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## Supplementary methods

Propensity score-matched analysis was performed to compare overall survival (OS) between stereotactic radiosurgery (SRS) and whole brain radiation therapy (WBRT). Time to brain metastasis (BM) diagnosis, age at small cell lung cancer (SCLC) diagnosis, disease stage, and receipt of chemotherapy were used for matching. Propensity matching was conducted in R using the MatchIt package and 1:1 neighbourhood matching without replacement.[1] General patient characteristics were calculated and compared before and after matching using the chi-square and Wilcoxon rank sum tests for categorical and continuous variables, respectively. Cox-proportional hazard regression models were used to assess differences between Kaplan-Meier survival curves in the propensity score-matched cohort.

## Supplementary results

Baseline characteristics of patients who received chemotherapy are shown in Table S2. Median OS among the 5552 patients who received chemotherapy was 10.64 months (95% CI, 10.32-10.91), with 6, 12, and 18-month survival estimates of 74.8 % (95% CI, 73.7-65.9%), 44.0% (95% CI, 42.7-45.3%), and 28.0% (95% CI, 26.8%-29.2%). Sex, age, disease stage, and receipt of prophylactic cranial irradiation (PCI) were significant prognostic factors for OS in univariable and multivariable analysis (Table S3).

Treatment of brain metastases among patients who did not receive prophylactic cranial irradiation
Among patients who presented with synchronous BM (n=1175) median OS from SCLC diagnosis was 9.61 months (95% CI, 3.42-27.43), 6.44 months (95% CI, 5.91-7.00), 95% CI, and 1.54 months (95% CI, 1.35-1.87) for patients who received SRS (n=22), WBRT (n=829), or no treatment (n=324) for their BM. Median OS from BM diagnosis was non-inferior between SRS and WBRT (4.88 months, 95% CI, 1.45-27.43, vs. 5.06 months, 95% CI, 4.34-5.59; HR, 0.66, 95% CI, 0.42-1.04, p=0.07), and in favour of SRS compared with no treatment (0.99 months, 95% CI, 0.79-1.28; HR, 0.24, 95% CI, 0.16-0.38, p<0.001). This remained unchanged in multivariable analysis (SRS vs WBRT: HR 0.69, 95% CI, 0.44-1.10, p=0.12; SRS vs no treatment: HR 0.29, 95% CI, 0.18-0.46, p<0.001).

1050 patients developed asynchronous BM and did not receive PCI. Median OS from time of SCLC diagnosis was 23.20 months (95% CI, 18.5-32.4), 11.70 months (95% CI, 11.17-12.60), and 10.0 months (95% CI, 9.23-10.60) for patients who received SRS (n=23), WBRT (n=571), or no treatment for their BM (n=329). Median OS from BM diagnosis was similar between SRS and WBRT (4.73 months, 95% CI, 3.12-10.84, vs. 2.60 months, 95% CI, 2.30-2.89; HR, 0.74, 95% CI, 0.49-1.12, p=0.15), and in favour of SRS compared with no treatment (0.79 months, 95% CI, 0.53-0.99; HR, 0.41, 95% CI, 0.27-0.63, p<0.001). This remained unchanged in multivariable analysis (SRS vs WBRT: HR 0.81, 95% CI, 0.58-1.35, p=0.58; SRS vs no treatment: HR 0.48, 95% CI, 0.31-0.73, p<0.001).

We performed a second propensity score-matched analysis using age, disease stage, and receipt of chemotherapy to calculate propensity scores to avoid confounding of post-indexing events (i.e. time to diagnosis of BM). Characteristics of this cohort are shown in Table S7. Median OS from time of SCLC diagnosis was 18.0 months (95% CI, 11.73-24.6) for patients who received SRS and 10.7 months (95% CI, 8.61-11.9; HR, 0.41, 95% CI, 0.26-0.67, p<0.001) for patients who received WBRT. Median OS from time of BM diagnosis was longer for patients who received SRS (4.73 months, 95% CI, 2.52-9.43) compared with WBRT (3.32 months, 95% CI, 1.81-7.39; HR, 0.58, 95% CI, 0.37-0.93, p=0.021; Figure S2).

