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Real-world treatment patterns and outcomes of patients with extensive disease small cell lung cancer

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Abstract

Objective: Clinical outcome data on patients with extensive disease small cell lung cancer (ED SCLC) treated in routine practice is limited. The aim of this retrospective study is to present data on treatment patterns and survival in an unselected patient population with ED SCLC.

Methods: All patients diagnosed with ED SCLC between 2008 and 2014 in six Dutch large teaching hospitals (Santeon network) were included. We collected data on patient characteristics, systemic treatments, overall survival (OS), dose reductions (<80% of initial dose) and early discontinuation (<4 cycles).

Results: From 792 diagnosed patients, 568 (72%) started with first-line treatment. Of these patients, 41% received second-line treatment. Only 68 patients received third-line treatment. For all treated patients, the mean age was 66 years. The majority (72%) had a performance status (ECOG) of 0 or 1 at diagnosis. Median OS of treated patients was 7.4 months. Of all patients with first-line treatment, 26% received <4 cycles and dose reductions were observed in 29%.

Conclusion: After first-line systemic treatment in ED SCLC the fraction of patients receiving subsequent lines of treatment is rapidly decreasing. This information is necessary as background for evaluation of the added value of future drugs under study for ED SCLC.

KEYWORDS

effectiveness, pharmacotherapy, real-world, small cell lung cancer, survival, treatment patterns

1 | INTRODUCTION

Of all patients diagnosed with lung cancer, small cell lung cancer (SCLC) represents 13% of the cases in the Netherlands (Netherlands Comprehensive Cancer Organisation, 2019). SCLC is an aggressive tumour which is frequently metastasized at time of diagnosis, and therefore the majority of patients is diagnosed with extensive disease (ED; Carney, 2002; Lally, Urbanic, Blackstock, Miller, & Perry, 2007). The median survival for patients without systemic therapy has been

Santeon SCLC Study Group collaborators are included in the Appendix.

reported to be 2 to 4 months (Carney, 2002; Meerbeeck, Fennell, & De Ruysscher, 2011).

Several studies have reported an improvement in survival after the introduction of chemotherapy in the 1970s (Janssen-Heijnen et al., 2012). Despite numerous clinical trials, systemic treatment for patients with SCLC has not changed significantly in the past several decades (Byers & Rudin, 2015; Pietanza, Byers, Minna, & Rudin, 2015). The standard of care in Europe for newly diagnosed ED SCLC is a platinum-based chemotherapy with etoposide (Fruh et al., 2013). In case of chemotherapy-resistant disease a second-line treatment with topotecan can be started (Ardizzoni, 2004; Fruh et al., 2013).

These treatment standards are based on clinical trial data, which often have excluded patients with a worse performance status, co-morbidities and high age. Therefore, the question remains if patients with ED SCLC in daily practice show the same outcomes as those in clinical trials. The recent German TLK study showed that platinum-based combination chemotherapies accounted for 93% of all first-line treatments in patients with ED SCLC (Steffens et al., 2019). At least 50% of the patients received a second-line treatment and 22% a third-line treatment. Regarding survival time, this study concluded similarity with data from previously randomised trials. A limitation is that they started with patients receiving systemic treatment thus not being able to report on the percentage of best supportive care only after diagnosis.

A recent systematic literature review on real-world effectiveness of SCLC treatments by Povsic et al. also emphasized the limited number of treatment options in SCLC and lack of good quality real-world data about outcomes (Povsic et al., 2019). The aim of the present study is to provide good quality data on treatment patterns, including best supportive care, and corresponding survival times in an unselected patient population with ED SCLC.

2 | PATIENTS AND METHODS

2.1 | Data source and study participants

This study was performed within a network of seven large (non-university) teaching hospitals in the Netherlands, named Santeon, which serves more than 12% of the Dutch patient population. We used the Santeon Care for Outcome (CfO) registry for identifying all patients diagnosed with ED SCLC between 2008 and 2014, and for collecting patient characteristics. Data on applied systemic pharmacotherapy for ED SCLC was derived from individual patient files. Furthermore, the Santeon Farmadatabase (SFD) was used for validation and collection of additional detailed data about systemic treatments. More details on the CfO registry and SFD can be found elsewhere (Cramer-van der Welle et al., 2018; Garde et al., 2019; Peters et al., 2017).

