## 1 Supplementary files

2 Table S1. The baseline characteristics of different treatment modalities in IV LCNEC

| Variable | Control ( $\mathrm{N}=179$ ) | Radiotherapy ( $\mathrm{N}=170$ ) | Chemotherapy ( $\mathrm{N}=318$ ) | Chemoradiotherapy ( $\mathrm{N}=427$ ) | p-value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Age |  |  |  |  | <0.001 |
| $<65$ | 129 (72.1\%) | 104 (61.2\%) | 177 (55.7\%) | 204 (47.8\%) |  |
| $\geq 65$ | 50 (27.9\%) | 66 (38.8\%) | 141 (44.3\%) | 223 (52.2\%) |  |
| Gender |  |  |  |  | 0.389 |
| Male | 92 (51.4\%) | 94 (55.3\%) | 188 (59.1\%) | 245 (57.4\%) |  |
| Female | 87 (48.6\%) | 76 (44.7\%) | 130 (40.9\%) | 182 (42.6\%) |  |
| Race |  |  |  |  | 0.709 |
| Black | 23 (12.8\%) | 20 (11.8\%) | 32 (10.1\%) | 61 (14.3\%) |  |
| White | 150 (83.8\%) | 142 (83.5\%) | 270 (84.9\%) | 347 (81.3\%) |  |
| Others | 6 (3.4\%) | 8 (4.7\%) | 16 (5\%) | 19 (4.4\%) |  |
| Marital status |  |  |  |  | 0.044 |
| Married | 88 (49.2\%) | 82 (48.2\%) | 180 (56.6\%) | 250 (58.5\%) |  |
| Unmarried | 91 (50.8\%) | 88 (51.8\%) | 138 (43.4\%) | 177 (41.5\%) |  |
| T stage |  |  |  |  | 0.013 |
| T0 | 4 (2.2\%) | 1 (0.6\%) | 7 (2.2\%) | 7 (1.6\%) |  |
| T1 | 27 (15.1\%) | 46 (27.1\%) | 48 (15.1\%) | 55 (12.9\%) |  |
| T2 | 54 (30.2\%) | 39 (22.9\%) | 74 (23.3\%) | 103 (24.1\%) |  |
| T3 | 36 (20.1\%) | 38 (22.4\%) | 82 (25.8\%) | 113 (26.5\%) |  |
| T4 | 58 (32.4\%) | 46 (27.1\%) | 107 (33.6\%) | 149 (34.9\%) |  |
| N stage |  |  |  |  | 0.030 |
| N0 | 48 (26.8\%) | 49 (28.8\%) | 57 (17.9\%) | 99 (23.2\%) |  |
| N1 | 21 (11.7\%) | 17 (10\%) | 27 (8.5\%) | 42 (9.8\%) |  |


| N2 | 77 (43\%) | 77 (45.3\%) | 152 (47.8\%) | 175 (41\%) |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
| N3 | 33 (18.4\%) | 27 (15.9\%) | 82 (25.8\%) | 111 (26\%) |  |
| Laterality |  |  |  |  | 0.582 |
| Left | 70 (39.1\%) | 63 (37.1\%) | 126 (39.6\%) | 172 (40.3\%) |  |
| Right | 99 (55.3\%) | 104 (61.2\%) | 181 (56.9\%) | 237 (55.5\%) |  |
| Others | 10 (5.6\%) | 3 (1.8\%) | 11 (3.5\%) | 18 (4.2\%) |  |
| Primary site |  |  |  |  | 0.042 |
| Main bronchus | 17 (9.5\%) | 9 (5.3\%) | 27 (8.5\%) | 33 (7.7\%) |  |
| Upper lobe | 70 (39.1\%) | 98 (57.6\%) | 157 (49.4\%) | 219 (51.3\%) |  |
| Middle lobe | 12 (6.7\%) | 5 (2.9\%) | 12 (3.8\%) | 19 (4.4\%) |  |
| Lower lobe | 50 (27.9\%) | 47 (27.6\%) | 83 (26.1\%) | 98 (23\%) |  |
| Others | 30 (16.8\%) | 11 (6.5\%) | 39 (12.3\%) | 58 (13.6\%) |  |
| Brain Metastasis |  |  |  |  | $<0.001$ |
| Yes | 37 (20.7\%) | 117 (68.8\%) | 29 (9.1\%) | 237 (55.5\%) |  |
| No | 142 (79.3\%) | 53 (31.2\%) | 289 (90.9\%) | 190 (44.5\%) |  |
| Bone Metastasis |  |  |  |  | 0.667 |
| Yes | 56 (31.3\%) | 64 (37.6\%) | 110 (34.6\%) | 147 (34.4\%) |  |
| No | 123 (68.7\%) | 106 (62.4\%) | 208 (65.4\%) | 280 (65.6\%) |  |
| Liver Metastasis |  |  |  |  | $<0.001$ |
| Yes | 60 (33.5\%) | 42 (24.7\%) | 145 (45.6\%) | 106 (24.8\%) |  |
| No | 119 (66.5\%) | 128 (75.3\%) | 173 (54.4\%) | 321 (75.2\%) |  |
| Lung Metastasis |  |  |  |  | $<0.001$ |
| Yes | 48 (26.8\%) | 29 (17.1\%) | 93 (29.2\%) | 77 (18\%) |  |
| No | 131 (73.2\%) | 141 (82.9\%) | 225 (70.8\%) | 350 (82\%) |  |

Abbreviations: LCNEC: large cell neuroendocrine carcinoma.

