

**Table S1** Search terms used in the Embase databases (search strings adapted for compatibility with other databases)

#	Search terms (Embase & Medline)
1	small cell lung cancer'/exp
2	small cell carcinoma'/exp
3	'sclc'
4	(pancoast* OR 'superior sulcus' OR 'pulmonary sulcus') NEXT/4 (tumo?r* OR syndrome*)
5	(small OR oat OR reserve OR round) NEXT/1 'cell' NEXT/1 (lung* OR pulmonary OR bronch*) NEXT/3 (cancer* OR neoplasm* OR carcinoma* OR tumo?r* OR lymphoma* OR metast* OR malignan* OR blastoma* OR carcinogen* OR adenocarcinoma* OR angiosarcoma* OR chondrosarcoma* OR sarcoma* OR teratoma* OR microcytic*)
6	1-5 (or)
7	Observational.tw
8	(retrospective NEXT/1 study).tw
9	(prospective NEXT/1 study).tw
10	(chart NEXT/1 review).tw
11	(expanded NEXT/1 access NEXT/1 program).tw
12	7-11 (OR)
13	6 AND 12
14	Humans/lim
15	EM 2000/01

\*truncated term - finds variant word endings e.g., child\* finds child, childhood, children

**Table S2** Treatments and outcomes reported in the included studies

Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
<b>Surgery</b>							
Ploenes <i>et al.</i>	2012	Germany	No. of patients = 29 Mean age, years = 62 (46–82) Gender (male) = 75.9%	Surgery = 100%	Surgery and CT [neoadjuvant] = 52% Surgery and CT [Adjuvant] = 48%	OS (median) = 89.4mo (surgery +neoadjuvant) 20.4mo (surgery)	Surgical resection could be beneficial in highly selected patients [cT1-2 cN0 cM0 disease] who can be completely resected. Adjuvant therapy is recommended following surgery
Ogawa <i>et al.</i>	2012	Japan	No. of patients = 15 Mean age, years = 64 (54–77) Gender (male) = 92%	Surgery = 32.7% Induction CT = 33% Adjuvant CT = 82%	Induction CT = 100% [PE] Adjuvant CT = 76.9% [PE] Other = 23.1%	OS (median) = 59.2mo	N/A
Zheng <i>et al.</i>	2013	China	No. of patients = 54 Mean age, years = 56 (32–76) Gender (male) = 72%	Surgery = 66.6% [Radical resection]; 33.3% [Non-radical resection] Pre-operative chemotherapy = 42.6%	N/A	OS (5yrs) = 73% [Radical resection and pre-op chemo]; 27% [Radical resection and no pre-op chemo]; 67% [Non-radical resection and pre-op chemo]; 67%[Non-radical resection and no pre-op chemo]	Pulmonary resection could improve survival for patients with early LS-SCLC. Systemic chemotherapy is recommended for all SCLC patients
Zhang <i>et al.</i>	2014	China	No. of patients = 153 Mean age, years = 56 (23–84) Gender (male) = 73.2%	Surgery = 32.7% CT = 100% RDT = 56% PCI = 50%	Surgery and CT = 78% [adjuvant] 22% [neoadjuvant]	OS (median) = 30.5mo (surgical) 16.5mo (non-surgical)	Pulmonary resection could improve the survival for I–IIIA stage SCLC. Systemic therapy is recommended for all patients with SCLC.
Bagshaw <i>et al.</i>	2019	USA	No. of patients = 59	Surgery = 100%	Stereotactic radiosurgery = 100%	OS (median) = 6.2mo	Patients with SCLC treated with SRS appear to have similar rates of local failure, distant failure, and neurologic death compared to historical controls of SRS for non-SCLC
Cifarelli <i>et al.</i>	2019	International	No. of patients = 232 Age (median) = 63 Gender (Male,%) = 50.5%	Surgery = 100%	Gamma knife radiosurgery = 100%	OS (1yr) = 28%; Local failure (1yr) = 31%; Distant brain failure (1yr) = 49%	SRS plays an important role in the management of brain metastases from SCLC, especially in salvage therapy following WBRT
<b>Chemotherapy/Chemoradiotherapy – Limited Stage</b>							
Scepanovic <i>et al.</i>	2010	Slovakia	No. of patients = 81 Median age, years = 57 Gender (male) = 80%	CCRT = 100%	CT [PE = 100%; Minimum = 4 cycles] RDT [44 Gy in 22 fractions = 50% ; 54–64 Gy in 27 to 32 fractions = 50%]	OS (1yr) = 98% (44Gy group), 100% (54-64 Gy group) PFS (1yr) = 42% (44Gy group), 65% (54-64 Gy group) OS (2yrs) = 5% (44Gy group), 53% (54-64 Gy group) PFS (2yrs) = 2% (44Gy group), 20% (54-64 Gy group)	Higher RDT doses resulted in improved time to progression and survival
Tada <i>et al.</i>	2010	Japan	No. of patients = 30 Gender (male) = 80%	CCRT = 100% PCI = 33.3%	CT [PE = 46%; PEI = 27%; PCE=17%; CE = 10%] RDT [45Gy in 30 fractions = 100%]	CR = 83% OS (2yrs) = 54% OS (5yrs) = 26%	N/A

**Table S2** (continued)

Table S2 (continued)

Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Dong <i>et al.</i>	2011	China	No. of patients = 166	CCRT = 29.5% SCRT = 37.3% CT = 33.2%	CT [CE/PE = 100%] RDT [Mean = 49.6 Gy]	ORR = 89.4% (CCRT), 67.2% (SCRT), 66% (CT) OS (median) = 29.7mo (CCRT), 22.6 mo (SCRT), 19.5 mo (CT) PFS (median) = 12.7mo (CCRT), 10.8mo (SCRT), 10.8mo (CT)	Chemoradiotherapy produce superior survival outcomes to CT alone. Similarly, CCRT results in increased survival vs SCRT
Hermes <i>et al.</i>	2011	Germany	No. of patients = 155 Median age, years = 63	CT= 100%	CT [CE = 100%]	Median OS = 18.7 mo (1–4 cycles) 18.5mo (5–6 cycles)	No. of cycles has limited impact on survival for patients with LS disease
Wzietek <i>et al.</i>	2011	Poland	No. of patients = 456	CCRT = 100% PCI = 37%	CT [PE = 100%] RDT dosing a) <45Gy b) 45Gy c) 45–54Gy d) >54Gy [No patient numbers provided ]	OS (1yrs) = 5% (<45Gy); 25% (45Gy), 12% (45–54Gy), 15% (>54Gy)	Higher dose TRT doses failed to show any survival advantage compared with standard doses (e.g. 45Gy)
Morimoto <i>et al.</i>	2014	Japan	No. of patients = 81	CCRT = 100%	CT [CE = 19% ; PE = 81%] RDT [45Gy in 30 fractions = 100%; Median overall treatment time = 24 days	N/A	N/A
Aynaci <i>et al.</i>	2016	Turkey	No. of patients = 129 Mean age, years = 60.1 Gender (male) = 96.9	CCRT = 8% SCRT = 76% PCI = 31.2%	CT [CE = 89%; CAV = 6.9] RDT [>50Gy = 50%]	OS (median) = 13.9mo DFS (median) = 18mo	CCRT and >50Gy provide an improved OS/DFS over SCRT
Matsuura <i>et al.</i>	2016	Japan	No. of patients = 19	CCRT = 100%	CT [CE or PE - no. of patients not stated] RDT [45 Gy in 30 fractions = 47.3%; 54 Gy in 36 fractions = 52.8%]	Median OS = 24 mo (45 Gy group), 41mo (54 Gy group) OS (3yrs) = 33.3% (45 Gy group), 60% (54 Gy group) PFS (3yrs) = 0% (45 Gy group), 40% (54 Gy group)	CCRT with 54 Gy results in slower time to progression and improved survival without increased toxicity, compared to 45 Gy
Chen <i>et al.</i>	2016	China	No. of patients = 177 Gender (male) = 87%	CCCT =100% CCRT = 100% Followed by consolidation CT = 40.6% PCI = 61.5%	CT (induction) [PE = 100%] RDT = 100%] Consolidation CT [TOP = 60%; Other = 40%]	PFS (Median) = 17mo (CCRT), 12.9mo (non-CCCT) OS (Median) = 31.6mo (CCRT), 24.8mo (non-CCCT)	Consolidation CT can improve survival outcomes following initial treatment with CCRT
Sas-Korczyńska <i>et al.</i>	2017	Poland	No. of patients = 217 Mean age, years = 60.3 Gender (male) = 65%	CCRT = 46.5% SCRT = 53.5% PCI = 60.4%	CT [PE = 100%; Mean no. of cycles = 4.9] RDT [TRT dose = 40-66]	DFS (5yrs) = 28% mo (CCRT); 14.3% (SCRT); OS (5yrs) = 27.3% (CCRT); 11.7% (SCRT)	CCRT leads to improved survival outcomes, delayed thoracic reoccurrence and reduced distant metastases vs SCRT
Chen <i>et al.</i>	2018	China	No. of patients = 118	HFRT = 48.3% CFRT = 51.7%		OS (5yrs) = 26%(HFRT), 24% (CFRT) PFS (5yrs) = 22% (HFRT), 22% (CFRT)	HFRT and CFRT produce similar survival outcomes. HFRT was associated with reduced toxicities

Table S2 (continued)