Study data were collected and managed using REDCap electronic data capture tools hosted at St. Antonius Hospital, Utrecht/Nieuwegein, the Netherlands (Harris et al., 2009). This study was approved by a medical research ethics committee (CMO registration number 2018-4338), with need for informed consent being waived because of the retrospective nature of the study and anonymous handling of data.

2.2 | Patient characteristics and systemic treatment per patient

The following patient characteristics were collected from the CfO: date of diagnosis, age at diagnosis, gender, ECOG performance status (PS), separate comorbidities (to calculate Charlson Comorbidity Index [CCI]) and date of death.

For every patient, all systemic treatments were extracted from both the individual patient files and the prescription data recorded in the SFD, including start and stop dates, number of cycles and dose, and whether it was first, second or further line of treatment. The initial systemic therapy following date of diagnosis was defined as first-line treatment. Switches from cisplatin to carboplatin due to toxicity were considered the same line. Second-line treatment was defined as systemic treatment applied after completion or discontinuation because of disease progression of first-line treatment. Re-induction treatment (systemic treatment with the same or similar regimen as administered in the previous line, ≥90 days after finishing first-line treatment) for chemo-sensitive patients was considered a subsequent line of treatment.

2.3 | Real-world treatment outcomes

The overall survival (OS) for all treated patients was calculated using time between start date of systemic treatment and date of death. For patients receiving best supportive care, date of diagnosis was used to calculate OS. Patients still alive at January 31, 2018 (date of update from Personal Records Database [BRP]) were given this end of follow-up date as imputed date of death (n = 7). Furthermore, progression-free survival (PFS) was calculated as time between start date of systemic treatment and date of progression when noted, or date of death in absence of acknowledged progression from the individual patient files.

As proxies for toxicity, the percentage of patients with dose reductions (<80% of the initial dose), early discontinuation (at least one cycle less than planned for that regimen) and/or switches were assessed within lines of treatment.

2.4 | Statistical analysis

Statistical Software (SPSS version 24 for Windows; IBM) was used for statistical analysis. In case of continuous data mean ± *SD* or median (range) was given, categorical data were analysed using chi-square and continuous data using *t* tests and one-way ANOVA when appropriate.

3 | RESULTS

3.1 | Patient characteristics

We identified 792 patients diagnosed with ED SCLC in the period 2008–2014, of which 568 (72%) started with first-line treatment. A combination therapy with cisplatin or carboplatin and etoposide is the most applied first-line systemic treatment (96% of all treated patients). Table 1 presents the baseline patient characteristics per systemic first-line treatment regimen, for all treated patients as a whole, and for patients who received best supportive care. For all treated patients, the mean age at diagnosis was 66 years; 45% were female. The majority of patients (72%) had an ECOG PS 0–1 at time of diagnosis and comorbidities were present in 57% of all patients (CCI > 0). For all patients with best supportive care, 87 patients (39%) had an ECOG PS 0–1 at time of diagnosis, but nevertheless did not start first-line treatment for various reasons, for example, personal preferences or very rapid progress of disease. Table A1 (appendix) presents the baseline characteristics for all treated patients on start of first, second or third-line treatment.

3.2 | Treatment patterns

Figure 1 shows the different treatment patterns of all patients towards best supportive care (BSC). Of all patients treated with first-line treatment, 41% (n = 231) received second-line treatment, of which 24% received topotecan. Apart from re-induction chemotherapy with platinum-etoposide (48%), taxane-based regimens were the most commonly used type of regimens (19%) in second-line. Only 68 patients (12%) received third-line treatment. In third-line, topotecan was most commonly applied (32%), followed by taxane-based regimens (31%). Twelve patients (18%) received re-induction treatment with a platinum-etoposide regimen. In fourth-line, topotecan was applied in half of the patients. Two patients subsequently received fifth-line systemic treatment.

3.3 | Outcomes

Median PFS and OS for all treated patients were 5.8 and 7.4 months, respectively. Median PFS and OS per line of systemic treatment were shown in Table 2. Median OS for patients with best supportive care (n = 224) was 0.9 months.

There was no difference in median OS for treated patients depending on year of diagnosis (p = .868). Furthermore, no significant difference was found in median OS for patients with second-line re-induction chemotherapy (platinum-etoposide) depending on time to progression from end date of first-line therapy (<6 months [n = 54] vs. ≥6 months [n = 55]): median OS from start date of second-line therapy was 5.6 and 7.0 months, respectively (p = .067).