5 Table S2. The baseline characteristics of different treatment modalities in IV SCLC

| Variable | Control ( $\mathrm{n}=2979$ ) | Radiotherapy ( $\mathrm{n}=1291$ ) | Chemotherapy( $\mathrm{n}=8242$ ) | Chemoradiotherapy(n=8427) | p -value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Age |  |  |  |  | $<0.001$ |
| $<65$ | 2264 (76\%) | 899 (69.6\%) | 5163 (62.6\%) | 4338 (51.5\%) |  |
| $\geq 65$ | 715 (24\%) | 392 (30.4\%) | 3079 (37.4\%) | 4089 (48.5\%) |  |
| Gender |  |  |  |  | $<0.001$ |
| Male | 1457 (48.9\%) | 626 (48.5\%) | 4349 (52.8\%) | 4267 (50.6\%) |  |
| Female | 1522 (51.1\%) | 665 (51.5\%) | 3893 (47.2\%) | 4160 (49.4\%) |  |
| Race |  |  |  |  | 0.005 |
| Black | 259 (8.7\%) | 139 (10.8\%) | 665 (8.1\%) | 797 (9.5\%) |  |
| White | 2578 (86.5\%) | 1095 (84.8\%) | 7235 (87.8\%) | 7272 (86.3\%) |  |
| Others | 142 (4.8\%) | 57 (4.4\%) | 342 (4.1\%) | 358 (4.2\%) |  |
| Marital status |  |  |  |  | $<0.001$ |
| Married | 1271 (42.7\%) | 574 (44.5\%) | 4268 (51.8\%) | 4659 (55.3\%) |  |
| Unmarried | 1708 (57.3\%) | 717 (55.5\%) | 3974 (48.2\%) | 3768 (44.7\%) |  |
| T stage |  |  |  |  | $<0.001$ |
| T0 | 46 (1.5\%) | 21 (1.6\%) | 119 (1.4\%) | 102 (1.2\%) |  |
| T1 | 337 (11.3\%) | 193 (14.9\%) | 866 (10.5\%) | 872 (10.3\%) |  |
| T2 | 735 (24.7\%) | 320 (24.8\%) | 1955 (23.7\%) | 1894 (22.5\%) |  |
| T3 | 684 (23\%) | 262 (20.3\%) | 1830 (22.2\%) | 1823 (21.6\%) |  |
| T4 | 1177 (39.5\%) | 495 (38.3\%) | 3472 (42.1\%) | 3736 (44.3\%) |  |
| N stage |  |  |  |  | $<0.001$ |
| N0 | 539 (18.1\%) | 239 (18.5\%) | 870 (10.6\%) | 961 (11.4\%) |  |
| N1 | 1590 (53.4\%) | 646 (50\%) | 4492 (54.5\%) | 4520 (53.6\%) |  |
| N2 | 208 (7\%) | 128 (9.9\%) | 528 (6.4\%) | 540 (6.4\%) |  |
| N3 | 642 (21.6\%) | 278 (21.5\%) | 2352 (28.5\%) | 2406 (28.6\%) |  |


| Laterality |  |  |  |  | 0.101 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Left | 1280 (43\%) | 513 (39.7\%) | 3424 (41.5\%) | 3460 (41.1\%) |  |
| Right | 1572 (52.8\%) | 725 (56.2\%) | 4478 (54.3\%) | 4665 (55.4\%) |  |
| Others | 127 (4.3\%) | 53 (4.1\%) | 340 (4.1\%) | 302 (3.6\%) |  |
| Primary site |  |  |  |  | $<0.001$ |
| Main bronchus | 316 (10.6\%) | 137 (10.6\%) | 980 (11.9\%) | 1100 (13.1\%) |  |
| Upper lobe | 1364 (45.8\%) | 646 (50\%) | 3815 (46.3\%) | 4234 (50.2\%) |  |
| Middle lobe | 114 (3.8\%) | 40 (3.1\%) | 332 (4\%) | 308 (3.7\%) |  |
| Lower lobe | 711 (23.9\%) | 282 (21.8\%) | 1821 (22.1\%) | 1635 (19.4\%) |  |
| Others | 474 (15.9\%) | 186 (14.4\%) | 1294 (15.7\%) | 1150 (13.6\%) |  |
| Brain Metastasis |  |  |  |  | $<0.001$ |
| Yes | 467 (15.7\%) | 768 (59.5\%) | 804 (9.8\%) | 3500 (41.5\%) |  |
| No | 2512 (84.3\%) | 523 (40.5\%) | 7438 (90.2\%) | 4927 (58.5\%) |  |
| Bone Metastasis |  |  |  |  | $<0.001$ |
| Yes | 893 (30\%) | 446 (34.5\%) | 3269 (39.7\%) | 3038 (36.1\%) |  |
| No | 2086 (70\%) | 845 (65.5\%) | 4973 (60.3\%) | 5389 (63.9\%) |  |
| Liver Metastasis |  |  |  |  | $<0.001$ |
| Yes | 1296 (43.5\%) | 383 (29.7\%) | 4402 (53.4\%) | 2714 (32.2\%) |  |
| No | 1683 (56.5\%) | 908 (70.3\%) | 3840 (46.6\%) | 5713 (67.8\%) |  |
| Lung Metastasis |  |  |  |  | $<0.001$ |
| Yes | 705 (23.7\%) | 231 (17.9\%) | 1865 (22.6\%) | 1534 (18.2\%) |  |
| No | 2274 (76.3\%) | 1060 (82.1\%) | 6377 (77.4\%) | 6893 (81.8\%) |  |

6 Abbreviations: SCLC: small cell lung cancer.