Patients who received PCI
Propensity score matching for age and disease stage identified 112 well-balanced patients treated with SRS (n=56) and WBRT (n=56, Table S11). Median OS from time of SCLC diagnosis was 25.0 months (95% CI, 23.9-28.80) for patients who received SRS and 22.10 months (95% CI, 20.0-26.2; HR, 0.64, 95% CI, 0.44-0.93, p=0.02) for patients who received WBRT. Median OS from time of BM diagnosis in the matched cohort was longer in patients who received salvage SRS (5.19 months, 95% CI, 3.02-8.71) compared with salvage WBRT (2.63 months, 95% CI, 1.84-4.47; HR, 0.53, 95% CI, 0.35-0.79, p=0.001; Figure S2).

**Table S1. Use of intracranial imaging at the time of diagnosis by year of diagnosis.**

|  | Diagnosis before 2011 (n=2919) | Diagnosis before 2011 (n=5768) | Overall |
|---|---|---|---|
| CT (n=6116) | 2259 (77.39%) | 3857 (66.87%) | 6116 |
| MRI (n=1823) | 342 (11.72%) | 1481 (25.68%) | 1823 |
| NA | 318 (10.89%) | 448 (7.77%) | 766 |

CT, computed tomography; MRI, magnetic resonance imaging; NA, not applicable

**Table S2. Baseline characteristics of patients who received chemotherapy stratified by disease stage.**

| Characteristic | Total, n = 5552 | ED, n = 3402 | LD, n = 1970 | Missing, n = 180 | P-value |
|---|---|---|---|---|---|
| Sex | | | | | <0.001 |
| F | 2779 (50%) | 1596 (47%) | 1101 (56%) | 82 (46%) | |
| M | 2773 (50%) | 1806 (53%) | 869 (44%) | 98 (54%) | |
| Age at SCLC diagnosis (years) | 66.00 (60.00, 72.00) | 66.00 (60.00, 72.00) | 66.00 (60.00, 73.00) | 67.00 (59.75, 73.00) | 0.3 |
| Diagnosis year | | | | | <0.001 |
| Before 2011 | 1592 (29%) | 885 (26%) | 610 (31%) | 97 (54%) | |
| After 2011 | 3960 (71%) | 2517 (74%) | 1360 (69%) | 83 (46%) | |
| ACG comorbidity categorization | | | | | <0.001 |
| Low | 1314 (24%) | 880 (26%) | 399 (20%) | 35 (19%) | |
| Moderate | 2248 (40%) | 1389 (41%) | 790 (40%) | 69 (38%) | |
| High | 1990 (36%) | 1133 (33%) | 781 (40%) | 76 (42%) | |
| ECOG PS | | | | | |
| 0 | 188 (17%) | SC | SC | SC | |
| 1 | 516 (47%) | SC | SC | SC | |
| 2 | 263 (24%) | SC | SC | SC | |
| 3 | 129 (12%) | SC | SC | SC | |
| ≥4 | 9 (<1%) | SC | SC | SC | |
| Unknown | 4447 | 2733 | 1552 | 162 | |
| Time to first brain imaging (days) | 14.00 (4.00, 29.00) | 11.00 (3.00, 26.00) | 17.00 (6.00, 33.00) | 23.00 (9.50, 48.50) | <0.001 |
| Unknown | 147 | 114 | 24 | 9 | |
| Imaging modality at first brain imaging | | | | | 0.004 |
| CT | 3929 (73%) | 2433 (74%) | 1364 (70%) | 132 (77%) | |
| MRI | 1476 (27%) | 855 (26%) | 582 (30%) | 39 (23%) | |
| Unknown | 147 | 114 | 24 | 9 | |
| Brain imaging at diagnosis | | | | | <0.001 |
| Yes | 4520 (84%) | 2822 (86%) | 1574 (81%) | 124 (73%) | |
| No | 885 (16%) | 466 (14%) | 372 (19%) | 47 (27%) | |
| Unknown | 147 | 114 | 24 | 9 | |
| Median time between follow-up brain imaging (days) | 105.00 (69.50, 161.50) | 95.50 (63.00, 143.25) | 123.00 (82.50, 196.00) | 117.00 (75.50, 203.62) | <0.001 |
| Unknown | 1336 | 971 | 317 | 48 | |
| Number of follow-up brain images | 3.00 (2.00, 4.00) | 2.00 (1.00, 4.00) | 3.00 (2.00, 5.00) | 3.00 (2.00, 5.00) | <0.001 |
| Unknown | 147 | 114 | 24 | 9 | |
| Receipt of PCI | | | | | <0.001 |
| Yes | 1758 (32%) | 755 (22%) | 950 (48%) | 53 (29%) | |
| No | 3794 (68%) | 2647 (78%) | 1020 (52%) | 127 (71%) | |
| BM diagnosis | | | | | <0.001 |
| Asynchronous | 1285 (23%) | 730 (21%) | 512 (26%) | 43 (24%) | |
| Synchronous | 697 (13%) | 689 (20%) | 0 (0%) | 8 (4.4%) | |

