smoking history (≥50 vs < 50 packs-year) | 1.78  | 1.04 | 3.06 | 12% | 0.04 | 2 | 3,703 |
| Pre-existing ILD | 2.36 | 0.65 | 8.58 | 42% | 0.19 | 2 | 3,703 |

Abbreviation: CI, confidence interval; CIP, checkpoint inhibitor pneumonitis; ICI, immune checkpoint inhibitor; ILD, interstitial lung disease; OR, odd ratio.

**Supplementary Table 6. Subgroup analysis. Pooled odds ratios assessing the risk factors for CIP in patients treated with ICIs according to regions.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk factors** | **Region** | **Pooled OR** | **Lower CI** | **Upper CI** | **I2** | **P value** | **Number of studies**  | **Number of participants** |
| Age (years) | Asia  | 0.99  | 0.96 | 1.01 | 0% | 0.33 | 4 | 590 |
|  | USA | 0.99  | 0.97 | 1.02 | 0% | 0.61 | 2 | 373 |
| Age (≥ 65 vs < 65) | Asia | 1.19 | 0.83 | 1.69 | 31% | 0.35 | 10 | 1,609 |
|  | USA | 1.03 | 0.89 | 1.18 | 54% | 0.71 | 2 | 82,465 |
| Sex (male vs female) | Asia | 1.03 | 0.87 | 1.22 | 6% | 0.75 | 19 | 57,441 |
|  | USA | 3.18  | 0.49 | 20.50 | 0% | 0.22 | 4 | 82,985 |
| Smoking history (ever smoker vs never smoker) | Asia | 1.43  | 1.14 | 1.80 | 0% | 0.002 | 15 | 5,871 |
|  | USA | 1.25 | 0.79 | 1.96 | 0% | 0.34 | 3 | 1,357 |
| Previous thoracic radiotherapy vs no radiotherapy | Asia | 1.81  | 1.30 | 2.53 | 19% | ＜0.001 | 9  | 2,014 |
|  | USA | 1.31  | 1.13 | 1.53 | 34% | ＜0.001 | 4 | 82,094 |
| Previous chemotherapy vs no chemotherapy | USA | 0.88  | 0.56 | 1.38 | 0% | 0.58 | 2 | 1042 |
| Stage IV | Asia | 0.84  | 0.51 | 1.40 | 0% | 0.51 | 4 | 656 |
| Squamous cell carcinoma | Asia | 1.31 | 0.96 | 1.80 | 0% | 0.09 | 11 | 1,540 |
|  | USA | 1.28  | 1.17 | 1.40 | 0% | ＜0.001 | 3 | 82,148 |
| Adenocarcinoma | Asia | 1.70 | 1.00 | 2.89 | 0% | 0.05 | 5 | 479 |
| Pre-existing respiratory disease | Asia | 2.14  | 1.00 | 4.58 | 77% | 0.05 | 4 | 707 |
|  | USA | 2.91 | 2.68 | 3.16 | 0% | ＜0.001 | 3 | 82,003 |
| Pre-existing ILD | Asia | 5.34 | 3.27 | 8.71 | 50% | ＜0.001 | 12 | 5,015 |
| Pre-existing ground glass attenuation | Asia | 11.48  | 1.13 | 116.74 | 75% | 0.04 | 2 | 282 |
| Pre-existing COPD | Asia | 2.39  | 0.49 | 11.56 | 68% | 0.28 | 2 | 3,675 |
|  | USA | 2.04 | 1.16 | 3.61 | 0% | 0.01 | 2 | 1,152 |
| Pre-existing pulmonary emphysema | Asia | 1.31  | 0.52 | 3.29 | 59% | 0.57 | 5 | 681 |
|  | USA | 2.67  | 0.55 | 13.06 | 68% | 0.22 | 2 | 375 |
| Pembrolizumab vs other ICIs | Asia | 1.88  | 0.67 | 5.31 | 69% | 0.23 | 2 | 350 |
|  | USA | 1.26 | 0.41 | 3.85 | 64% | 0.69 | 3 | 1,357 |
| Nivolumab vs other ICIs | USA | 3.28  | 1.37 | 7.84 | 0% | 0.008 | 2 | 1,042 |
| ICI monotherapy | Asia | 2.37  | 0.36 | 15.73 | 82% | 0.37 | 2 | 338 |
| Combined therapy | Asia | 1.41 | 0.62 | 3.18 | 61% | 0.41 | 3 | 396 |
|  | USA | 1.19 | 0.86 | 1.63 | 41% | 0.31 | 2 | 81,833 |
| PD-L1 ≥1%vs < 1% | Asia | 1.07 | 0.52 | 2.18 | 25% | 0.86 | 5 | 593 |
|  | USA | 1.01 | 0.77 | 1.31 | 0% | 0.96 | 2 | 81,943 |
| NLR (≥ 5 vs < 5) | Asia | 1.11 | 0.57 | 2.15 | 0% | 0.76 | 2 | 368 |