Of all patients with first-line treatment, dose reductions were present in 29%, early discontinuation in 26%, and switches in 8% of the patients (Table 3). Multivariate analysis showed a statistically significant association of age, ECOG PS and CCI with the occurrence of one or more proxies for toxicity (p = .046, .004 and .017, respectively).

4 | DISCUSSION

This study showed that after first-line systemic treatment in ED SCLC the fraction of patients receiving subsequent lines is rapidly decreasing. From 792 diagnosed patients, 72% started with first-line treatment. Of these patients, 41% received second-line treatment and only 12% third-line treatment. The median OS from start of first-line treatment is 7.4 months. Combination therapy with platinum-etoposide is the most applied first-line systemic treatment (96% of all treated patients).

This is one of the few studies that provide a complete overview of treatment patterns and corresponding outcomes for an unselected population of patients with ED SCLC. To the best of our knowledge, the German TLK study of Steffens et al. (2019) and the cohort study of Tendler et al. (2020) are the only other recent studies including

TABLE 1 Baseline characteristics ED SCLC patients with first-line treatment

	Carboplatin-etoposide	Cisplatin-etoposide	CDE	Other	All treated patients	All patients with BSC
Patients, *n*	335	209	15	9	568	224
Age at diagnosis, median (min–max)	68 (39–88)	64 (42–84)	68 (49–78)	61 (52–87)	66 (39–88)	74 (44–92)
Male, *n* (%)	203 (61)	93 (45)	13 (87)	2 (22)	311 (55)	129 (58)
Comorbidities (CCI ≥ 1), *n* (%)	197 (59)	112 (54)	9 (60)	6 (67)	324 (57)	144 (64)
Missing	0	0	0	0	0	9 (4)
ECOG PS, *n* (%)						
0–1	240 (72)	156 (75)	11 (73)	4 (44)	411 (72)	87 (39)
≥2	83 (25)	46 (22)	4 (27)	5 (56)	138 (24)	113 (50)
Missing	12 (4)	7 (3)	0	0	19 (3)	24 (11)

Abbreviations: BSC, best supportive care; CCI, Charlson Comorbidity Index; CDE, cyclophosphamide-doxorubicin-etoposide; ECOG PS, Eastern Cooperative Oncology Group Performance Status.