| | | | | | |
|---|---|---|---|---|---|
| No record of BM diagnosis | 3570 (64%) | 1983 (58%) | 1458 (74%) | 129 (72%) | |
| Age at BM diagnosis (years) | 66.00 (59.00, 72.00) | 66.00 (59.00, 71.00) | 66.00 (59.00, 73.00) | 66.00 (59.00, 70.00) | 0.3 |
| NA | 3570 | 1983 | 1458 | 129 | |
| Time to BM diagnosis (months) | 8.77 (3.48, 16.92) | 6.37 (1.61, 10.97) | 15.57 (8.77, 35.97) | 10.78 (5.68, 27.41) | <0.001 |

Values are displayed as median (IQR) or n (%). Between-group comparisons were made using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables. SC: values between 1 and 5, or complementary values that can be used to back-calculate small cells, redacted according to administrative privacy regulations due to re-identification risk.

BM, brain metastasis; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; ED, extensive stage disease; LD, limited stage disease; MRI, magnetic resonance imaging; NA, not applicable; SC, small cell; SCLC, small cell lung cancer

**Table S3. Univariable and multivariable analysis of overall survival in patients who received chemotherapy with complete data on covariates (n=4983).**

| Variable | No. total | No. events | Median OS | Univariable analysis HR | Multivariable analysis HR |
|---|---|---|---|---|---|
| Sex | | | | | |
| Female | 2779 | 2545 | 11.76 (95% CI, 11.37-12.22) | 1.25 (95% CI, 1.18-1.32), p<0.001 | 1.19 (95% CI, 1.13-1.26), p<0.001 |
| Male | 2773 | 2606 | 9.63 (95% CI, 9.33-9.92) | | |
| Age | | | | | |
| <65 years | 2372 | 2161 | 11.53 (95% CI, 11.04-11.96) | 0.85 (95% CI, 0.81-0.9), p<0.001 | 0.85 (95% CI, 0.80-0.89), p<0.001 |
| ≥65 years | 3180 | 2990 | 9.92 (95% CI, 9.63-10.32) | | |
| Year of diagnosis | | | | | |
| Before 2011 | 1592 | 1525 | 10.84 (95% CI, 10.22-11.37) | 1.01 (95% CI, 0.95-1.07), p>0.5 | NS |
| After 2011 | 3960 | 3626 | 10.51 (95% CI, 10.22-10.87) | | |
| Disease stage | | | | | |
| LD | 1970 | 1672 | 17.81 (95% CI, 17.15-18.89) | 0.39 (95% CI, 0.37-0.42), p<0.001 | 0.41 (95% CI, 0.43-0.48), p<0.001 |
| ED | 5664 | 5558 | 5.26 (95% CI, 4.9-5.55) | | |
| ACG comorbidity index | | | | | |
| Low | 1314 | 1228 | 10.58 (95% CI, 9.99-11.17) | 0.99 (95% CI, 0.94-1.05), p>0.5 | NS |
| Moderate | 2248 | 2077 | 10.94 (95% CI, 10.41-11.4) | 0.92 (95% CI, 0.88-0.97), p=0.001 | |
| High | 1990 | 1846 | 10.32 (95% CI, 9.92-10.81) | Ref. | |
| Receipt of PCI | | | | | |
| Yes | 1758 | 1541 | 8.94 (95% CI, 1.12-22.47) | 0.66 (95% CI, 0.62-0.71), p<0.001 | 0.77 (95% CI, 0.72-0.82), p<0.001 |
| No | 3794 | 3610 | 9.66 (95% CI, 9.43-9.92) | | |

Multivariable Cox proportional hazards regression analyzes were performed adjusting for variables significant in univariable analysis.

