



BRIEF REPORT

Symptoms and Experiences with Small Cell Lung Cancer: A Mixed Methods Study of Patients and Caregivers

D. Gwyn Bebb · Cressida Murray · Andromachi Giannopoulou · Enriqueta Felip

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ABSTRACT

Introduction: Understanding of the patient-perceived symptom burden of small cell lung cancer (SCLC) is limited. The objective of this study was to explore patients' experiences with SCLC, identify which treatment-/disease-related symptoms have the greatest impact on their well-being, and gain caregiver perspectives.

HumanBranding Inc., Toronto, ON, Canada, (Cressida Murray); Amgen (Europe) GmbH, Rotkreuz, Switzerland (Andromachi Giannopoulou): affiliation during the conduct of the study.

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D. G. Bebb (✉)
Global Development, Amgen, One Amgen Centre Drive, Thousand Oaks, CA 91320, USA
e-mail: dbebb01@amgen.com

D. G. Bebb
Cumming School of Medicine, University of Calgary, 3285 Hospital Drive, NW, Calgary, AB T2N 4N1, Canada

C. Murray
HumanBranding Inc., Toronto, ON, Canada

A. Giannopoulou
Amgen (Europe) GmbH, Rotkreuz, Switzerland

E. Felip
Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain

Methods: A noninterventional, cross-sectional, multimodal, mixed methods study was conducted from April–June 2021. Adult patients with SCLC and unpaid caregivers were eligible to participate. Patients' experiences, captured via 5-day video diaries and follow-up interviews, were scored 1–10 on how bothersome the patients perceived each symptom/symptomatic adverse event. Patients indicated if they believed a symptom was disease or treatment related. Caregivers participated in an online community board.

Results: The study included nine patients (five with extensive-stage [ES] disease, four with limited-stage [LS] disease) and nine caregivers. Except for one patient/caregiver pairing, patients and caregivers were unmatched. The most common impactful symptoms in patients with ES-SCLC were shortness of breath, fatigue, coughing, chest pain, and nausea/vomiting; in LS-SCLC, these were fatigue and shortness of breath. Among patients with ES disease, SCLC had a high impact on physical (leisure/hobbies, work, sleep, ability to do household chores and errands/responsibilities outside home), social (family dynamics, extrafamilial social interaction), and emotional (mental health) aspects. Patients with LS-SCLC faced the long-term physical effects of treatment, financial implications, and emotional toll of an uncertain prognosis. SCLC had a high personal and psychologic burden among caregivers, whose duties consumed much of their time. Caregivers observed similar symptoms and impacts of SCLC as those reported by patients.

Conclusions: This study provides valuable insight into patient- and caregiver-perceived burden of SCLC and can inform the design of prospective studies. Clinicians should seek to understand patients' opinions and priorities before making treatment decisions.

Keywords: Caregiver; Interview; Mixed methods; Patient-reported outcome; Qualitative; Small cell lung cancer

Key Summary Points

Why carry out this study?

Current understanding of the patient-perceived symptom burden of small cell lung cancer (SCLC) is limited

We conducted a noninterventional, cross-sectional, multimodal, mixed methods study to explore patients' experiences with SCLC, identify which treatment-/disease-related symptoms have the greatest impact on their well-being, and gain perspectives from patients' caregivers

What was learned from the study?

Data collected from online video diaries and webcam interviews highlighted that the symptomatic burden of disease in patients with SCLC is substantial. Patients with extensive-stage disease ($n = 5$) struggle with the physical, social, and emotional impact, whereas patients with limited-stage disease ($n = 4$) experience social and financial challenges

Based on data collected from online community boards, caregivers for those with SCLC ($n = 9$) experienced a high personal and psychologic burden, with caregiving duties consuming much of their time

This study provides valuable insight into the patient- and caregiver-perceived burden of SCLC, which may help to inform the design of future prospective studies. In clinical practice, clinicians should seek to understand patients' opinions and priorities to ensure that interventions are selected appropriately.

INTRODUCTION

Lung cancer causes approximately 20% of all cancer-related deaths, making it the world's most deadly form of cancer [1]. Small cell lung cancer (SCLC) is an aggressive subtype that accounts for ~ 15% of lung cancers and is strongly associated with smoking [2–4]. Approximately 30% of patients present with disease confined to one hemithorax (limited-stage [LS] disease), but most individuals have disease that cannot be encompassed within a single radiotherapy field (extensive-stage [ES] disease) [2, 3, 5].