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Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
O Hara <i>et al.</i>	2018	Japan	No. of patients = 254 Mean age, years = 64 Gender (male) = 77.1%	CCRT = 61% SCRT = 12% CT = 16% PCI = 38.5%	CT [CE = 22.8%; PE = 54.7%] RDT [45 Gy in 1.5 fractions twice a day = 62.8% ; 50 Gy in 25 fractions = 18.5%; No RDT = 16%]	Complete tumour response = 35% (CCRT); 18% (SCRT); 11% (CT) OS (Median) = 41.1 mo (CCRT); 38.1mo (SCRT); 15.6mo (CT) OS (5yrs) = 41% (CCRT); 36% (SCRT); 15.4% (CT)	SCRT produce comparable treatment outcomes to CCRT
Sukaichai <i>et al.</i>	2019	Thailand	No. of patients = 35 Age (median) = 61 Gender (Male,%) = 83%	CT = 80% PCI = 3%	CT [PE=51.4%; CE=28.7%]	OS (Median) = 17.7mo (LS), 5.9mo (ES)	The OS of the limited stage SCLC patients at our hospital was comparable to landmark studies. Most received sequential chemoradiation treatment
Matsuura <i>et al.</i>	2019	Japan	No. of patients = 13	CCRT = 100%	CT [PE/CE=100%] RDT [54Gy in 36 fractions in 18 days=100%]	OS (1yr) = 100%; OS (2yrs) = 92.3%; OS (3yrs) = 72.5%; PFS (1yr) = 76.9%; PFS (2yrs) = 53.9%; PFS (3yrs) = 53.9%	AHF-TRT of 54 Gy with concurrent PE or CE regimens resulted in a better OS and PFS without an increase in the severity of toxicity
Chemotherapy/Chemoradiotherapy – Extensive stage							
Zhu <i>et al.</i>	2011	China	No. of patients = 119 Mean age, years = 61 Gender (male) = 80.7%	CT = 49.6% CRT = 50.4% PCI = 1.6%	CT [PE = 87.4%; CE = 12.6%] CRT = 40-60Gy PCI = 1.6%	OS (median) = 17mo (CRT), 9.3mo (CT) OS (2yr) = 35% (CRT), 17% (CT) OS (5yr) = 7.1% (CRT), 5.1% (CT)	TRT added to CT improved OS in ES-SCLC patients.
Forde <i>et al.</i>	2012	UK	No. of patients = 81	CT = 39% SCRT = 61%	Not available	N/A	N/A
Luan <i>et al.</i>	2015	China	No. of patients = 167 Mean age, years = 59 Gender (male) = 82.6%	CT = 50.1% CCRT = 49.1% PCI = 2.9%	CT [PE= 77%; CE= 23%]	OS (median) = 18mo (CCRT), 12mo (CT) PFS (median) = 9mo (CCRT), 6mo (CT) OS (2yrs) = 35.3% (CCRT), 14.5% (CT) OS (5yrs) = 2.4% (CCRT), 2.4% (CT)	TRT added to CT improved OS in ES-SCLC patients.
Kim <i>et al.</i>	2017	Korea	No. of patients = 88 Mean age, years = 71 [65–83] Gender (male) = 82%	CT=100%	CT [etoposide-based regimen = 100%]	N/A	N/A
Li-Ming <i>et al.</i>	2017	China	No. of patients = 306 Mean age, years = 60 Gender (male) = 72%	CT = 55.5% CCRT = 44.5% PCI = 8.8%	CT [ etoposide-based regimen = 100%]	OS (2yrs) = 21.4% (CCRT), 10.3% (CT) PFS (2yrs) = 7.7% (CCRT), 4.6% (CT)	TRT added to CT improved OS in ES-SCLC patients. High TRT doses improved OS over lower doses
Mellemgaard <i>et al.</i>	2017	Denmark	No. of patients = 200	CT = 100%	CT [oral etoposide= 42%; IV etoposide= 58%]	OS (median) = 227 days (etoposide oral), 235 days (etoposide IV) PFS (median) = 140 days (etoposide oral), 195 days(etoposide IV)	IV and oral produced similar OS but longer PFS with the IV schedule for ES-SCLC

Table S2 (continued)

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Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Elegbede <i>et al.</i>	2018	Canada	No. of patients = 242 Mean age, years = 68	CT = 40% CRT = 60% PCI = 12.4%	Not available	N/A	In contrast to advanced NSCLC, systemic treatment uptake was high. However, <20% of patients followed through with PCI
Sallam <i>et al.</i>	2018	UK	No. of patients = 671	CT = 100%	[CE=94%; PE=6%] Platinum + E (4 cycles) = 86%; Platinum + E (>4 cycles) = 14%	OS (median) = 11mo [4 cycles], 12mo [>4cycles] PFS (median) = 8mo [4 cycles], 9mo [>4cycles]	There is a lack of clinical benefit by extending first-line platinum combination treatment beyond four cycles in selected patients. This supports limiting the number of cycles to four until the superiority of a longer regimen is identified in a randomized study.
Sedef <i>et al.</i>	2019	Turkey	No. of patients = 117 Age (median) = 61 Gender (Male,%) = 90%	CT=100%	CT [PE/CE=100%]	OS (median) = 13mo PFS (median) = 8mo	Complete response and recurrent free time were the prognostic factors for ES SCLC patients in our study
Shirasawa <i>et al.</i>	2019	Japan	No. of patients = 161 Age (median) = 72 Gender (Male,%) = 85%	CT=100%	Not available	OS (median) w/ interstitial pneumonia = 7.1mo, PFS (median) w/out interstitial pneumonia = 10.0mo	Systemic chemotherapy was effective even in ED-SCLC patients with IP
Sukaichai <i>et al.</i>	2019	Thailand	No. of patients = 35 Age (median) = 61 Gender (Male,%) = 83%	CT = 80% PCI = 3%	CT [PE=51.4%; CE=28.7%]	OS (Median) = 5.9mo (ES)	The OS of the limited stage SCLC patients at our hospital was comparable to landmark studies. Most received sequential chemoradiation treatment
Mixed treatment cohorts							
Demeter <i>et al.</i>	2003	Canada	No. of patients = 100 Gender (male) = 75% Mean age, years = 61.9 Stage of disease = 33% [LS] 67% [ES]	CT= [LS = 86%; ES=64%] CRT= [LS = 83%; ES=63%]	Not available	OS (2yrs) = 22% [LS], 4% [ES]	N/A
Debevec <i>et al.</i>	2005	Slovenia	No. of patients= 51 Stage of disease = 47% [LS] 53% [ES]	Not available	Not available	OS (1yr) = 45% [LS], 10% [ES] OS (5yr) = 0%	N/A
Thammakumpee <i>et al.</i>	2007	Thailand	No. of patients = 116 Mean age, years = 63 (42–87) Gender (male) = 93% Stage of disease = 42% [LS], 58% [ES]	CT = 26% CRT= 28% RT= 20% BSC= 26%	PE = 97% (of CT/CRT patients)	OS (1yr) = 41% [LS], 22.4% [ES] OS (2yr) = 12.5%[LS], 3% [ES]	Response to chemotherapy was about 50% and median survival was significantly better than in patients without chemotherapy for both limited- and extensive-stage patients.
Sugiyama <i>et al.</i>	2007	Japan	No. of patients= 94 Mean age, years = 66 Gender (male) = 83% Stage of disease = 44.7% [LS], 55.3% [ES]	CT=100%	PE = 60% CE = 21% Other = 19%	Not available	N/A