95% CI, 95% confidence interval; ACG, Adjusted Clinical Groups; HR, hazard ratio; NS, not significant; OS, overall survival; PCI, prophylactic cranial irradiation

**Figure S1. Cumulative incidence of brain metastases stratified by disease stage.**
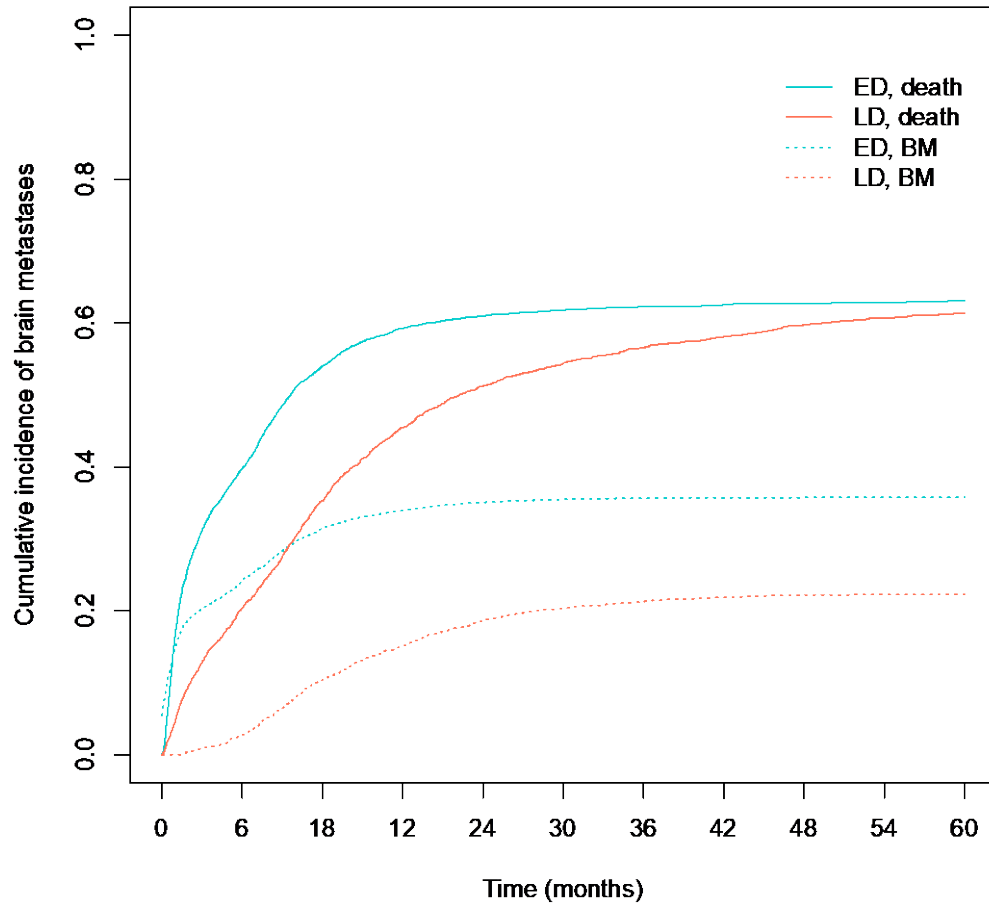


BM, brain metastases; ED, extensive stage disease; LD, limited stage disease

**Table S4. Baseline characteristics of patients who were diagnosed with brain metastases and did not receive prophylactic cranial irradiation stratified by type of intracranial treatment modality.**

| Characteristic | Overall, n = 2225 | SRS, n = 45 | WBRT, n = 1527 | None, n = 653 | P-value |
|---|---|---|---|---|---|
| Sex | | | | | 0.2 |
| F | 1034 (49%) | 25 (56%) | 723 (47%) | 338 (52%) | |
| M | 1064 (51%) | 20 (44%) | 804 (53%) | 315 (48%) | |
| Age at SCLC diagnosis (years) | 66.00 (59.00, 72.00) | 64.00 (57.00, 72.00) | 65.00 (58.00, 71.00) | 68.00 (60.00, 74.00) | <0.001 |
| Diagnosis year | | | | | <0.001 |
| Before 2011 | 625 (30%) | 0 (0%) | 1007 (66%) | 161 (25%) | |
| After 2011 | 1473 (70%) | 45 (100%) | 520 (34%) | 492 (75%) | |
| ACG comorbidity categorization | | | | | 0.11 |
| Low | 624 (28%) | 9 (20%) | 413 (30%) | 446 (29%) | |
| Moderate | 867 (39%) | 22 (49%) | 548 (39%) | 597 (39%) | |
| High | 734 (33%) | 14 (31%) | 439 (31%) | 484 (32%) | |
| SCLC stage | | | | | <0.001 |
| LD | 298 (15%) | 15 (35%) | 215 (15%) | 105 (17%) | |
| ED | 1725 (85%) | 28 (65%) | 1265 (85%) | 520 (83%) | |
| Unknown | 75 | 2 | 47 | 28 | |
| ECOG PS | | | | | 0.13 |
| 0 | 58 (17%) | SC | SC | SC | |
| 1 | 154 (45%) | SC | SC | SC | |
| 2 | 75 (22%) | SC | SC | SC | |
| 3 | 51 (15%) | SC | SC | SC | |
| ≥4 | SC | SC | SC | SC | |
| Unknown | 1,883 | 39 | 1,256 | 588 | |
| Time to first brain imaging (days) | 9.00 (1.50, 25.00) | 10.00 (4.00, 26.00) | 9.00 (1.00, 24.00) | 8.00 (2.00, 27.00) | 0.13 |
| Unknown | 10 | SC | SC | SC | |
| Imaging modality at first brain imaging | | | | | <0.001 |
| CT | 1698 (77%) | SC | SC | SC | |
| MRI | 517 (23%) | SC | SC | SC | |
| Unknown | 10 | 0 | SC | 8 | |
| Brain imaging at diagnosis | | | | | 0.5 |
| No | 313 (14%) | SC | SC | SC | |
| Yes | 1902 (86%) | SC | SC | SC | |
| Unknown | 10 | SC | SC | SC | |
| Receipt of chemotherapy | | | | | <0.001 |
| Yes | 704 (32%) | 7 (16%) | 424 (28%) | 273 (42%) | |
| No | 1521 (68%) | 38 (84%) | 1103 (72%) | 380 (58%) | |
| BM diagnosis | | | | | <0.001 |