Abbreviation: CI, confidence interval; CIP, checkpoint inhibitor pneumonitis; COPD, Chronic obstructive pulmonary disease; ICI, immune checkpoint inhibitor; ILD, interstitial lung disease; NLR, neutrophil lymphocyte ratio; OR, odd ratio; PD-L1, programmed death-ligand 1.

**Supplementary Table 7. Subgroup analysis. Pooled odds ratios assessing the risk factors for CIP in patients treated with ICIs according to cancer types.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk factors** | **Cancer type** | **Pooled OR** | **Lower CI** | **Upper CI** | **I2** | **P value** | **Number of studies** | **Number of participants** |
| Age (years) | NSCLC | 0.99  | 0.97 | 1.01 | 0% | 0.42 | 4 | 596 |
| Age (≥ 65 vs < 65) | NSCLC | 1.03  | 0.91 | 1.16 | 23% | 0.66 | 7 | 82,537 |
|  | Lung cancer | 0.84 | 0.38 | 1.82 | 64% | 0.65 | 3 | 512 |
| Sex (male vs female) | NSCLC | 2.31  | 0.93 | 5.72 | 0% | 0.07 | 15 | 87,209 |
|  | Lung cancer | 1.05 | 0.58 | 1.92 | 41% | 0.87 | 4 | 827 |
| Smoking history (ever smoker vs never smoker) | NSCLC | 1.45 | 1.14 | 1.84 | 0% | 0.002 | 12 | 5,283 |
|  | Lung cancer | 1.37 | 0.81 | 2.31 | 0% | 0.24 | 3 | 731 |
| Race (African vs. Caucasian) | NSCLC | 0.99 | 0.87 | 1.12 | 0% | 0.86 | 2  | 81,833 |
| Previous thoracic radiotherapy vs no radiotherapy | NSCLC | 1.40  | 1.15 | 1.69 | 46% | ＜0.001 | 10 | 83,418 |
|  | Lung cancer | 2.46 | 1.63 | 3.71 | 0% | ＜0.001 | 4 | 896 |
| ECOG (PS≥2 vs <2) | NSCLC | 1.16 | 0.73 | 1.83 | 0% | 0.53 | 9 | 1,476 |
|  | Lung cancer | 1.58  | 0.56 | 4.45 | 69% | 0.38 | 5 | 708 |
| Stage IV | NSCLC | 0.85  | 0.55 | 1.32 | 0% | 0.48 | 4 | 619 |
| Squamous cell carcinoma | NSCLC | 1.27  | 1.17 | 1.38 | 0% | ＜0.001 | 11 | 82,939 |
|  | Lung cancer | 1.72  | 0.92 | 3.23 | 40% | 0.09 | 3 | 585 |
| Pre-existing respiratory disease | NSCLC | 2.40 | 1.74 | 3.30 | 91% | ＜0.001 | 4 | 82,170 |
