Table S1 Introduction of the included studies. SCLC, small cell lung cancer; NSCLC, non-small cell lung cancer; HNSCC, head and neck squamous cell cancer; PD-1, programmed death 1; PD-L1, programmed death-ligand 1; CTLA-4, cytotoxic T-lymphocyte-associated antigen 4; SoC, standard of care; ECOG PS, eastern cooperative oncology group performance status; TC, tumor cells; CPS, combined positive score.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Median (range)**  **Age (years)** | | **Males**  **(%)** | | **Tumor P****D-L1 expression** | | | | | | **Never smokers**  **(%)** | | **ECOG PS** | | | | **Note** |
| **PD-1/PD-L1+CTLA-4 inhibitors** | **SoC** | **PD-1/PD-L1+CTLA-4 inhibitors** | **SoC** | **PD-1/PD-L1+CTLA-4**  **inhibitors** | | | **SoC** | | | **PD-1/PD-L1+CTLA-4**  **inhibitors** | **SoC** | **PD-1/PD-L1+CTLA-4**  **inhibitors** | | **SoC** | |
| **<1%**  **(%)** | **≥1%**  **(%)** | **Unknown**  **(%)** | **<1%**  **(%)** | **≥1%**  **(%)** | **Unknown**  **(%)** | **0**  **(%)** | **1**  **(%)** | **0**  **(%)** | **1**  **(%)** |
| Baas et al.  2021 | 69 (65-75) | 69 (62-75) | 77.2 | 77.2 | 18.8 | 76.6 | 4.6 | 25.8 | 72.5 | 1.7 | 41.9 | 40.4 | 37.6 | 62.4 | 42.4 | 57.3 | - |
| Peters et al.  2021 |
| Doki et al.  2022 | 63  (28-81) | 64  (26-81) | 82.8 | 84.9 | 51.4 | 48.6 | 0 | 51.5 | 48.5 | 0 | 17.5 | 21.0 | 46.5 | 53.5 | 47.5 | 52.5 | - |
| Goldman  et al.  2020 | 63  (58-68) | 63  (57-68) | 75.4 | 68.4 | 0 | 0 | 100 | 0 | 0 | 100 | 5.6 | 5.6 | 40.7 | 59.3 | 33.5 | 66.5 | No requirements concerning  PD-L1 expression at study entry |
| Hellmann  et al.  2019 | 64  (26-87) | 64  (29-87) | 67.4 | 66.0 | 32.1 | 67.9 | 0 | 31.9 | 68.1 | 0 | 13.6 | 13.4 | 35.0 | 64.7 | 32.8 | 66.2 | - |
| Motzer  et al.  2018 | 62  (26-85) | 61  (21-85) | 73.9 | 71.3 | 66.8 | 23.6 | 9.6 | 65.9 | 27.0 | 7.1 | NA | NA | NA | NA | NA | NA | intermediate- and poor-risk patients |
| Paz-Ares  et al.  2021 | 65  (59-70) | 65  (58-70) | 69.8 | 70.4 | 37.4 | 56.2 | 6.4 | 36.0 | 57.0 | 7.0 | 12.7 | 14.5 | 31.3 | 68.4 | 31.3 | 68.4 | - |
| Powles  et al.  2020 | 68  (60-73) | 68  (60-73) | 74.9 | 79.7 | NA | NA | NA | NA | NA | NA | 28.7 | 29.4 | 55.3 | 44.4 | 54.9 | 44.8 | 60% patients PD-L1 TC ≥25% |
| Rizvi et al.  2020 | 65  (34-87) | 65  (35-85) | 72.4 | 65.4 | 20.4 | 79.6 | 0 | 22.3 | 77.7 | 0 | 15.3 | 13.0 | 39.9 | 60.1 | 43.2 | 56.2 | - |
| Owonikoko  et al.  2021 | 64 (39-85) | 64 (44-84) | 64.5 | 63.6 | NA | NA | NA | NA | NA | NA | 7.2 | 4.7 | 39.8 | 60.2 | 37.5 | 62.5 | 47.0% patients  PD-L1 CPS ≥1% |
| Chen et al.  2020 | 65 (39-87) | 64 (36-85) | 62 | 77 | NA | NA | NA | NA | NA | NA | NA | NA | 28 | 72 | 28 | 72 | - |
