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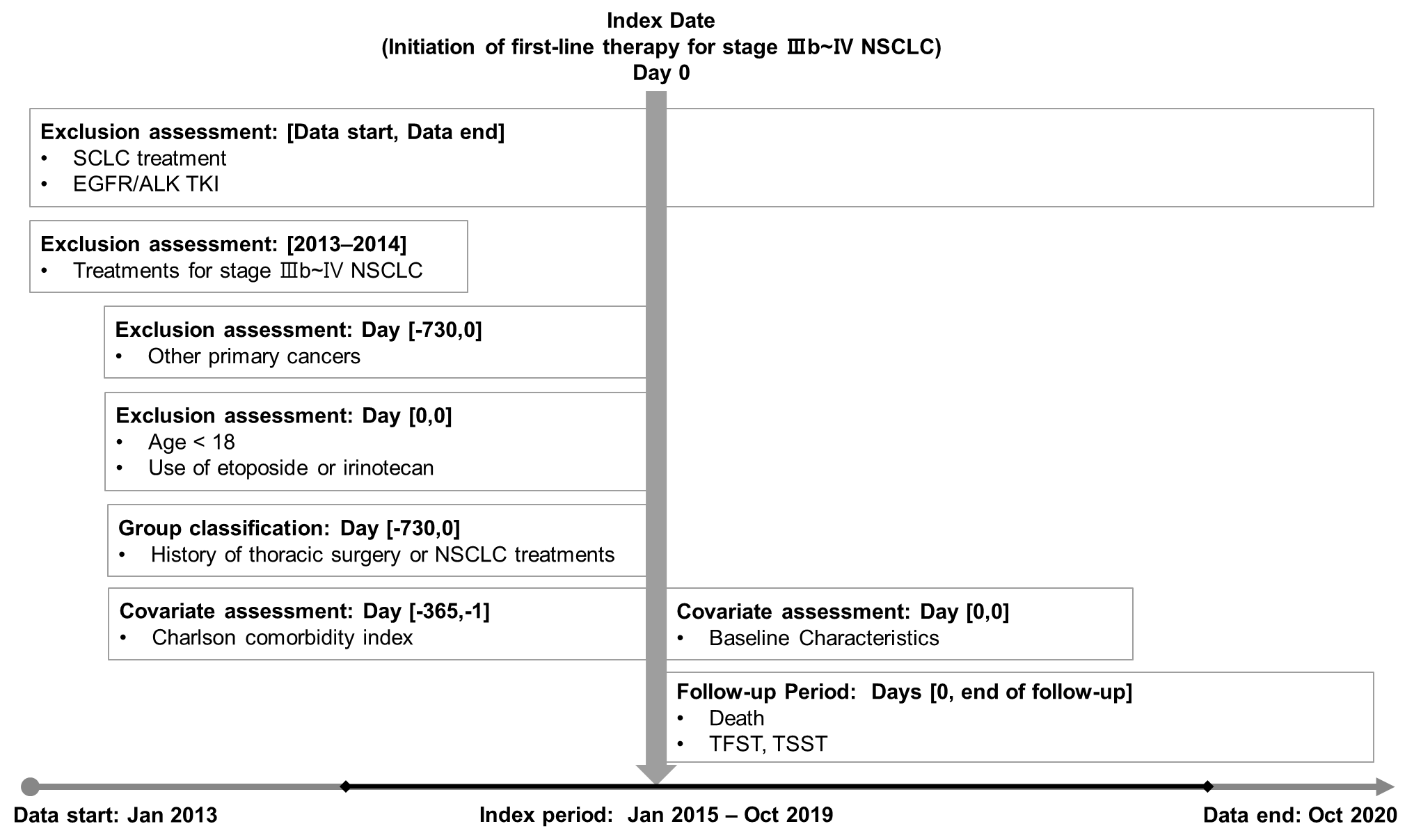
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**S1 Fig. Study design**