Table S2 (continued)

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Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Duarte <i>et al.</i>	2008	Brazil	No. of patients= 62 Mean age, years = 60.6 Gender (male) = 71.2% Stage of disease = 59% [LS]; 41% [ES]	CT=100%	PE = 69% CE= 31%	Not available	N/A
Li <i>et al.</i>	2009	China	No. of patients = 126 Age group, years = 84 [<70], 42 [>70] Gender (male) = 69% Stage of disease = 49% [LS], 51% [ES]	CT=100%	PE = 65.8% CAV = 34.2%	OS (median) = 13mo [<70], 12mo [>70] PFS (median) = 8mo [<70], 7mo [>70]	SCLC patients 70 years or older may tolerate and benefit from standard chemotherapy regimens (EP or CAV) with or without RT
Noguchi <i>et al.</i>	2010	Japan	No. of patients = 83 Age group, years = 38 [70- 79], 45 [>80] Gender (Male, %) = 68% Stage of disease = 70% [LS], 30% [ES]	CT = 38.6% CRT= 25.3% RT= 4.8% BSC= 31.3%	Not available	OS (median, ES) = 9.2mo [70–79], 10.3mo [>80] OS (2yrs, ES) = 28% [70–79], 17% [>80]	Combination chemotherapy with or without TRT is feasible for patients aged 80 years with SCLC with PS 0 to 1, and even those with PS 2 to 3 or moderate comorbidities can benefit from these treatments
Devbhandari <i>et al.</i>	2010	UK	No. of patients= 67			OS (5yr) = 18% [LS = 33%, ES = 3%]	N/A
Garcia Prim <i>et al.</i>	2010	Spain	No. of patients= 98			OS (2yr) = 26.4% OS (median) = 8.83mo [LS]; 8.43mo [ES]	N/A
Nakao <i>et al.</i>	2010	Japan	No. of patients = 30 Age group, years = 35% [<70], 55% [>70] Stage of disease = 35% [LS], 55%[ES]	CT =100%	AMR = 100%	OS (median) = 301 days PFS (median) = 86 days	N/A
Lebau <i>et al.</i>	2011	France	No. of patients= 239 Mean age, years = 61 (50–72) Gender (Male, %) = 71% Stage of disease = 54.3% [LS], 45.7% [ES]	CT = 100%	PCDE = 44% PE = 32% Other = 24%	Complete response = 56% [PCDE]; 26% [PE] Objective response = 75% [PCDE]; 40% [PE]	N/A
Hermes <i>et al.</i>	2012	Germany	No. of SCLC patients = 397 Mean age, years = 63 [LS- SCLC] 61 [ES-SCLC] Stage of disease = 39% [LS]; 61% [ES]	CT = 28% [LS-SCLC], 95% [ES-SCLC] CCRT = 72% [LS-SCLC], 5% [ES-SCLC] PCI = 33% [LS- SCLC],22% [ES-SCLC]	CE = 98.1% [LS], 81.4% [ES] PE = 1.7% [LS], 6.1% [ES] Other CT = 0.2% [LS], 12.5% [ES]	OS (median) = 18.6mo [LS], 8.7mo [ES] PFS (median) = 7.2mo [LS], 3.55mo [ES]	N/A
Fisher <i>et al.</i>	2012	Canada	No. of patients= 171 Age group, years = 111 [75- 79], 60 [>80] Gender (male) = 56.7% Stage of disease = 23% [LS]; 77% [ES]	CT = 100%	PE = 47% CE = 31% Oral etoposide = 21%	Outcomes presented as univariable and multivariable analyses	Elderly patients who are able to initiate chemotherapy are able to tolerate treatment and receive survival benefits from it

Table S2 (continued)

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Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Molina-Guillen <i>et al.</i>	2012	Spain	No. of patients = 40 Mean age, years = 65.3 Gender (male) = 90% Stage of disease = 37.5% [LS], 62.5% [ES]	CT = 100%	Platinum based (CE or PE) = 100%	PFI >6mo (ES patients) = 28%	Platinum based chemotherapy has been shown to be more effective in SCLC patients when they start the treatment at LS disease than ES. The 73.3% of the patients diagnosed and treated at the LS had a PFI longer than 6 months. However, only 28% of the patients who started the treatment at the ES reached a PFI longer than 6 months
Fujitani <i>et al.</i>	2013	Japan	No. of patients = 42 Mean age, years = 69 Gender (male) = 85.7% Stage of disease = 26.2% [LS]; 73.8% [ES]	CT = 100%	PE = 73.8% PC = 26.2%	OS (median) = 391 days [PE] Not reached [PC]	Physicians preferred PE for older patients as first-line therapy Survival outcomes tended to be better longer in the PC group
Postmus <i>et al.</i>	2013	Western Europe, Eastern Europe and Korea	No. of patients = 507 Mean age, years = 65.4 Gender (male) = 73% Stage of disease = 34% [LS], 66% [ES]	CT = 59% CRT = 67% [LS only] PCI = 26% [LS = 34%, ED = 22%]	CT (first line) PE = 90.7%; CAV = 3.9%; CYC = 3.9%; Other = 2.5%	OS (median) = 10.6mo [all patients]; 17.8mo [LS]; 8.7mo [ES]	The combination of platinum and etoposide remains first choice of chemotherapy at first line and often at relapse, followed by topotecan starting from second-line and beyond.
Islam <i>et al.</i>	2015	Australia	No. of patients = 41 Age group, years = 100% (>70) Stage of disease = 22% [LS], 78% [ES]	CT = 78% [All ES patients] CRT = 22% [All LS patients] PCI = 26% [LS = 34%, ED = 22%]	Not available	OS (median) = 355 days [LS], 310 [ES] PFS (median) = 204 days [LS], 155 days [ES]	Elderly patients can be treated with standard doublet chemotherapy; however, dose reductions are required for a significant number of patients
Li <i>et al.</i>	2016	China	No. of patients = 77 Stage of disease = 42.7% [LS], 55.3% [ES]	Untreated = [LS = 32.4%; ES = 47.6%] CT = [LS = 38.2%; ES = 47.6%] CRT = [LS = 29.4%; ES = 2.4%]	Not available	OS (median) = 14.23mo [LS], 12.5mo [ES]	N/A
Al Farsi <i>et al.</i>	2017	Canada	No. of patients = 185 Mean age, years = 64 Gender (male) = 50% Stage of disease = 37% [LS], 63% [ES]	CT = 51% CRT = 49% PCI = 43.2% [LS = 64%, ES = 39%]	PE = 53% CE = 47%	Incidence of relapse = 73% Time to relapse = 9.2mo [LS = 14.3mo, ES = 7.5mo]	<50% of eligible SCLC patients receive PCI. CNS relapse occurs frequently and more commonly in patients who do not receive PCI. Implementation of PCI in routine clinical practice appears to influence patterns of recurrence.
Silva <i>et al.</i>	2017	Portugal	No. of patients = 144 Mean age, years = 65 [42–87] Gender (male) = 79.9% Stage of disease = 25% [LS], 75% [ES]	CT = 100%	PE = 95.1%	ORR = 64% OS (median) = 5.5mo	Clinical practice at the centre represented that presented in the current literature. New treatments and predictive biomarkers for SCLC are urgently needed