| | | | | | |
|---|---|---|---|---|---|
| Asynchronous | 1050 (47%) | 23 (51%) | 698 (46%) | 329 (50%) | |
| Synchronous | 1175 (56%) | 22 (49%) | 829 (59%) | 324 (50%) | |
| Age at BM diagnosis (years) | 67.00 (60.00, 73.00) | 66.00 (59.00, 74.00) | 66.00 (59.00, 72.00) | 69.00 (61.00, 75.00) | <0.001 |
| Time to BM diagnosis (months) | 2.10 (0.33, 8.08) | 10.71 (0.95, 17.18) | 2.10 (0.33, 7.89) | 1.87 (0.33, 8.35) | <0.001 |

Values are displayed as median (IQR) or n (%). Between-group comparisons were made using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables. SC: values between 1 and 5, or complementary values that can be used to back-calculate small cells, redacted according to administrative privacy regulations due to re-identification risk.

BM, brain metastasis; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; ED, extensive stage disease; LD, limited stage disease; MRI, magnetic resonance imaging; NA, not applicable; SC, small cell; SCLC, small cell lung cancer

**Table S5. Univariable and multivariable analysis of overall survival from brain metastasis diagnosis by type of intracranial treatment modality among patients who developed brain metastases and did not receive prophylactic cranial irradiation.**

| BM Treatment modality | Median OS from BM diagnosis (months) | Univariable analysis HR | Multivariable analysis HR |
|---|---|---|---|
| Overall (n=2225) | 2.50 (95% CI, 2.33-2.69) | NA | NA |
| SRS (n=45) | 4.73 (95% CI, 2.66-9.43) | Ref. | Ref. |
| WBRT (n=1527) | 3.55 (95% CI, 3.29-3.84) | 0.74 (95% CI, 0.54-1.01), p=0.054 | 0.83 (95% CI, 0.61-1.14), p=0.253 |
| None (n=563) | 0.85 (95% CI, 0.76-1.02) | 0.34 (95% CI, 0.25-0.47), p<0.001 | 0.39 (95% CI, 0.28-0.54), p<0.001 |

Multivariable Cox proportional hazards regression analyzes were performed adjusting for variables significant in univariable analysis.

95% CI, 95% confidence interval; BM, brain metastasis; HR, hazard ratio; NA, not applicable; OS, overall survival; Ref., reference value; SRS, stereotactic radiosurgery; WBRT, whole brain radiation therapy

**Table S6. Baseline characteristics of propensity score-matched cohort for overall survival analysis of patients who did not receive prophylactic cranial irradiation. Propensity score matching was performed on the basis of stage, diagnosis age, receipt of chemotherapy, and time to development of brain metastases.**