|  | Lung cancer | 2.84  | 1.63 | 4.94 | 0% | ＜0.001 | 2 | 480 |
| Pre-existing abnormal CT findings | NSCLC | 1.33 | 1.02 | 1.74 | 0% | 0.03 | 3 | 3,854 |
| Pre-existing ILD | NSCLC | 5.81 | 3.07 | 10.99 | 54% | ＜0.001 | 7 | 4,336 |
|  | Lung cancer | 5.06 | 1.13 | 22.72 | 67% | 0.03 | 4 | 607 |
| Pre-existing radiation-induced pneumonitis | NSCLC | 1.82  | 0.46 | 7.26 | 66% | 0.40 | 3 | 464 |
| Pre-existing COPD | NSCLC | 2.39  | 0.49 | 11.56 | 68% | 0.28 | 2 | 3,765 |
| Pre-existing pulmonary emphysema | NSCLC | 1.20  | 0.57 | 2.52 | 0% | 0.63 | 3 | 386 |
|  | Lung cancer | 2.58 | 0.66 | 10.11 | 73% | 0.18 | 2 | 411 |
| Pembrolizumab vs other ICIs | NSCLC | 1.05  | 0.40 | 2.78 | 65% | 0.92 | 3 | 488 |
| Nivolumab vs other ICIs | NSCLC | 1.79  | 0.42 | 7.72 | 74% | 0.43 | 2 | 385 |
| ICI monotherapy | NSCLC | 1.40 | 0.84 | 2.36 | 0% | 0.20 | 2 | 81,792 |
| Combined therapy  | NSCLC | 1.15  | 0.90 | 1.47 | 14% | 0.25 | 4 | 82,064 |
| Treatment line (=1) | NSCLC | 1.04  | 0.51 | 2.09 | 0% | 0.92 | 2 | 344 |
| Treatment line (≥2) | NSCLC | 1.06 | 0.86 | 1.30 | 0% | 0.60 | 6 | 4,538 |
|  | Lung cancer | 1.76 | 1.03 | 3.02 | 0% | 0.04 | 2 | 270 |
| PD-L1 ≥1%vs < 1% | NSCLC | 1.01  | 0.78 | 1.30 | 2% | 0.94 | 6 | 82,221 |
| NLR | NSCLC | 1.04 | 1.01 | 1.08 | 0% | 0.01 | 2 | 253 |
| NLR (≥ 5 vs < 5) | NSCLC | 1.25 | 0.65 | 2.40 | 0% | 0.51 | 2 | 271 |
| LDH (>240 vs ≤240 IU/L) | NSCLC | 1.04  | 0.23 | 4.69 | 71% | 0.96 | 2 | 324 |
| CRP (mg/dL) ≥1 vs <1 | NSCLC | 1.10  | 0.44 | 2.75 | 38% | 0.84 | 2 | 303 |

Abbreviation: CI, confidence interval; CIP, checkpoint inhibitor pneumonitis; CRP, c-reactive protein; COPD, Chronic obstructive pulmonary disease; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; ICI, immune checkpoint inhibitor; ILD, interstitial lung disease; LDH, lactate dehydrogenase; NLR, neutrophil lymphocyte ratio; OR, odd ratio; PD-L1, programmed death-ligand 1; PS, performance status.

