**Supplementary material: contents**

Supplementary S1 Fig. Study design

Supplementary S2 Fig. Patient flowchart

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

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

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

Supplementary S1 Table. Treatment regimens for inclusion and exclusion

Supplementary S2 Table. Treatment regimens included in the analysis

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

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

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

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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 | belotecancyclophosphamide+doxorubicin+cisplatincyclophosphamide+doxorubicin+vincristinecyclophosphamide+etoposide+vincristineifosfamide+carboplatinifosfamide+doxorubicinifosfamide+etoposide+vincristine+carboplatintopotecantopotecan+carboplatintopotecan+cisplatintopotecan+etoposidetopotecan+ifosfamide | Study period |
| NSCLC first-line palliative treatment- Chemotherapy | Included | bevacizumab+gemcitabine+cisplatinbevacizumab+paclitaxel+carboplatindocetaxeldocetaxel+carboplatindocetaxel+cisplatindocetaxel+vinorelbinegemcitabinegemcitabine+carboplatingemcitabine+cisplatingemcitabine+vinorelbinepaclitaxelpaclitaxel+carboplatinpaclitaxel+cisplatinpaclitaxel+ifosfamidepaclitaxel+vinorelbinepemetrexed+cisplatinpemetrexed+carboplatinvinorelbinevinorelbine+carboplatinvinorelbine+cisplatinvinorelbine+ifosfamidevinorelbine+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+cisplatinbevacizumab+paclitaxel+carboplatindocetaxeldocetaxel+vinorelbinedocetaxel+vinorelbine+carboplatindocetaxel+vinorelbine+cisplatingemcitabinegemcitabine+vinorelbinegemcitabine+vinorelbine+carboplatingemcitabine+vinorelbine+cisplatinirinotecanpaclitaxel+etoposide+carboplatinpaclitaxel+etoposide+cisplatinpaclitaxel+ifosfamidepaclitaxel+ifosfamide+carboplatinpaclitaxel+ifosfamide+cisplatinpaclitaxel+vinorelbinepaclitaxel+vinorelbine+carboplatinpaclitaxel+vinorelbine+cisplatinpemetrexedpemetrexed+cisplatinpemetrexed+carboplatinatezolizumabnivolumabpembrolizumab | 2013–2014 |
| Stage IIIB–IV NSCLC treatment\*- EGFR/ALK TKI | Excluded | afatinibalectinibbrigatinibceritinibcrizotiniberlotinibgefitinibosimertinib | 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+cisplatinbevacizumab+paclitaxel+carboplatindocetaxeldocetaxel+carboplatindocetaxel+cisplatindocetaxel+vinorelbinegemcitabinegemcitabine+carboplatingemcitabine+cisplatingemcitabine+vinorelbinepaclitaxelpaclitaxel+carboplatinpaclitaxel+cisplatinpaclitaxel+ifosfamidepaclitaxel+vinorelbinepemetrexed+cisplatinpemetrexed+carboplatinvinorelbinevinorelbine+carboplatinvinorelbine+cisplatinvinorelbine+ifosfamidevinorelbine+ifosfamide+cisplatin |
| Immunotherapy\* | atezolizumab (±chemotherapy)nivolumab (±chemotherapy)pembrolizumab (±chemotherapy)  |
| Second and subsequent-line palliative treatment | Chemotherapy | docetaxeldocetaxel+carboplatindocetaxel+cisplatindocetaxel+vinorelbinedocetaxel+vinorelbine+carboplatindocetaxel+vinorelbine+cisplatinetoposide+carboplatinetoposide+carboplatin+ifosfamideetoposide+cisplatinetoposide+cisplatin+ifosfamidegemcitabinegemcitabine+carboplatingemcitabine+cisplatingemcitabine+vinorelbinegemcitabine+vinorelbine+carboplatingemcitabine+vinorelbine+cisplatinirinotecanirinotecan+carboplatinirinotecan+cisplatinpaclitaxelpaclitaxel+carboplatinpaclitaxel+cisplatinpaclitaxel+etoposide+carboplatinpaclitaxel+etoposide+cisplatinpaclitaxel+ifosfamidepaclitaxel+ifosfamide+carboplatinpaclitaxel+ifosfamide+cisplatinpaclitaxel+vinorelbinepaclitaxel+vinorelbine+carboplatinpaclitaxel+vinorelbine+cisplatinpemetrexedpemetrexed+cisplatinpemetrexed+carboplatinvinorelbinevinorelbine+carboplatinvinorelbine+cisplatinvinorelbine+ifosfamidevinorelbine+ifosfamide+cisplatin |
| Immunotherapy | atezolizumabnivolumabpembrolizumab |
| \* 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 rangeAll percentages may not add to a total of 100% because of rounding. |