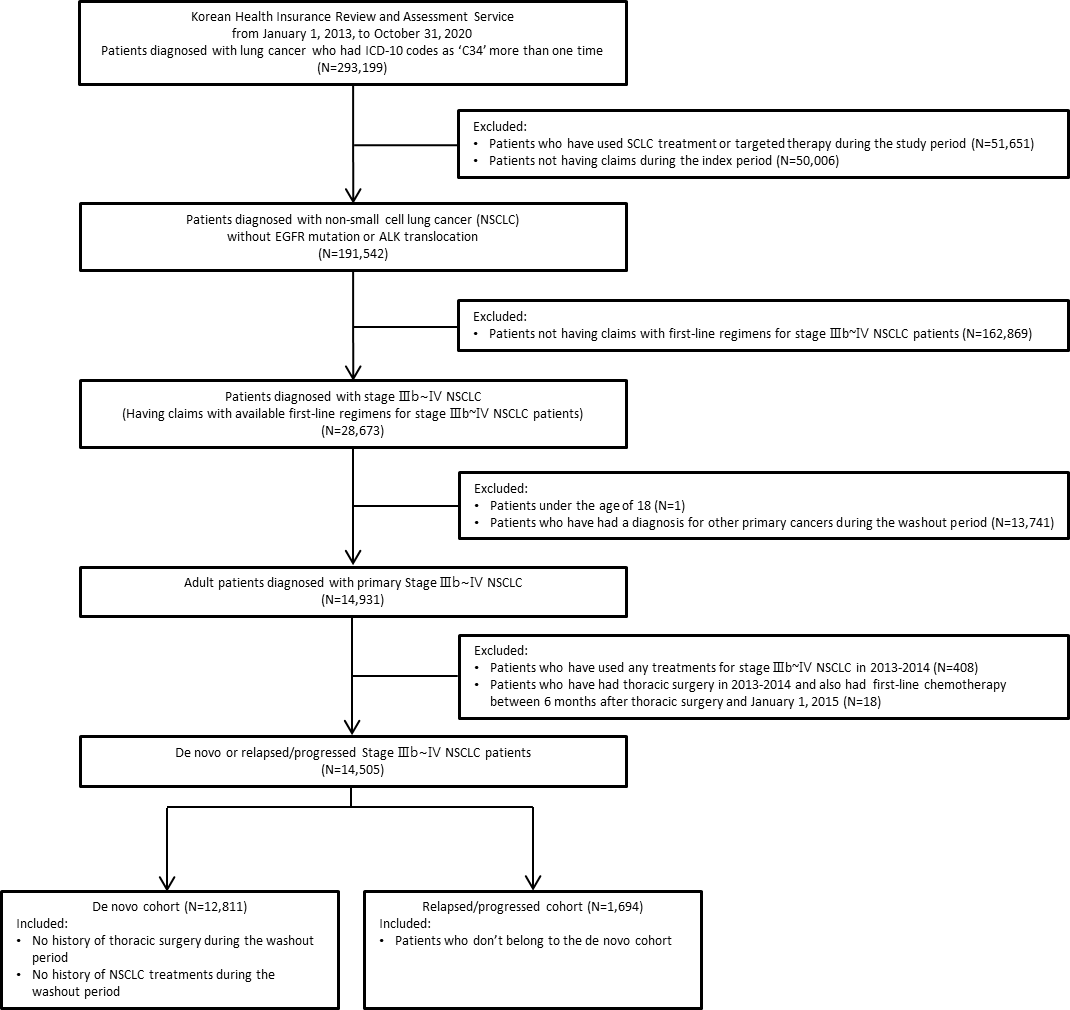
ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; TKI, tyrosine kinase inhibitor