**Supplementary Table 8. Subgroup analysis. Pooled odds ratios assessing the risk factors for CIP in patients treated with ICIs according to treatment** **regime.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk factors** | **Treatment** | **Adjusted OR** | **Lower CI** | **Upper CI** | **I2** | **P value** | **Number of studies** | **Number of participants** |
| Age (years) | Monotherapy | 0.98 | 0.95 | 1.01 | 0% | 0.24 | 3 | 507 |
| Age (≥ 65 vs < 65) | Monotherapy | 2.14  | 1.06 | 4.33 | 0% | 0.03 | 3 | 441 |
| Sex (male vs female) | Monotherapy | 1.23 | 0.83 | 1.82 | 15% | 0.29 | 9 | 4,823 |
| Smoking history (ever smoker vs never smoker) | Monotherapy | 1.32  | 0.84 | 2.08 | 22% | 0.23 | 7 | 4,515 |
| Previous thoracic radiotherapy vs no radiotherapy | Monotherapy | 1.71  | 0.75 | 3.92 | 60% | 0.21 | 4 | 581 |
| ECOG (PS≥2 vs <2) | Monotherapy | 1.20 | 0.63 | 2.28 | 48% | 0.57 | 7 | 1,084 |
| Stage IV | Monotherapy | 0.97 | 0.50 | 1.88 | 0% | 0.94 | 2 | 318 |
| Squamous cell carcinoma | Monotherapy | 1.04 | 0.66 | 1.64 | 0% | 0.86 | 5 | 697 |
| Adenocarcinoma | Monotherapy | 1.58  | 0.85 | 2.95 | 0% | 0.15 | 3 | 412 |
| Pre-existing respiratory disease | Monotherapy | 3.97 | 0.38 | 41.97 | 88% | 0.25 | 2 | 242 |
| Pre-existing abnormal CT findings | Monotherapy | 1.39 | 1.06 | 1.82 | 0% | 0.02 | 3 | 3,970 |
| Pre-existing ILD | Monotherapy | 5.49  | 3.21 | 9.40 | 47% | ＜0.001 | 8 | 4,609 |
| Pre-existing radiation-induced pneumonitis | Monotherapy | 2.70  | 0.81 | 9.02 | 0% | 0.11 | 2 | 379 |
| Pre-existing pulmonary emphysema | Monotherapy | 0.87 | 0.31 | 2.49 | 43% | 0.80 | 3 | 502 |
| Pembrolizumab vs other ICIs | Monotherapy | 1.88 | 0.67 | 5.31 | 69% | 0.23 | 2 | 350 |
| Treatment line (≥2) | Monotherapy | 0.97  | 0.74 | 1.28 | 6% | 0.83 | 5 | 4,273 |
| PD-L1 ≥1%vs < 1% | Monotherapy | 0.67 | 0.12 | 3.68 | 74% | 0.65 | 2 | 318 |
| NLR (≥ 5 vs < 5) | Monotherapy | 1.11 | 0.57 | 2.15 | 0% | 0.76 | 2 | 368 |
| LDH (>240 vs ≤240 IU/L) | Monotherapy | 0.91  | 0.28 | 2.95 | 54% | 0.87 | 2 | 311 |

Abbreviation: CI, confidence interval; CIP, checkpoint inhibitor pneumonitis; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; ICI, immune checkpoint inhibitor; ILD, interstitial lung disease; LDH, lactate dehydrogenase; NLR, neutrophil lymphocyte ratio; OR, odd ratio; PD-L1, programmed death-ligand 1; PS, performance status.