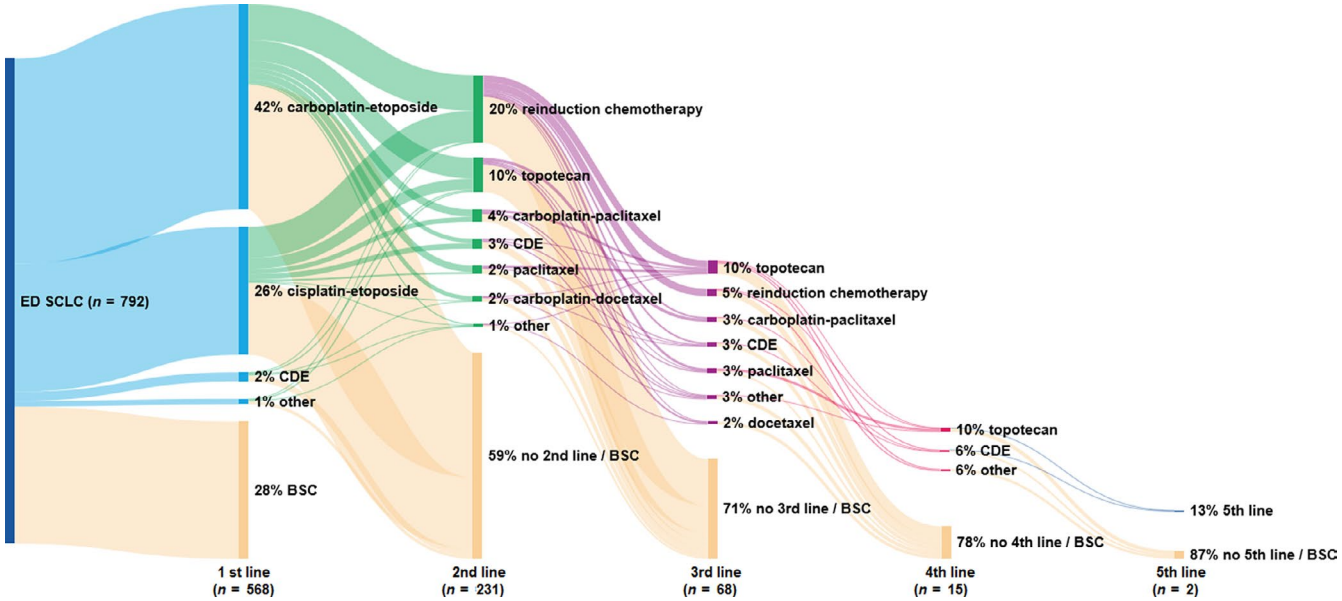

FIGURE 1 Treatment patterns of ED SCLC patients. BSC, best supportive care; CDE, cyclophosphamide-doxorubicin-etoposide

TABLE 2 PFS and OS of treated patients from start date of corresponding line

	1st line (*n* = 568 treated)	2nd line (*n* = 231)	3rd line (*n* = 68)	4th line (*n* = 15)	5th line (*n* = 2)
Median PFS (months)	5.8	3.4	3.4	3.7	4.7
Median OS (months)	7.4	4.6	3.7	5.1	6.0

Abbreviations: OS, overall survival; PFS, progression-free survival.

TABLE 3 Toxicity in patients with first-line treatment

Regimen	Dose reduction (%)	Early discontinuation (%)	Switch (%)
Carboplatin-etoposide (*n* = 335)	26	27	2
Cisplatin-etoposide (*n* = 209)	35	23	18
CDE (*n* = 15)	40	33	7
Other (*n* = 9)	22	44	22
Overall	29	26	8

Abbreviation: CDE, cyclophosphamide-doxorubicin-etoposide.

such data. Our findings are in line with Steffens et al. with regard to low percentages of patients receiving a second and third-line. Furthermore, we found a comparable percentage of platinum-based combination chemotherapy as first-line treatment. In addition to Steffens et al., our study revealed that 28% of all patients diagnosed with ED SCLC received best supportive care only. This means that the statement of Steffens et al. that their results may not be generalised to the small group of patients not receiving any systemic treatment concerns more than a quarter of all patients diagnosed with ED SCLC (Steffens et al., 2019).

In contrast to the German TLK study, we found a lower median OS from first-line treatment (7.4 months, compared to 10.7 as found by Steffens et al.), whereas Tendler et al. reported a median OS of 7.0 months, which is in line with our findings. These differences may be related to differences in cohort selection. The TLK study included patients who received at least one palliative *line* of treatment, whereas in our study and in the study of Tendler et al. all patients who started first-line treatment were included (i.e. at least one *cycle* of treatment). The possibility exists that some patients have not made it into the Steffens et al. cohort because of early discontinuation of treatment due to rapid progression or toxicity. The remaining patients do have a better prognosis which is reflected in a longer median survival. Furthermore, it is not inconceivable that the process of prospective enrolment of patients in the TLK study might have caused selection bias by missing patients with poor prognosis. For example, Steffens et al. reported 39% of all patients with CCI ≥ 1 and 17% with ECOG PS ≥ 2, compared to 57% and 24% in our population treated with first-line systemic treatment. Another contrast with the German TLK Study is that in second-line regimens with paclitaxel or docetaxel were applied

more often in our population (19% vs. <3%). This is in contrast with the clinical practice guidelines in the US and Europe recommending topotecan for patients eligible for second-line treatment in case of chemotherapy-resistant disease (Ardizzoni, 2004; Fruh et al.,; Rudin et al., 2015). Topotecan is the only second-line drug approved by the FDA (US Food and Drug Administration). One reason for this divergence from guidelines could be Netherlands based research of Groen et al. who observed a high response rate and mild toxicity of second-line carboplatin-paclitaxel in CDE-resistant SCLC patients (Groen et al., 1999).

A strength of this study is that it is based on a large unselected real-world population of patients diagnosed with ED SCLC, geographically spread over the Netherlands. In addition, this study is based on high-resolution data with a very low number of missing values.