S1 Table. Treatment regimens for inclusion and exclusion

| **Treatment type** | **Incl./excl.** | **Therapy** | **Time frame** |
| --- | --- | --- | --- |
| SCLC treatment | Excluded | belotecan  cyclophosphamide+doxorubicin+cisplatin  cyclophosphamide+doxorubicin+vincristine  cyclophosphamide+etoposide+vincristine  ifosfamide+carboplatin  ifosfamide+doxorubicin  ifosfamide+etoposide+vincristine+carboplatin  topotecan  topotecan+carboplatin  topotecan+cisplatin  topotecan+etoposide  topotecan+ifosfamide | Study period |
| NSCLC first-line palliative treatment  - Chemotherapy | Included | bevacizumab+gemcitabine+cisplatin  bevacizumab+paclitaxel+carboplatin  docetaxel  docetaxel+carboplatin  docetaxel+cisplatin  docetaxel+vinorelbine  gemcitabine  gemcitabine+carboplatin  gemcitabine+cisplatin  gemcitabine+vinorelbine  paclitaxel  paclitaxel+carboplatin  paclitaxel+cisplatin  paclitaxel+ifosfamide  paclitaxel+vinorelbine  pemetrexed+cisplatin  pemetrexed+carboplatin  vinorelbine  vinorelbine+carboplatin  vinorelbine+cisplatin  vinorelbine+ifosfamide  vinorelbine+ifosfamide+cisplatin | Index period |
| NSCLC first-line palliative treatment  - Immunotherapy | Included | atezolizumab (±chemotherapy)  nivolumab (±chemotherapy)  pembrolizumab (±chemotherapy) |
| Stage IIIB–IV NSCLC treatment | Excluded | bevacizumab+gemcitabine+cisplatin  bevacizumab+paclitaxel+carboplatin  docetaxel  docetaxel+vinorelbine  docetaxel+vinorelbine+carboplatin  docetaxel+vinorelbine+cisplatin  gemcitabine  gemcitabine+vinorelbine  gemcitabine+vinorelbine+carboplatin  gemcitabine+vinorelbine+cisplatin  irinotecan  paclitaxel+etoposide+carboplatin  paclitaxel+etoposide+cisplatin  paclitaxel+ifosfamide  paclitaxel+ifosfamide+carboplatin  paclitaxel+ifosfamide+cisplatin  paclitaxel+vinorelbine  paclitaxel+vinorelbine+carboplatin  paclitaxel+vinorelbine+cisplatin  pemetrexed  pemetrexed+cisplatin  pemetrexed+carboplatin  atezolizumab  nivolumab  pembrolizumab | 2013–2014 |
| Stage IIIB–IV NSCLC treatment\*  - EGFR/ALK TKI | Excluded | afatinib  alectinib  brigatinib  ceritinib  crizotinib  erlotinib  gefitinib  osimertinib | Study period |
| \* Regimens reimbursed for adjuvant therapy are not included.  ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; TKI, tyrosine kinase inhibitor | | | |

S2 Table. Treatment regimens included in the analysis

| **Treatment type** | **Treatment Class** | **Therapy** |
| --- | --- | --- |
| First-line  palliative treatment | Chemotherapy | bevacizumab+gemcitabine+cisplatin  bevacizumab+paclitaxel+carboplatin  docetaxel  docetaxel+carboplatin  docetaxel+cisplatin  docetaxel+vinorelbine  gemcitabine  gemcitabine+carboplatin  gemcitabine+cisplatin  gemcitabine+vinorelbine  paclitaxel  paclitaxel+carboplatin  paclitaxel+cisplatin  paclitaxel+ifosfamide  paclitaxel+vinorelbine  pemetrexed+cisplatin  pemetrexed+carboplatin  vinorelbine  vinorelbine+carboplatin  vinorelbine+cisplatin  vinorelbine+ifosfamide  vinorelbine+ifosfamide+cisplatin |
| Immunotherapy\* | atezolizumab (±chemotherapy)  nivolumab (±chemotherapy)  pembrolizumab (±chemotherapy) |
| Second and subsequent-line palliative treatment | Chemotherapy | docetaxel  docetaxel+carboplatin  docetaxel+cisplatin  docetaxel+vinorelbine  docetaxel+vinorelbine+carboplatin  docetaxel+vinorelbine+cisplatin  etoposide+carboplatin  etoposide+carboplatin+ifosfamide  etoposide+cisplatin  etoposide+cisplatin+ifosfamide  gemcitabine  gemcitabine+carboplatin  gemcitabine+cisplatin  gemcitabine+vinorelbine  gemcitabine+vinorelbine+carboplatin  gemcitabine+vinorelbine+cisplatin  irinotecan  irinotecan+carboplatin  irinotecan+cisplatin  paclitaxel  paclitaxel+carboplatin  paclitaxel+cisplatin  paclitaxel+etoposide+carboplatin  paclitaxel+etoposide+cisplatin  paclitaxel+ifosfamide  paclitaxel+ifosfamide+carboplatin  paclitaxel+ifosfamide+cisplatin  paclitaxel+vinorelbine  paclitaxel+vinorelbine+carboplatin  paclitaxel+vinorelbine+cisplatin  pemetrexed  pemetrexed+cisplatin  pemetrexed+carboplatin  vinorelbine  vinorelbine+carboplatin  vinorelbine+cisplatin  vinorelbine+ifosfamide  vinorelbine+ifosfamide+cisplatin |
| Immunotherapy | atezolizumab  nivolumab  pembrolizumab |
| \* Immunotherapies are not reimbursed in Korea as the first-line therapy during the study period. Thus, patients treated with immunotherapies in the first line would have paid 100% of the drug cost according to the Health Insurance Review and Assessment Service guidance. | | |