Table S2 (continued)

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Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Zhou <i>et al.</i>	2017	China	No. of patients = 523 Median age, years = 59 [27–87] Gender (male) = 79.3% Stage of disease = 26.8% [LS]; 73.2% [ES]	CT = 50.9% [LS = 39.3%, ES=55.1%] CRT= 49.1% [LS = 60.7, ES=44.9%] PCI = 12.6% [LS = 23.6%, ES = 8.6%]	All patients received either PE, CE, C+IRI or P +IRI	OS (median) = 21mo [LS] 13mo [ES] Other outcomes present as univariable and multivariable analyses	Limited stage disease and good response to initial therapy predicted a better survival for SCLC patients
Aquin <i>et al.</i>	2018	Canada	No. of patients = 531 Stage of disease = 30.2% [LS], 69.8% [ES]	CT=100%	PE = 73.8% CE = 26.2%	OS (median) = 322 days [PE] 224days [CE] Other outcomes present as univariable and multivariable analyses	Carboplatin appears to be an equally effective treatment option for SCLC, facilitating equivalent survival while avoiding toxicity
El Benna <i>et al.</i>	2018	Tunisia	No. of patient s= 60 Mean age, years = 61 [±6.5] Gender (male) = 95% Stage of disease = 33.3% [LS], 66.7% [ES]	CT=100%	CE/PE = 85%; Other =15%	N/A	Patients with SCLC are highly responsive to chemotherapy and radiation therapy. Long-term prognosis remains poor, with relapse and disease recurrence occurring in almost all cases
Hong <i>et al.</i>	2018	China	No. of patients= 999 Age group, years = 61.3% [<60], 38.7% [>60] Gender (male) = 69.3% Stage of disease = 59.1% [LS], 40.9% [ES]	Surgery +CRT = 5.9% [LS = 9.9%; ] CT = 55.1% [LS = 52.5%, ES = 56.8%] CRT= 33.5% [LS = 33.2, ES = 32.8%]	PE = 89.3% [LS = 88.8%, ES = 90.1%] Non-PE = 10.7% [LS = 11.2%, ES = 9.9%]	OS (1yr) = 50.5% [LS], 32.2% [ES] OS (2yr) = 14.5%[LS], 8.7% [ES] OS (3yr) = 3.1% [LS], 2.6% [ES]	Several factors, including patient, tumour, and treatment characteristics and serum LDH levels are independent prognostic factors for OS and PFS in Chinese patients with SCLC
Lattuca-Truc <i>et al.</i>	2018	France	No. of patients= 529 Median age, years = 64 Gender (male) = 77% Stage of disease = 42% [LS], 58% [ES]	CT = 35% CRT= 65% PCI = [1997-09 = 26%, 2009-19= 32%]	Platinum based (CE or PE) =96%	Median OS = 12mo [1997-09=13mo, 2009-17= 11mo]	Since 1997 there was no improvement in survival nor response rate to chemotherapy in SCLC patients. There is a desperate need for new approaches in this setting
Saber <i>et al.</i>	2018	Egypt	No. of patients= 24	CT = 84%	PE/CE =100%	OS (median) = 7.7mo PFS (median) = 5.4mo	N/A
Cramer-Van Der Welle <i>et al.</i>	2019	Netherlands	No. of patients= 501 Age (mean) = 66 Gender (Male,%) = 67% Stage of disease = 100%[ES]	CT = 100%	Not available	OS (median) = 7.4mo	After first line systemic treatment in ED SCLC the fraction of patients receiving subsequent lines of treatment is rapidly decreasing
Incanc <i>et al.</i>	2019	Turkey	No. of patients= 177 Age (mean) = 56 Gender (Male,%) = 91% Stage of disease = 41% [LS]; 59%[ES]	CT = 100%	PE = 100%	Not available	We evaluated the relationship between NLR and SCLC, and found that NLR is a potential prognostic serum marker in patients with SCLC
Chemotherapy/Chemoradiotherapy 2 <sup>nd</sup> /3 <sup>rd</sup> line – Extensive stage							
Asai <i>et al.</i>	2012	Japan	No. of patients= 36 [second-line = 12%, third-line = 88%] Mean age, years= 69 [47–83] Gender (male) = 89% Prior therapies [CE= 62%, PE = 25%, other = 13%]	CT	AMR = 100%	OS (median) = 5.1mo PFS (median) = 2.9mo	AMR has the potential to be effective tool for the treatment of elderly patients (i.e. >70 years) with R/R SCLC