**Supplementary Table 9. Subgroup analysis. Pooled odds ratios assessing the risk factors for CIP in patients treated with ICIs according to ICI types.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk factors** | **ICI type** | **Pooled OR** | **Lower CI** | **Upper CI** | **I2** | **P value** | **Number of studies** | **Number of participants** |
| Age (years) | PD-1 | 0.99  | 0.97 | 1.01 | 0% | 0.25 | 5 | 758 |
| Age (≥ 65 vs < 65) | PD-1 | 1.81 | 0.83 | 3.95 | 0% | 0.14 | 2 | 311 |
| Sex (male vs female) | PD-1 | 1.22  | 0.90 | 1.67 | 0% | 0.20 | 9 | 4,797 |
|  | Nivolumab  | 1.47 | 0.76 | 2.86 | 39% | 0.25 | 4 | 4,084 |
| Smoking history (ever smoker vs never smoker) | PD-1 | 1.30  | 0.80 | 2.12 | 29% | 0.29 | 7 | 4,489 |
|  | Nivolumab | 1.41 | 1.01 | 1.97 | 0% | 0.05 | 4 | 4,084 |
| Previous thoracic radiotherapy vs no radiotherapy | PD-1 | 2.09  | 0.90 | 4.87 | 64% | 0.09 | 5 | 679 |
| ECOG (PS≥2 vs <2) | PD-1 | 1.23  | 0.64 | 2.37 | 45% | 0.53 | 7 | 1,058 |
|  | Nivolumab | 1.06  | 0.45 | 2.47 | 0% | 0.90 | 2 | 389 |
| Squamous cell carcinoma | PD-1 | 1.17  | 0.72 | 1.91 | 0% | 0.52 | 5 | 671 |
|  | Nivolumab | 1.18 | 0.56 | 2.49 | 0% | 0.66 | 2 | 295 |
| Adenocarcinoma | PD-1 | 1.80 | 0.62 | 5.22 | 40% | 0.28 | 2 | 232 |
| Pre-existing respiratory disease | PD-1 | 4.98  | 1.85 | 13.37 | 46% | 0.001 | 3 | 287 |
| Pre-existing ILD | PD-1 | 5.42  | 3.10 | 9.48 | 49% | ＜0.001 | 7 | 4,382 |
|  | Nivolumab | 3.27  | 2.00 | 5.33 | 23% | ＜0.001 | 3 | 3,883 |
| Pre-existing ground glass attenuation | PD-1 | 11.48 | 1.13 | 116.74 | 75% | 0.04 | 2 | 282 |
| Pre-existing radiation-induced pneumonitis | PD-1 | 1.49 | 0.31 | 7.27 | 64% | 0.62 | 3 | 483 |
| Pre-existing pulmonary emphysema | PD-1 | 1.09 | 0.34 | 3.47 | 60% | 0.88 | 4 | 465 |
| Treatment line (≥2) | PD-1 | 0.91 | 0.61 | 1.35 | 23% | 0.62 | 4 | 4,093 |
| PD-L1 (TPS) ≥1%vs < 1% | PD-1 | 1.32  | 0.55 | 3.19 | 0% | 0.54 | 2 | 221 |
| NLR | PD-1 | 1.04 | 1.01 | 1.08 | 0% | 0.01 | 2 | 253 |
| CRP (mg/dL) ≥1 vs <1 | PD-1 | 0.69  | 0.34 | 1.42 | 0% | 0.31 | 2 | 311 |

Abbreviation: CI, confidence interval; CIP, checkpoint inhibitor pneumonitis; CRP, c-reactive protein; ECOG, Eastern Cooperative Oncology Group; ICI, immune checkpoint inhibitor; ILD, interstitial lung disease; NLR, neutrophil lymphocyte ratio; OR, odd ratio; PD-L1, programmed death-ligand 1; PS, performance status.