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**S2 Fig. Patient flow chart**

ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; ICD-10, International Classification of disease 10th revision; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer

**S3 Table. Hazard ratio for time to first subsequent treatment or death**

|  | Hazard ratio (95% CI) |
| --- | --- |

| **Variable** | | **Total (n = 14,505)** | **De novo patients**  **(n = 12,811)** | **Relapsed/progressed patients (n = 1,694)** |
| --- | --- | --- | --- | --- |
| **De novo vs. relapsed/progressed** | | |  |  |
|  | Relapsed/progressed | reference | - | - |
|  | De novo | 1.09 (1.03–1.15) | - | - |
| **Age group** | | |  |  |
|  | < 60 | reference | reference | reference |
|  | 60–69 | 1.08 (1.03–1.14) | 1.10 (1.04–1.16) | 1.00 (0.86–1.16) |
|  | 70–79 | 1.18 (1.12–1.24) | 1.19 (1.13–1.26) | 1.07 (0.92–1.25) |
|  | ≥ 80 | 1.32 (1.22–1.42) | 1.30 (1.20–1.41) | 1.58 (1.19–2.10) |
| **Sex** | | |  |  |
|  | Female | reference | reference | reference |
|  | Male | 1.36 (1.29–1.44) | 1.35 (1.27–1.43) | 1.46 (1.23–1.73) |
| **CCI** | | |  |  |
|  | < 3 | reference | reference | reference |
|  | ≥ 3 | 1.03 (0.99–1.07) | 1.02 (0.98–1.06) | 1.09 (0.97–1.22) |
| **Insurance type** | | |  |  |
|  | National health insurance | reference | reference | reference |
|  | Medical aid or veterans | 1.13 (1.05–1.21) | 1.12 (1.04–1.21) | 1.16 (0.94–1.43) |
| **Type of hospital at initiation of first-line therapy** | | |  |  |
|  | Tertiary hospital | reference | reference | reference |
|  | Others | 1.04 (1.00–1.08) | 1.04 (1.00–1.09) | 1.01 (0.89–1.15) |
| **Geographic region of hospital** | | |  |  |
|  | Capital area | reference | reference | reference |
|  | Metropolitans | 1.01 (0.96–1.06) | 1.03 (0.98–1.08) | 0.88 (0.76–1.03) |
|  | Rural | 0.96 (0.91–1.01) | 0.95 (0.90–1.00) | 1.00 (0.85–1.17) |
| **Index year** | | |  |  |
|  | Pre-immunotherapy | reference | reference | reference |
|  | Post-immunotherapy | 0.79 (0.76–0.82) | 0.79 (0.76–0.82) | 0.81 (0.73–0.91) |
| CCI, charlson comorbidity index; CI, confidence interval | | | | |