Table S2 (continued)



Table S2 (continued)

Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Inomata <i>et al.</i>	2014	Japan	No. of patients= 19 Mean age, years = 68 [47–78] Gender (male) = 94.7% Prior therapies [first-line platinum = 100%; second-line re-challenged platinum = 57.1%]	CT	Platinum doublet = 15.7% AMR = 47.4% TOP = 21% IRI = 10.4% PTX = 5.2%	OS (median) = 8.5mo	Numerous prognostic factors identified for improved OS in third-line SCLC
Morise <i>et al.</i>	2014	Japan	No. of patients= 57 Mean age, years = 70 [51–83] Gender (male) = 91% Prior therapies [PE = 47%, CE = 46%, RDT = 42, PCI = 23%]	CT	IRI=100%	ORR = 32% OS (median) = 5.3mo PFS (median) = 2.9mo	Low dose IRI has the potential to be an effective option for third-line SCLC with favourable toxicity
Murakami <i>et al.</i>	2015	Japan	No. of patients= 39 Mean age, years = 68 Gender (male) = 87.2%	CT	Re-challenge (existing platinum) = 33.3% AMR = 51.2% Other= 15.5%	OS (median) = 44.2mo [re-challenge], 20.9mo [AMR] PFS (median) = 8.2mo [re-challenge], 4.9mo [AMR]	Platinum re-challenge therapy provide better outcomes than single agent chemotherapy for relapsed SCLC
Aktas <i>et al.</i>	2016	Turkey	No. of ES-SCLC patients = 255 No. of ES-SCLC patients receiving second-line therapy = 117 [primary resistant = 17%, platinum sensitive = 83%] No. of ES-SCLC patients receiving third-line therapy = 25 [primary resistant = 12%, platinum sensitive = 88%] Mean age, years= 57 [39–74] Gender (Male,%) = 92%	CT (second-line and third-line regimen provided)	IRI/TOP = 44% TOP/IRI = 56%	OS (median) = 18mo [IRI/TOP], 14mo [TOP/IRI] PFS (median) = 14wks [IRI/TOP], 12wks [TOP/IRI]	Sequential monotherapy of TOP and IRI provide a considerable contribution to OS but sequencing of treatment provides similar outcomes
Granados <i>et al.</i>	2017	Spain	No. of patients= 83 Mean age, years = 58 [43–81] Gender (male) = 83.2% Prior therapies [CE= 38.7%, PE = 60.3%]	CT	PTX+GCB = 100%	OS (median) = 172 days PFS (median) = 148 days Treatment cessation (toxicity) = 14.4%	PTX+GCB is a well-tolerated regimen for relapsed SCLC and contributes to OS and PFS
Itotani <i>et al.</i>	2017	Japan	No. of patients= 21 Mean age, years = 70 [±5.6] Gender (male) = 85.7% ILD = 100%	CT	C+PTX =100%	OS (median) = 7.1mo PFS (median) = 3.5mo	In previously treated SCLC patients with ILD who had received more than one cytotoxic chemotherapy regimen, C+PTX is an effective treatment regimen
Minemura <i>et al.</i>	2017	Japan	No. of patients = 86 Mean age, years = 74 [70–84] Stage of disease = 48% [sensitive relapse], 52% [refractory relapse]	CT	AMR = 100%	OS (median) = 7.6mo [sensitive relapse], 5.5mo [refractory relapse] PFS (median) = 4mo [sensitive relapse], 2.7mo [refractory relapse]	Amrubicin demonstrated anti-tumour activity in both sensitive and refractory relapsed SCLC patients

Table S2 (continued)

Table S2 (continued)

Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Yu <i>et al.</i>	2017	Japan	No. of patients= 54	CT	IRO+NED = 63% IRO+P = 37%	OS (median) = 62wks (IRO+NED), 58wks (IRO+P) PFS (median) = 23wks (IRO+NED), 19wks (IRO+P)	Irinotecan plus platinum is effective and tolerable for refractory and relapsed small cell lung cancer
Wang <i>et al.</i>	2017	China	No. of patients= 82	CT	IRO+PE = 54% TOP = 46%	OS (median) = 16.3 (IRO+PE), 10.1mo (TOP) PFS (median) = 6.2 (IRO+NED), 4.1 (IRO+P)	Combined chemotherapy with PEI is not inferior to topotecan monotherapy at second-line treatment
Zhang <i>et al.</i>	2018	China	No. of patients= 78	CT	P+E+IRO = 15.7% TOP = 47.4%	OS (median) = 16.3mo [PE+IRO] 13.1mo [66]	Combination chemotherapy with C+E+IRO could be considered as a second-line treatment option in patients with relapsed sensitive SCLC
von Eiff <i>et al.</i>	2018	Germany	No. of patients= 185 Mean age, years = 64 Gender (male) = 64.3% Prior therapies = 100% [CE/PE]	CT	PTX = 100%	OS (median) = 100 days PFS (median) = 48 days	Patients in good condition and without cerebral/hepatic metastases benefit from PTX therapy in relapsed SCLC
Saijo <i>et al.</i>	2019	Japan	No. of patients= 17 Gender (Male,%) = 71.1%	CT	PTX = 44.7%	OS (median) = 2.7mo; PFS (median) = 3.6mo	Although PTX-containing regimens demonstrated promising anti-tumor activity against relapsed SCLC with IIPs, the survival benefit was limited because of the high incidence of PTX-related AE of IIPs and treatment-related death
Moharana <i>et al.</i>	2019	India	No. of patients= 12	CT	PTX/IRI = 100%	PFS (median) 1.5mo	Weekly Paclitaxel in 2nd line may have favourable toxicity profile and response rate comparable to Irinotecan or Temozolomide
Moser	2019	Israel	No. of patients= 235 Age (median) = 64 Gender (Male,%) = 61% Prior therapies= 100%[PE]	CT	Not available	OS (median) = 11.8m	Overall survival for SCLC patients in a real world setting was found to be similar to those reported in clinical trials
Sugiyama <i>et al.</i>	2019	Japan	No. of patients= 31 Age (mean) = 69 Gender (Male,%) = 85%	CT	PTX = 100%	OS (median) = 4.4mo, PFS (median) = 2.2mo	PTX monotherapy showed moderate efficacy with acceptable toxicity in heavily treated patients with R/R SCLC patients
Sone <i>et al.</i>	2018	Japan	No. of patients = 31 Mean age, years = 72 (>65) Gender (male) = 83.9%	CT = 100%	CT [AMR=100%]	OS (median) = 11.6mo PFS (median) = 5.4mo	AMR has the potential to be an effective regimen for elderly patients with ES-SCLC, in particular for patients with relapsed SCLC
Zhao <i>et al.</i>	2019	China	No. of patients= 116 Age ≤65 (180), >65 (92) Gender (Male,%) = 84.9%	CT	TOP/PTX/DTX=100%	OS (median) IRI = 595d; TOP = 154d; PTX = 168.5d; DTX = 184d; PFS (median) IRI = 91d; TOP = 74.5d; PTX = 81d; DTX = 50d	Second-line chemotherapy with TPT in SCLC patients may provide better overall survival benefits

Table S2 (continued)

Table S2 (continued)

Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Prophylactic Cranial Irradiation (PCI)							
Stanic <i>et al.</i>	2010	Slovenia	No. of patients= 356 Gender (male) = 75% Mean age, years = 61.9 Stage of disease = 48% [LS], 52% [ES]	PCI = 6% CT = 41% CRT = 48.5%	N/A	OS (median) = 21.9mo [PCI] 12.13mo [no PCI] Brain metastases = 25%	Increased median survival time and decreased incidence for brain metastases in patients with PCI. Recommendation to perform PCI in patients with LS disease and good performance status
Nakahara <i>et al.</i>	2012	Japan	No. of patients= 17 Mean age, years = 66 [52–78]	PCI = 100%	N/A	Brain metastases (%) = 35% Dementia (incidence) = 29% Gait disturbance (incidence) = 18%	Impact of PCI on neurocognitive functioning is significant and should be weighed against survival benefits, especially in older patients
Ramlov <i>et al.</i>	2012	Denmark	No. of patients= 118 Gender (male) = 43% Stage of disease = 62.7% [LS], 37.3% [ES]	PCI = 100% Surgery = 6% CRT = 53% Palliative CT/CRT = 41%	N/A	OS (median) = 24mo [LS], 12mo [ES] Cerebral reoccurrence (%) = 17%	PCI lowers likelihood of developing brain metastases in SCLC
Ozawa <i>et al.</i>	2014	Japan	No. of patients= 124 Mean age, years = 65 Stage of disease = 100% [LS]	PCI = 23.3%	N/A	OS (median) = 25.5mo [PCI] 34.5mo [no PCI] Brain metastases (2yrs) = 45.5% [PCI] 29.9% [no PCI]	PCI does not benefit patients with LS-SCLC in conjunction with periodical brain screening and thoracic radiotherapy
Zhu <i>et al.</i>	2014	China	No. of patients= 193 Mean age, years = 56 Stage of disease = 100% [LS]	PCI = 34.7% Surgery = 100%	N/A	OS (2y) = 92.5% [PCI] 63.2%, [non-PCI] OS (5yr) = 54.9% [PCI], 47.8% [non-PCI] Brain metastases free survival (2yrs) = 96.8% [PCI], 79.4% [non-PCI]	PCI improves survival and lowers likelihood of developing brain metastases in patients with surgically resected SCLC
Bang <i>et al.</i>	2015	Canada	No. of patients= 399 Stage of disease = 100% [ES]	PCI = 17.3% (uptake pre-2008=24.2%; post- 2008=57.6%)	N/A	OS (median) = 14mo [PCI], 8.2mo [No PCI] Brain metastases (2yrs) = 40.6% [PCI] 43.8% [No PCI]	PCI in the setting of at least partial response to chemotherapy was found to have a survival benefit and prolongation of time to brain metastasis
Zeng <i>et al.</i>	2016	China	No. of patients= 175 Mean age, years = 55 Gender (male) = 73.7% Stage of disease = 88.6% [LS], 11.4% [ES]	PCI = 100%	N/A	OS (5yr) = 48% Brain metastases free survival (2yrs) = 54.9% [PCI]	
Qiu <i>et al.</i>	2016	China	No. of patients= 399 Mean age, years = 55 (25–79) Gender (male) = 81% Stage of disease = 100% [LS]	PCI = 46.4% CRT = 100%	N/A	OS (median) = 32.6mo [Early PCI], 40.9 [Late PCI], 21.5 mo [No PCI] Brain metastases (2yrs) = 13% [PCI], 42% [No PCI]	PCI significantly decreased the incidence of brain metastases and improved the overall survival rate in patients with LS-SCLC. Early PCI administered within 6 months of the start of first- line chemotherapy was as effective as late PCI (PCI that was administered 6 months later)