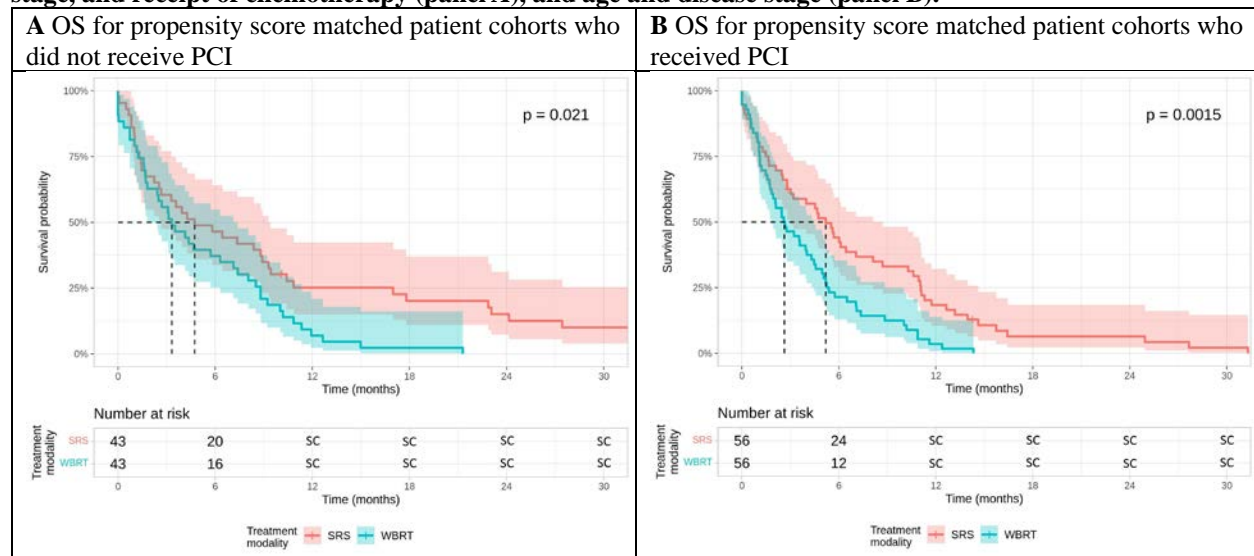| Characteristic | Overall, n = 86 | WBRT, n = 43 | SRS, n = 43 | P-value |
|---|---|---|---|---|
| Sex | | | | 0.13 |
| F | 43 (50%) | 18 (42%) | 25 (58%) | |
| M | 43 (50%) | 25 (58%) | 18 (42%) | |
| Age at SCLC diagnosis (years) | 64.00 (57.50, 74.75) | 65.00 (60.00, 76.00) | 64.00 (57.00, 72.50) | 0.50 |
| SCLC stage | | | | 0.40 |
| LD | 34 (40%) | 19 (44%) | 15 (35%) | |
| ED | 52 (60%) | 24 (56%) | 28 (65%) | |
| Receipt of chemotherapy | | | | 0.30 |
| Yes | 68 (79%) | 32 (74%) | 36 (84%) | |
| No | 18 (21%) | 11 (26%) | 7 (16%) | |
| Time to BM diagnosis | 223.50 (23.50, 495.00) | 201.00 (25.00, 487.00) | 248.00 (19.00, 499.00) | 0.70 |
| Time to radiation therapy (months) | 164.50 (32.25, 382.00) | 113.00 (24.00, 372.50) | 225.00 (38.50, 389.50) | 0.40 |

Values are displayed as median (IQR) or n (%). Between-group comparisons were made using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

**Table S7. Baseline characteristics of propensity score-matched cohort for overall survival analysis of patients who did not receive prophylactic cranial irradiation. Propensity score matching was performed on the basis of stage, diagnosis age, and receipt of chemotherapy.**

| Characteristic | Overall, n = 86 | WBRT, n = 43 | SRS, n = 43 | P-value |
|---|---|---|---|---|
| Sex | | | | 0.13 |
| F | 43 (50%) | 18 (42%) | 25 (58%) | |
| M | 43 (50%) | 25 (58%) | 18 (42%) | |
| Age at SCLC diagnosis (years) | 64.00 (57.00, 72.75) | 64.00 (57.00, 72.50) | 64.00 (57.00, 72.50) | >0.9 |
| SCLC stage | | | | >0.9 |
| LD | 56 (65%) | 28 (65%) | 28 (65%) | |
| ED | 30 (35%) | 15 (35%) | 15 (35%) | |
| Receipt of chemotherapy | | | | >0.9 |
| Yes | 14 (16%) | 7 (16%) | 7 (16%) | |
| No | 72 (84%) | 36 (84%) | 36 (84%) | |
| Time to BM diagnosis | 177.50 (33.00, 427.75) | 134.00 (38.00, 265.00) | 248.00 (19.00, 499.00) | 0.30 |
| Time to radiation therapy (months) | 142.00 (33.25, 285.50) | 89.00 (27.00, 253.00) | 225.00 (38.50, 389.50) | 0.15 |