| Ferris et al. 2020 | 61  (23-81) | 61  (22-82) | 84.6 | 83.1 | 28.3 | 71.7 | 0 | 28.5 | 71.5 | 0 | 22.7 | 21.3 | 25.9 | 74.1 | 31.7 | 68.3 | - |
| Planchard  et al.  2020 | 63 (26-81) | 65 (42-83) | 66.1 | 68.6 | 41.4 | 58.6 | 0 | 49.2 | 50.8 | 0 | 20.1 | 17.8 | 33.3 | 66.7 | 33.9 | 66.1 | All patients PD-L1 TC <25% |

Table S2 Summarize of OS in subgroups of patients with different clinical features. N+I, nivolumab plus ipilimumab; D+T, durvalumab plus tremelimumab; PD-L1, programmed death-ligand 1; OS, overall survival; No, number; HR, hazard ratio; CI, confidence interval; TC, tumor cells; PS, performance status.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Population | Subgroup | No. of studies | Test of association | | | Test of heterogeneity | |
| HR | 95%CI | *p* value | *I*2 | *p* value |
| Aged <65 years | N+I | 6 | 0.70 | 0.63-0.78 | <0.00001 | 48% | 0.09 |
|  | D+T | 5 | 0.82 | 0.72-0.94 | 0.003 | 37% | 0.18 |
| Aged ≥65 years | - | - | - | - | - | - | - |
| Aged 65-74 years | N+I | 4 | 0.72 | 0.62-0.82 | <0.00001 | 0% | 0.55 |
| Aged ≥75 years | - | - | - | - | - | - | - |
| Female | - | - | - | - | - | - | - |
| Male | N+I | 6 | 0.72 | 0.67-0.79 | <0.00001 | 36% | 0.16 |
|  | D+T | 5 | 0.87 | 0.78-0.97 | 0.010 | 0% | 0.66 |
| PS 0 | N+I | 5 | 0.75 | 0.60-0.94 | 0.01 | 62% | 0.03 |
|  | D+T | 4 | 0.77 | 0.66-0.91 | 0.002 | 0% | 0.57 |
| PS 1 | N+I | 5 | 0.77 | 0.70-0.84 | <0.00001 | 0% | 0.69 |
| Active or previous smoker | N+I | 3 | 0.70 | 0.63-0.77 | <0.00001 | 0% | 0.38 |
|  | D+T | 2 | 0.81 | 0.69-0.96 | 0.01 | 0% | 0.36 |
| Never smoker | - | - | - | - | - | - | - |
| With liver metastases | - | - | - | - | - | - | - |
| Without liver metastases | N+I | 4 | 0.71 | 0.64-0.79 | <0.00001 | 0% | 0.50 |
|  | D+T | 2 | 0.82 | 0.71-0.96 | 0.02 | 1% | 0.31 |
| With brain metastases | N+I | 2 | 0.50 | 0.30-0.83 | 0.007 | 63% | 0.10 |
| Without brain metastases | N+I | 2 | 0.75 | 0.67-0.84 | <0.00001 | 0% | 0.99 |
|  | D+T | 1 | 0.81 | 0.66-0.98 | 0.03 | - |  |
| With bone metastases | N+I | 3 | 0.70 | 0.59-0.84 | 0.0001 | 0% | 0.94 |
| Without bone metastases | N+I | 3 | 0.70 | 0.62-0.79 | <0.00001 | 0% | 0.42 |
| Asian | - | - | - | - | - | - | - |
| White population | D+T | 1 | 0.81 | 0.66-0.98 | 0.03 | - | - |
| PD-L1 expression on <1% of TC | N+I | 5 | 0.76 | 0.63-0.93 | 0.007 | 58% | 0.05 |
|  | D+T | 3 | 0.76 | 0.61-0.94 | 0.01 | 37% | 0.21 |
| PD-L1 expression on ≥1% of TC | N+I | 5 | 0.69 | 0.62-0.77 | <0.00001 | 31% | 0.22 |
| PD-L1 expression on ≥1% and <50% of TC | - | - | - | - | - | - | - |
| PD-L1 expression on ≥50% of TC | N+I | 2 | 0.69 | 0.56-0.85 | 0.0006 | 0% | 0.79 |
| Low tumor mutational burden | N+I | 3 | 0.80 | 0.67-0.95 | 0.010 | 0% | 0.47 |
| High tumor mutational burden | N+I | 3 | 0.72 | 0.59-0.88 | 0.001 | 0% | 0.81 |