**Supplementary Table 10. Sensitivity analysis of incidence of CIP in patients treated with ICIs by omitting the study one by one.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ID** | **First author** | **Year** | **Incidence**  | **Study exclude, incidence (95%CI)** | **Study exclude, I2** |
| 1 | Asada [38] | 2021 | 0.14 | 0.17 [0.17, 0.18] | 97% |
| 2 | Barrón [46] | 2020 | 0.22 | 0.16 [0.16, 0.16] | 98% |
| 3 | Chao [26] | 2022 | 0.12 | 0.16 [0.16, 0.16] | 98% |
| 4 | Chen [36] | 2021 | 0.29 | 0.16 [0.16, 0.16] | 98% |
| 5 | Chu [45] | 2020 | 0.18 | 0.16 [0.16, 0.16] | 98% |
| 6 | Cui [56] | 2018 | 0.33 | 0.16 [0.16, 0.16] | 98% |
| 7 | Fukihara [51] | 2019 | 0.16 | 0.16 [0.16, 0.16] | 98% |
| 8 | Hata [44] | 2020 | 0.20 | 0.16 [0.16, 0.16] | 98% |
| 9 | Husain [35] | 2021 | 0.11 | 0.16 [0.16, 0.16] | 98% |
| 10 | Isono [34] | 2021 | 0.15 | 0.16 [0.16, 0.16] | 98% |
| 11 | Jerzy [29] | 2021 | 0.19 | 0.13 [0.13, 0.13] | 94% |
| 12 | Jung [33] | 2021 | 0.10 | 0.16 [0.16, 0.16] | 98% |
| 13 | Komiya [55] | 2018 | 0.15 | 0.16 [0.16, 0.16] | 98% |
| 14 | Li [43] | 2020 | 0.04 | 0.16 [0.16, 0.16] | 97% |
| 15 | Lin [32] | 2021 | 0.50 | 0.16 [0.16, 0.16] | 98% |
| 16 | Mamesaya[50] | 2019 | 0.09 | 0.16 [0.16, 0.16] | 98% |
| 17 | Moda [49] | 2019 | 0.09 | 0.16 [0.16, 0.16] | 98% |
| 18 | Nakahama [54] | 2018 | 0.12 | 0.16 [0.16, 0.16] | 98% |
| 19 | Nakanishi [48] | 2019 | 0.17 | 0.16 [0.16, 0.16] | 98% |
| 20 | Okada [42] | 2020 | 0.19 | 0.16 [0.16, 0.16] | 98% |
| 21 | Owen [53] | 2018 | 0.10 | 0.16 [0.16, 0.16] | 98% |
| 22 | Shimoji [31] | 2020 | 0.10 | 0.16 [0.16, 0.16] | 98% |
| 23 | Stahlbaum [30] | 2021 | 0.67 | 0.16 [0.16, 0.16] | 98% |
| 24 | Sugano [41] | 2020 | 0.12 | 0.16 [0.16, 0.16] | 98% |
| 25 | Sukari [47] | 2019 | 0.15 | 0.16 [0.16, 0.16] | 98% |
| 26 | Suresh [16] | 2018 | 0.19 | 0.16 [0.16, 0.16] | 98% |
| 27 | Suzuki [40] | 2020 | 0.14 | 0.16 [0.16, 0.16] | 98% |
| 28 | Tamiya [57] | 2017 | 0.12 | 0.16 [0.16, 0.16] | 98% |
| 29 | Wang [25] | 2022 | 0.34 | 0.16 [0.16, 0.16] | 98% |
| 30 | William [37] | 2021 | 0.10 | 0.16 [0.16, 0.16] | 98% |
| 31 | Yamaguchi [52] | 2018 | 0.15 | 0.16 [0.16, 0.16] | 98% |
| 32 | Yamaguchi [28] | 2021 | 0.12 | 0.16 [0.16, 0.16] | 98% |
| 33 | Yamaguchi [24] | 2022 | 0.14 | 0.16 [0.16, 0.16] | 98% |
| 34 | Yamamoto [27] | 2022 | 0.10 | 0.16 [0.16, 0.16] | 98% |
| 35 | Zhang [39] | 2020 | 0.17 | 0.16 [0.16, 0.16] | 98% |

Abbreviation: CI, confidence interval; CIP, checkpoint inhibitor pneumonitis; ICI, immune checkpoint inhibitor.

**Supplementary Table 11. Sensitivity analysis by omitting the study one by one (risk factor: previous thoracic radiotherapy).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ID** | **First author** | **Year** | **Pooled OR** | **Study exclude, pooled OR** | **Study exclude, I2** |
| **1** | Cui [56] | 2018 | 3.34 [1.51, 7.39] | 1.32 [1.21, 1.45] | 46% |
| **2** | Jerzy [29] | 2021 | 1.29 [1.18, 1.41] | 2.40 [1.67, 3.43] | 0% |
| **3** | Lin [32] | 2021 | 1.95 [0.75, 5.07] | 1.33 [1.22, 1.46] | 60% |
| **4** | Mamesaya [50] | 2019 | 1.95 [1.13, 3.37] | 1.33 [1.21, 1.45] | 57% |
| **5** | Nakahama [54] | 2018 | 3.96 [1.35, 11.62] | 1.33 [1.22, 1.45] | 50% |
| **6** | Stahlbaum [30] | 2021 | 9.14 [1.15, 72.64] | 1.33 [1.22, 1.46] | 52% |
| **7** | Sugano [41] | 2020 | 1.26 [0.33, 4.81] | 1.34 [1.23, 1.46] | 61% |