The limitations of this study primarily relate to the retrospective nature of the data collection and the time frame under study (2008–2014), which can possibly affect the generalisability of our findings to present daily clinical practice. On the other hand, we captured a time frame of >7 years without any effect of calendar year on the findings. Recently, improved OS and PFS were reported with the addition of atezolizumab (Horn et al., 2018) or durvalumab (Paz-Ares et al., 2019) to chemotherapy in first-line compared to chemotherapy alone. The latest National Comprehensive Cancer Network (NCCN) guidelines included these chemo-immunotherapy regimens as a first-line option for ED SCLC patients (National Comprehensive Cancer Network®, 2019). Future studies capturing more recent years are needed to discover how these new treatment options find their way in routine practice. Furthermore, due to the retrospective nature of the data collection, some data items were not captured, for example, site of metastases and the use of radiotherapy. Consequently, a statement about the impact of radiotherapy and the localisation of metastases on treatment prognosis was not possible.

Our findings are of interest when designing clinical trials for future drugs under study for ED SCLC. We showed that the number of patients who will be eligible for a second and/or third line of systemic therapy is limited in real-world. Furthermore, insight in treatment patterns is helpful to payers when considering the budget impact (e.g. expected patient volume) of novel treatment options when they come available.

In conclusion, after first-line systemic treatment in ED SCLC the fraction of patients receiving subsequent lines of treatment is rapidly decreasing. This information is necessary as background for the evaluation of the added value of future drugs under study for ED SCLC.

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CONFLICT OF INTEREST

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REFERENCES

Ardizzoni, A. (2004). Topotecan in the treatment of recurrent small cell lung cancer: An update. *The Oncologist*, *9*(Suppl. 6), 4–13. https://doi.org/10.1634/theoncologist.9-90006-4

Byers, L. A., & Rudin, C. M. (2015). Small cell lung cancer: Where do we go from here? *Cancer*, *121*, 664–672. https://doi.org/10.1002/cncr.29098

Carney, D. N. (2002). Lung cancer – Time to move on from chemotherapy. *New England Journal of Medicine*, *346*, 126–128. https://doi.org/10.1056/NEJM200201103460211

Cramer-van der Welle, C. M., Peters, B. J. M., Schramel, F., Klungel, O. H., Groen, H. J. M., van de Garde, E. M. W., & Santeon NSCLC Study Group. (2018). Systematic evaluation of the efficacy-effectiveness gap of systemic treatments in metastatic nonsmall cell lung cancer. *European Respiratory Journal*, *52*(6). https://doi.org/10.1183/13993003.01100-2018

Fruh, M., De Ruysscher, D., Popat, S., Crino, L., Peters, S., & Felip, E. (2013). Small-cell lung cancer (SCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*, *6*, vi99–vi105. https://doi.org/10.1093/annonc/mdt178

Groen, H. J., Fokkema, E., Biesma, B., Kwa, B., van Putten, J. W., & Postmus, P. E. (1999). Paclitaxel and carboplatin in the treatment of small-cell lung cancer patients resistant to cyclophosphamide, doxorubicin, and etoposide: A non-cross-resistant schedule. *Journal of Clinical Oncology*, *17*, 927–932. https://doi.org/10.1200/JCO.1999.17.3.927

Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009). Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics*, *42*, 377–381. https://doi.org/10.1016/j.jbi.2008.08.010

Horn, L., Mansfield, A. S., Szczesna, A., Havel, L., Krzakowski, M., Hochmair, M. J. … Liu, S. V. (2018). First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *New England Journal of Medicine*, *379*, 2220–2229. https://doi.org/10.1056/NEJMoa1809064

Janssen-Heijnen, M. L., Karim-Kos, H. E., van der Drift, M. A., Groen, H. J., Ho, V. K., Koning, C. & de Vries, E. (2012). Modest improvements of survival for patients with small cell lung cancer aged 45 to 59 years only, diagnosed in the Netherlands, 1989 to 2008. *Journal of Thoracic Oncology*, *7*, 227–232. https://doi.org/10.1097/JTO.0b013e3182370e4c

Lally, B. E., Urbanic, J. J., Blackstock, A. W., Miller, A. A., & Perry, M. C. (2007). Small cell lung cancer: Have we made any progress over the last 25 years? *The Oncologist*, *12*, 1096–1104. https://doi.org/10.1634/theoncologist.12-9-1096

National Comprehensive Cancer Network®. (2019). Clinical practice guidelines in oncology – Small cell lung cancer. Version 2.2020 - November 15, 2019. Retrieved from NCCN.org

Netherlands Comprehensive Cancer Organisation. (2019). Retrieved from www.cijfersoverkanker.nl. Accessed March 14, 2019.