Values are displayed as median (IQR) or n (%). Between-group comparisons were made using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

**Figure S2. Median overall survival from time of brain metastasis diagnosis among propensity score matched cohorts of patients who did not (panel A) and did (panel B) receive prophylactic cranial irradiation stratified by intracranial treatment modality for total. Propensity scores were calculated on the basis of age, disease stage, and receipt of chemotherapy (panel A), and age and disease stage (panel B).**

| A OS for propensity score matched patient cohorts who did not receive PCI | B OS for propensity score matched patient cohorts who received PCI |
|---|---|
|  |  |

Kaplan-Meier methods were used to analyze overall survival in months from time of BM diagnosis. Cox-proportional hazard regression models were used to assess differences between Kaplan-Meier survival curves. SC: values between 1 and 5, or complementary values that can be used to back-calculate small cells, redacted according to administrative privacy regulations due to re-identification risk.

OS, overall survival; PCI, prophylactic cranial irradiation; SC, small cell; SRS, stereotactic radiosurgery; WBRT, whole brain radiation therapy

**Table S8. Baseline characteristics of patients who were diagnosed with brain metastases and did not receive prophylactic cranial irradiation stratified by type of intracranial treatment modality.**

| Characteristic | Overall, n = 461 | SRS, n = 57 | WBRT, n = 127 | None, n = 227 | P-value |
|---|---|---|---|---|---|
| Sex | | | | | 0.3 |
| F | 241 (52%) | 24 (42%) | 68 (54%) | 149 (54%) | |
| M | 220 (48%) | 33 (58%) | 59 (46%) | 128 (46%) | |
| Age at SCLC diagnosis (years) | 63.00 (56.00, 68.00) | 61.00 (54.00, 65.00) | 62.00 (54.00, 66.50) | 64.00 (58.00, 70.00) | <0.001 |
| Diagnosis year | | | | | <0.001 |
| Before 2011 | 153 (33%) | 9 (16%) | 56 (44%) | 88 (32%) | |
| After 2011 | 308 (67%) | 48 (84%) | 71 (56%) | 189 (68%) | |
| ACG comorbidity categorization | | | | | 0.025 |
| Low | 121 (26%) | 13 (23%) | 45 (35%) | 63 (23%) | |
| Moderate | 206 (45%) | 24 (42%) | 57 (45%) | 125 (45%) | |
| High | 134 (29%) | 20 (35%) | 25 (20%) | 89 (32%) | |
| SCLC stage | | | | | <0.001 |
| LD | 208 (45%) | 21 (37%) | 49 (39%) | 138 (50%) | |
| ED | 243 (53%) | 35 (61%) | 72 (57%) | 136 (49%) | |
| Unknown | 10 | SC | 6 | SC | |
| ECOG PS | | | | | >0.5 |
| 0 | 28 (22%) | SC | SC | SC | |
| 1 | 66 (53%) | SC | SC | SC | |
| 2 | 26 (21%) | SC | SC | SC | |
| ≥3 | SC | SC | SC | SC | |
| Unknown | 1,883 | 39 | 1,256 | 588 | |
| Time to first brain imaging (days) | 15.00 (6.00, 31.00) | 14.00 (6.00, 27.00) | 17.00 (6.00, 36.50) | 15.00 (5.00, 31.00) | 0.5 |
| Unknown | SC | 0 | 0 | SC | |
| Imaging modality at first brain imaging | | | | | 0.3 |
| CT | 307 (67%) | SC | SC | SC | |
| MRI | 153 (33%) | SC | SC | SC | |
| Unknown | SC | SC | SC | SC | |
| Brain imaging at diagnosis | | | | | 0.3 |
| No | SC | SC | SC | SC | |
| Yes | SC | SC | SC | SC | |
| Unknown | SC | SC | SC | SC | |
| Age at BM diagnosis (years) | 65.00 (58.00, 70.00) | 63.00 (57.00, 68.00) | 64.00 (56.50, 69.00) | 66.00 (60.00, 73.00) | <0.001 |
| Time to BM diagnosis (months) | 14.92 (10.58, 22.57) | 19.32 (13.54, 24.08) | 18.10 (13.86, 23.23) | 12.55 (9.46, 19.81) | <0.001 |

Values are displayed as median (IQR) or n (%). Between-group comparisons were made using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables. SC: values between 1 and 5, or complementary values that can be used to back-calculate small cells, redacted according to administrative privacy regulations due to re-identification risk.