Table S2 (continued)

Table S2 (continued)

Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Matutino <i>et al.</i>	2017	Brazil	No. of patients= 46 Stage of disease = 100% [ES]	PCI = 35% CT (platinum) = 100%	N/A	OS (median) = 20.94mo [PCI], 11.05 mo [No PCI] PFS (median) = 10.32mo [PCI], 7.66 mo [No PCI] Brain metastases (2yrs) = 19% [PCI], 53% [No PCI]	Careful patient selection for PCI can improve not only brain metastases but also patient survival.
Mamesaya <i>et al.</i>	2017	Japan	No. of patients= 79 Mean age, years = 67 (34-83) Gender (male) = 68% Stage of disease = 100% [LS]	PCI = 73.4% [CR =26.5%; PR = 46.8%] CRT = 100%	N/A	OS (median) = Not reached [CR and PCI] 3.2yrs [PR and PCI] Not reached [No PCI] PFS (median) = 7.8yrs [CR and PCI] 1.2yrs [PR and PCI] 1.7yrs [No PCI] Brain metastases (3yrs) = 11.6% [CR and PCI] 34.6% [PR and PCI] 38.1% [No PCI]	PCI may not add clinical benefit to LS-SCLC patients who did not achieve CR after initial therapy if absence of bone metastases could be confirmed by MRI immediately before PCI administration
Soon <i>et al.</i>	2018	Singapore	No. of patients= 71 Gender (male) = 83.6% Stage of disease = 100% [ES]	PCI = 22.5% CT = 77.5% [Platinum based = 93%] CRT = 22.5%	N/A	Outcomes presented as univariable and multivariable analyses	Increased utilisation of PCI was observed after publication of the EORTC trial (2006) and PCI was associated with improved survival in patients with at least stable disease following initial chemotherapy
Srivastava <i>et al.</i>	2018	New Zealand	No. of patients= 245 Gender (male) = 45% Mean age, years = 63 Stage of disease = 100% [ES]	PCI = 19.5% CT = 89.4% CRT = 11.6%	N/A	OS (median) = 14.3mo [PCI], 6.3mo [No PCI]	Patients who received PCI had improved survival, although this positive association is no longer observed after stratifying patient according to treatment (i.e. chemotherapy and radiotherapy) characteristic
Boskovic <i>et al.</i>	2019	Serbia	No. of patients= 200	PCI = 100%	N/A	OS (median) PCI = 19.0m Control = 15.4m	The authors strongly believe that PCI should remain a standard of care for patients with SCLC, after response to initial treatment
Liu <i>et al.</i>	2019	China	No. of patients= 385	PCI = 41% CRT = 100%	N/A	OS (median) = 57m; OS (2yrs) = 72.3%; OS (3yrs) = 56.6%; OS (5yrs) = 47.1%	PCI was associated with a significant survival benefit for LS-SCLC patients who had CR to chemoradiotherapy, and prolonged the time to BM, and reduced the cumulative incidence of BM
Cabrero <i>et al.</i>	2019	Not available	No. of patients= 98 Stage of disease = 40% [LS] 60% [ES]	PCI = 37.5% RT = 34.7%	N/A	No significant difference in survival between the group treated with RT	We didn't find any difference with PCI or CI in overall survival and BR. A high proportion of the patients in both groups (with/ without BM at diagnosis) didn't receive radiotherapy, due to a very poor clinical status

Table S2 (continued)

**Table S2** (continued)

Author	Year	Country	Patient characteristics	Treatment received	Regimen	Outcomes	Conclusion
Chung <i>et al.</i>	2019	Not available	No. of patients= 190 Stage of disease = 100% [ES]	PCI = 27.9%	N/A	OS (1yr) PCI = 45%; No-PCI = 50%; BMFS (1yr) PCI = 86.9%; No-PCI = 52.5%, BMFS (2yr) PCI = 49.8%; No-PCI = 12.7%	Four prognostic factors are associated with a high risk of symptomatic brain metastasis in ED-SCLC: presence of extrathoracic metastases, FDG-PET uptake in BM or spleen, PD after chemotherapy, and high Hb level
Maintenance Chemotherapy							
Yan <i>et al.</i>	2018	China	No. of patients = 25	Maintenance CT	Apatanib	OS (median) = 17mo PFS (median) = 8.3mo	Maintenance apatinib was safe and achieved encouraging PFS and OS in extensive-stage SCLC.

AMR=amrubicin, adriamycin, and vincristine, BSC=best supportive care, CAV=cyclophosphamide, adriamycin and vincristine, CE=cisplatin and etoposide, CFRT=conventional fractionation radiotherapy, CR=complete response, CRT=chemoradiotherapy, CCT=concurrent chemotherapy, CCRT=concurrent chemoradiotherapy, CNS=central nervous system, CT=chemotherapy, DFS=disease-free survival, E=etoposide, ES=extensive stage, HFRT=hypofractionated frequency radiotherapy, IRI=irinotecan, IV= intravenous, LDH=lactate dehydrogenase, LS=limited stage, M=extent of external organ involvement (metastases), N=regional lymph node involvement, NSCLC=non-small cell lung cancer, ORR=overall response rate, OS=overall survival, PC=paclitaxel and carboplatin, PCDE=cisplatin, cyclophosphamide, doxorubicin and etoposide, PE=cisplatin and etoposide, PFI=, PS=performance score, PCI=prophylactic cranial irradiation, PEI=cisplatin, etoposide, and ifosfamide, PFS=progression-free survival, RDT=radiotherapy, SCLC=small cell lung cancer, SCRT=sequential chemoradiotherapy, TRT=thoracic radiotherapy, T=characteristics of the primary tumour