Paz-Ares, L., Dvorkin, M., Chen, Y., Reinmuth, N., Hotta, K., Trukhin, D., … Williamson, M. (2019). Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): A randomised, controlled, open-label,

phase 3 trial. *Lancet*, *394*, 1929–1939. https://doi.org/10.1016/S0140-6736(19)32222-6

Peters, B. J. M., Cramer-Vd Welle, C. M., Smit, A. A. J., Schramel, F., & van de Garde, E. M. W.; Santeon NSCLC Study Group. (2017). Trends in prescribing systemic treatment and overall survival for non-small cell lung cancer stage IIIB/IV in the Netherlands: 2008–2012. *Cancer Epidemiology*, *51*, 1–6. https://doi.org/10.1016/j.canep.2017.08.001

Pietanza, M. C., Byers, L. A., Minna, J. D., & Rudin, C. M. (2015). Small cell lung cancer: Will recent progress lead to improved outcomes? *Clinical Cancer Research*, *21*, 2244–2255. https://doi.org/10.1158/1078-0432.CCR-14-2958

Povsic, M., Enstone, A., Wyn, R., Kornalska, K., Penrod, J. R., & Yuan, Y. (2019). Real-world effectiveness and tolerability of small-cell lung cancer (SCLC) treatments: A systematic literature review (SLR). *PLoS ONE*, *14*, e0219622. https://doi.org/10.1371/journal.pone.0219622

Rudin, C. M., Ismaila, N., Hann, C. L., Malhotra, N., Movsas, B., Norris, K., … Giaccone, G. (2015). Treatment of small-cell lung cancer: American Society of Clinical Oncology Endorsement of the American College of Chest Physicians Guideline. *Journal of Clinical Oncology*, *33*, 4106–4111. https://doi.org/10.1200/JCO.2015.63.7918

Steffens, C. C., Elender, C., Hutzschenreuter, U., Dille, S., Binninger, A., Spring, L., … Marschner, N. (2019). Treatment and outcome of 432 patients with extensive-stage small cell lung cancer in first, second and third line – Results from the prospective German TLK cohort study. *Lung Cancer*, *130*, 216–225. https://doi.org/10.1016/j.lungcan.2019.02.026

Tendler, S., Zhan, Y., Pettersson, A., Lewensohn, R., Viktorsson, K., Fang, F., & De Petris, L. (2020). Treatment patterns and survival outcomes for small-cell lung cancer patients – A Swedish single center cohort study. *Acta Oncologica*, *59*(4), 388–394. https://doi.org/10.1080/0284186X.2019.1711165

van de Garde, E. M. W., Plouvier, B. C., Fleuren, H., Haak, E. A. F., Movig, K. L. L., Deenen, M. J., & van Hulst, M. (2019). Pharmacotherapy within a learning healthcare system: Rationale for the Dutch Santeon Farmadatabase. *European Journal of Hospital Pharmacy*, *26*, 46–50. https://doi.org/10.1136/ejhpharm-2017-001329

van Meerbeeck, J. P., Fennell, D. A., & De Ruysscher, D. K. (2011). Small-cell lung cancer. *Lancet*, *378*, 1741–1755. https://doi.org/10.1016/S0140-6736(11)60165-7

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APPENDIX

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TABLE A1 Baseline characteristics ED SCLC patients on start of first, second, or third line treatment

	All treated patients in first-line	All treated patients in second-line	All treated patients in third-line
Patients, *n* (%)	568	231	68
Age at diagnosis, median (min-max)	66 (39–88)	64 (39–83)	62 (46–81)
Male, *n* (%)	311 (55)	118 (51)	35 (51)
Comorbidities (CCI ≥ 1), *n* (%)	324 (57)	121 (52)	33 (49)
Missing	0	0	0
ECOG PS, *n* (%)			
0–1	411 (72)	182 (79)	58 (85)
≥2	138 (24)	42 (18)	9 (13)
Missing	19 (3)	7 (3)	1 (1)

Abbreviations: BSC, best supportive care; CCI, Charlson Comorbidity Index; CDE, cyclophosphamide-doxorubicin-etoposide; ECOG PS, Eastern Cooperative Oncology Group Performance Status.