**Supplementary Table 12. Sensitivity analysis by omitting the study one by one (risk factor: pre-existing respiratory disease).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ID** | **First author** | **Year** | **Pooled OR** | **Study exclude, pooled OR** | **Study exclude, I2** |
| 1 | Cui [56]  | 2018 | 2.86 [1.45, 5.64] | 2.50 [1.86, 3.35] | 89% |
| 2 | Isono [34] | 2021 | 1.36 [1.11, 1.67] | 2.91 [2.68, 3.16] | 0% |
| 3 | Jerzy [29] | 2021 | 2.91 [2.68, 3.16] | 2.22 [1.23, 4.02] | 64% |
| 4 | Stahlbaum [30] | 2021 | 5.40 [1.02, 28.59] | 2.48 [1.87, 3.28] | 89% |
| 5 | William [37] | 2021 | 2.79 [1.07, 7.27] | 2.51 [1.88, 3.35] | 89% |

**Supplementary Table 13. Sensitivity analysis by omitting the study one by one (risk factor: pre-existing ILD).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ID** | **First author** | **Year** | **Pooled OR** | **Study exclude, pooled OR** | **Study exclude, I2** |
| **1** | Isono [34] | 2021 | 4.35 [1.22, 15.45] | 6.10 [2.99, 12.44] | 66% |
| **2** | Okada [42] | 2020 | 0.78 [0.14, 4.35] | 6.82 [3.61, 12.88] | 60% |
| **3** | Shimoji [31] | 2020 | 6.42 [1.96, 21.03] | 5.78 [2.85, 11.70] | 65% |
| **4** | Sugano [41] | 2020 | 14.70 [2.16, 100.05] | 5.37 [2.81, 10.26] | 63% |
| **5** | Yamaguchi [52] | 2018 | 9.53 [2.47, 36.77] | 5.46 [2.79, 10.71] | 63% |
| **6** | Yamaguchi [28] | 2021 | 5.92 [2.07, 16.93] | 5.87 [2.85, 12.06] | 65% |
| **7** | Yamaguchi [24] | 2022 | 19.07 [4.24, 85.76] | 5.00 [2.71, 9.24] | 56% |
| **8** | Yamamoto [27] | 2022 | 2.62 [1.85, 3.71] | 6.98 [3.75, 13.01] | 36% |
| **9** | Zhang [39] | 2020 | 20.13 [3.64, 111.33] | 5.11 [2.74, 9.51] | 58% |

**Supplementary Table 14. Sensitivity analysis by omitting the study one by one (risk factor: pre-existing pulmonary emphysema).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ID** | **First author** | **Year** | **Pooled OR** | **Study exclude, pooled OR** | **Study exclude, I2** |
| **1** | Chen [36] | 2021 | 5.67 [1.66, 19.37] | 2.06 [0.61, 6.98] | 53% |
| **2** | Isono [34] | 2021 | 2.09 [0.64, 6.76] | 3.02 [0.70, 12.96] | 68% |
| **3** | Stahlbaum [30] | 2021 | 7.28 [1.37, 38.68] | 2.11 [0.67, 6.62] | 58% |
| **4** | Yamaguchi [52] | 2018 | 0.68 [0.16, 2.89] | 3.94 [1.85, 8.40] | 0% |

**Supplementary Figure 6. Quality assessment of the included studies.**

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**Supplementary Figure 7. Funnel plot of the incidence of CIP for the search of publication bias.**

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**Supplementary Figure 8. Funnel plot of the risk factors of CIP for the search of publication bias.**

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