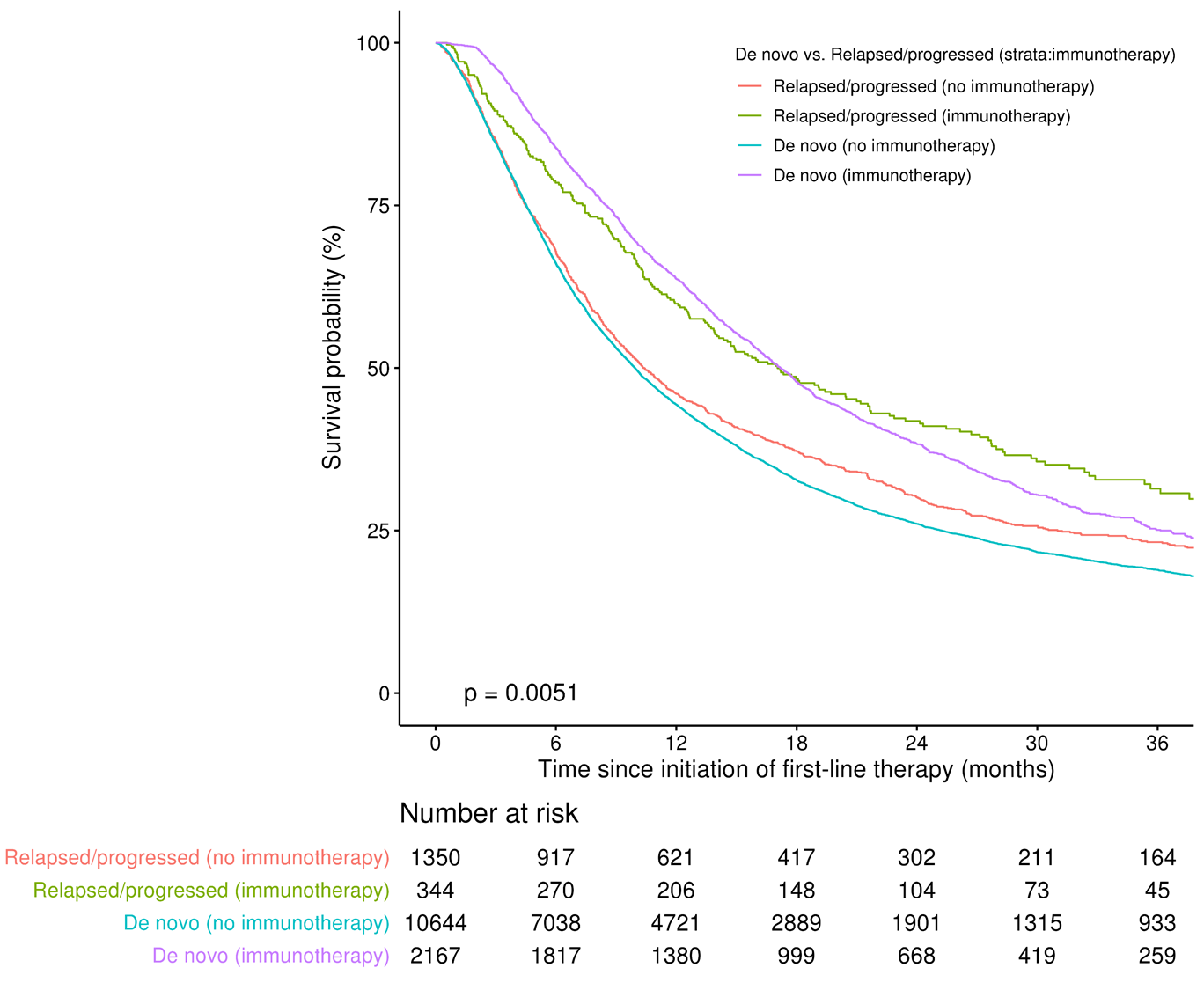
**S3 Fig. Results of sensitivity analysis on overall survival when cytotoxic chemotherapy used within 5 months is considered adjuvant therapy**

CI, confidence interval



**S4 Fig. Overall survival of de novo and relapsed/progressed advanced non-small cell lung cancer patients from the 1-year landmark**

CI, confidence interval



**S5 Fig. Overall survival in de novo and relapsed/progressed advanced non-small cell lung cancer stratified by immunotherapy use**