BM, brain metastasis; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; ED, extensive stage disease; LD, limited stage disease; MRI, magnetic resonance imaging; NA, not applicable; SC, small cell; SCLC, small cell lung cancer

**Table S9. Univariable and multivariable analysis of overall survival from brain metastasis diagnosis by type of intracranial treatment modality among patients who developed brain metastases and received prophylactic cranial irradiation.**

| BM Treatment modality | Median OS from BM diagnosis (months) | Univariable analysis HR | Multivariable analysis HR |
|---|---|---|---|
| Overall (n=461) | 1.97 (95% CI, 1.68-2.37) | NA | NA |
| SRS (n=57) | 5.19 (95% CI, 3.02-8.12) | Ref. | Ref. |
| WBRT (n=127) | 2.20 (95% CI, 1.84-3.22) | 0.65 (95% CI, 0.47-0.89), p=0.007 | 0.64 (95% CI, 0.46-0.88), p=0.006 |
| None (n=277) | 1.58 (95% CI, 1.31-1.97) | 0.61 (95% CI, 0.46-0.82), p<0.001 | 0.61 (95% CI, 0.45-0.82), p=0.001 |

Multivariable Cox proportional hazards regression analyzes were performed adjusting for variables significant in univariable analysis.

95% CI, 95% confidence interval; BM, brain metastasis; HR, hazard ratio; NA, not applicable; OS, overall survival; Ref., reference value; SRS, stereotactic radiosurgery; WBRT, whole brain radiation therapy

**Table S10. Baseline characteristics of propensity score-matched cohort for overall survival analysis of patients who received prophylactic cranial irradiation and developed brain metastases. Propensity score matching was performed on the basis of stage, diagnosis age, and time to brain metastases.**

| Characteristic | Overall, n = 112 | WBRT, n = 56 | SRS, n = 56 | P-value |
|---|---|---|---|---|
| Sex | | | | 0.4 |
| F | 52 (46%) | 28 (50%) | 24 (43%) | |
| M | 60 (54%) | 28 (50%) | 32 (57%) | |
| Age at SCLC diagnosis (years) | 61.00 (55.00, 66.00) | 63.50 (55.00, 66.00) | 60.50 (54.00, 65.00) | 0.5 |
| SCLC stage | | | | 0.4 |
| LD | 46 (41%) | 25 (45%) | 21 (38%) | |
| ED | 66 (59%) | 31 (55%) | 35 (62%) | |
| Time to BM diagnosis | 558.00 (425.00, 785.00) | 540.50 (451.50, 797.50) | 590.00 (416.50, 741.75) | >0.9 |
| Time to radiation therapy (months) | 533.00 (371.25, 741.75) | 547.00 (395.50, 791.25) | 509.00 (360.75, 709.00) | 0.3 |

Values are displayed as median (IQR) or n (%). Between-group comparisons were made using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

**Table S11. Baseline characteristics of propensity score-matched cohort for overall survival analysis of patients who received prophylactic cranial irradiation and developed brain metastases. Propensity score matching was performed on the basis of stage and diagnosis age.**

| Characteristic | Overall, n = 112 | WBRT, n = 56 | SRS, n = 56 | P-value |
|---|---|---|---|---|
| Sex | | | | 0.13 |
| F | 56 (50%) | 32 (57%) | 24 (43%) | |
| M | 56 (50%) | 24 (43%) | 32 (57%) | |
| Age at SCLC diagnosis (years) | 61.50 (54.00, 67.00) | 62.00 (54.75, 67.00) | 60.50 (54.00, 65.00) | 0.5 |
| SCLC stage | | | | 0.7 |
| LD | 40 (36%) | 19 (34%) | 21 (38%) | |
| ED | 72 (64%) | 37 (66%) | 35 (62%) | |
| Time to BM diagnosis | 558.50 (411.75, 716.00) | 539.50 (404.00, 693.00) | 590.00 (416.50, 741.75) | 0.4 |
| Time to radiation therapy (months) | 17.76 (12.16, 23.04) | 18.04 (12.53, 22.97) | 16.72 (11.85, 23.29) | 0.6 |

Values are displayed as median (IQR) or n (%). Between-group comparisons were made using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

References

1.	Ho D, Imai K, King G, Stuart EA. MatchIt: Nonparametric Preprocessing for Parametric Causal Inference. *Journal of Statistical Software* 2011; **42**(8): 1 - 28.