**S4 Table. Median overall survival in de novo and relapsed/progressed advanced non-small cell lung cancer stratified by immunotherapy use**

|  | Number of patients | Median overall survival (months) | 95% Confidence interval (months) |
| --- | --- | --- | --- |
| De novo (immunotherapy) | 2,167 | 17.2 | 16.4–18.0 |
| De novo (No immunotherapy) | 10,644 | 10.0 | 9.7–10.2 |
| Relapsed/progressed (immunotherapy) | 344 | 17.1 | 14.0–21.6 |
| Relapsed/progressed (No immunotherapy) | 1,350 | 10.4 | 9.5–11.51 |

**S5 Table. Top five regimens and their time to treatment discontinuation (median, IQR)**

|  | Number of patients (%) | | | Time to treatment discontinuation (months), median (IQR) | | |
| --- | --- | --- | --- | --- | --- | --- |
| Total | De novo patients | Relapsed/progressed patients | Total | De novo patients | Relapsed/progressed patients |
| First-line regimen | 14,505 (100.0) | 12,811 (100.0) | 1,694 (100.0) | 2.5 (1.6–3.4) | 2.6 (1.7–3.4) | 2.1 (1.4–3.2) |
| Paclitaxel+platinum | 4,758 (32.8) | 4,387 (34.2) | 371 (21.9) | 2.1 (1.8–3.1) | 2.1 (1.8–3.1) | 1.9 (1.5–2.5) |
| Pemetrexed+platinum | 4,063 (28.0) | 3,763 (29.4) | 300 (17.7) | 2.8 (1.8–3.3) | 2.9 (1.8–3.3) | 2.8 (1.7–3.2) |
| Gemcitabine+platinum | 4,042 (27.9) | 3,631 (28.3) | 411 (24.3) | 2.7 (1.4–3.9) | 2.7 (1.4–3.9) | 2.6 (1.3–3.5) |
| Gemcitabine | 430 (3.0) | 337 (2.6) | 93 (5.5) | 1.5 (0.9–3.1) | 1.5 (0.9–3.1) | 1.5 (1.2–3.0) |
| Docetaxel+platinum | 329 (2.3) | 295 (2.3) | 34 (2.0) | 2.8 (1.5–4.3) | 2.9 (1.6–4.4) | 1.5 (0.8–2.8) |
| Others | 883 (6.1) | 398 (3.1) | 485 (28.6) | 2.1 (1.2–3.5) | 2.3 (1.4–3.4) | 1.9 (1.1–3.5) |
| Second-line regimen | 5.973 (100.0) | 5,314 (100.0) | 659 (100.0) | 2.1 (1.3–4.0) | 2.1 (1.4–4.0) | 2.1 (1.3–3.9) |
| Docetaxel | 1,127 (18.9) | 996 (18.7) | 131 (19.9) | 1.7 (1.2–3.0) | 1.7 (1.2–3.0) | 1.7 (1.2–2.9) |
| Gemcitabine+platinum | 946 (15.8) | 860 (16.2) | 86 (13.1) | 2.3 (1.3–3.3) | 2.3 (1.3–3.3) | 2.2 (1.3–3.2) |
| Pembrolizumab | 822 (13.8) | 765 (14.4) | 57 (8.7) | 3.5 (1.5–10.5) | 3.5 (1.5–10.1) | 3.5 (1.6–16.6) |
| Nivolumab | 688 (11.5) | 617 (11.6) | 71 (10.8) | 2.8 (1.4–7.5) | 2.8 (1.4–7.4) | 2.3 (1.3–7.8) |
| Paclitaxel+platinum | 404 (6.8) | 373 (7.0) | 31 (4.7) | 2.0 (1.5–3.0) | 2.0 (1.5–3.0) | 2.2 (1.4–3.2) |
| Others | 1,986 (33.3) | 1,703 (32.1) | 283 (42.9) | 2.0 (1.2–3.6) | 2.0 (1.2–3.6) | 2.0 (1.2–3.5) |
| IQR, interquartile range  All percentages may not add to a total of 100% because of rounding. | | | | | | |