The prognosis for patients with SCLC is poor, with a 5-year survival rate of ~ 6% typically reported [2, 6]. However, the duration of survival is affected by disease stage. Patients with LS-SCLC have median survival rates of up to 30 months and 5-year survival rates of approximately 15–30%, and some patients are treated with curative intent [2, 7, 8]. ES disease is deemed incurable and treatment is palliative in nature; median survival rates are reported to be in the range of 7–13 months [9–11].

Patients presenting with SCLC are likely to be experiencing symptoms, the profile of which depends on the location and size of the tumor(s) [2, 3]. The symptoms of localized disease include cough, wheezing, dyspnea, and hemoptysis. Approximately two-thirds of patients present with metastases affecting the contralateral lung, brain, liver, adrenal glands, bone, or bone marrow. Extrapulmonary disease may cause neurologic problems, nerve pain, fatigue, anorexia, and weight loss [2, 3].

Studies in advanced lung cancer have identified fatigue, dyspnea, depression, and anxiety as key symptoms associated with reduction in patients' quality of life (QoL) [12, 13]. However, our understanding of the patient-perceived symptom burden of SCLC is limited.

We performed a mixed methods study to (1) explore patients' experiences with SCLC, (2) identify which treatment- and disease-related symptoms have the greatest impact on patients' well-being, and (3) gain perspectives from caregivers of patients with SCLC on the impact of disease.

METHODS

This noninterventional, cross-sectional, multimodal, mixed methods remote research study was conducted in the USA between April and June 2021. Participants were recruited through professional qualitative recruiting firms via their advocacy connections and internal resources and through public and private social media groups. Interested candidates were screened for inclusion in the study as per the criteria listed below. The study was not restricted to any specific locations/regions in the USA, and data were collected via online platforms or telephonic interviews. In accordance with ethical practice and the requirements of most peer-reviewed journals, and to comply with human participant research requirements, ethics approval was obtained prior to the initiation of study procedures. The protocol was reviewed and approved by the Western Copernicus Group Institutional Review Board as well as the Amgen internal Observational Research Review Group, and the study was conducted in accordance with Good Clinical Practice. All study participants provided informed consent to participate in the study; participants were provided with a consent information sheet that clearly stated which data were being collected and that the data may be published. Patients also voiced their consent before participating in the study interviews. Each participant received financial compensation of \$150–300, with the exact amount based on the method of participation.

Patients

Patients aged ≥ 18 years with a self-reported clinical diagnosis of SCLC who received first-line treatment with a platinum-containing regimen (including cisplatin or carboplatin; also self-reported) were eligible to participate. They were required to understand, read, and speak English sufficiently to complete questionnaires and hold a conversation. To gather insights regarding the impact of disease on their daily lives, patients were asked to participate in an online video diary study. Patients were asked to keep a video diary for 5 days, designed to take

10–15 min at any point during the course of each day, and record the symptoms, thoughts, and feelings they were experiencing. Study participants were also asked open-ended questions about their disease history and treatments and the associated social, physical, and emotional impacts. Details of questions and activities are provided in resource 1 in the Supplementary Material. Upon completion of the online diary, each respondent participated in a 60-min follow-up interview, conducted via webcam. Details regarding answers provided in the video diary were requested. Patients assigned scores from 1 to 10 to their disease symptoms and symptomatic adverse events to indicate how bothersome each one was. Study participants were also asked whether they felt that their symptoms were an effect of the disease or treatment, and initial responses were checked via additional questions (e.g., regarding the timing of symptoms or changes in severity).

Caregivers

Individuals aged ≥ 18 years providing unpaid care for patients meeting the above inclusion criteria (either currently or if the patient had died within the preceding 12 months) were enrolled. To be designated a caregiver, an individual's duties had to include accompanying the patient to doctor visits and taking part in decision-making around medication. As with the patients, it was a requirement for caregivers to understand, read, and speak English sufficiently to complete questionnaires and hold a conversation. Each caregiver was asked to join a 5-day online caregiver community board (30 min per day), where they could read responses of other caregivers and interact with each other. Details of activities/questions are provided in resource 2 in the Supplementary Material.

Patients and Caregivers

In addition to the activities described above, webcam interviews were conducted with one patient and caregiver pair to bring together perspectives from the two groups. The patient

Table 1 Patients' baseline and disease characteristics

Characteristic	Overall (<i>N</i> = 9)	Extensive-stage patients (<i>n</i> = 5)	Limited-stage patients (<i>n</i> = 4)
Age (years), mean (range)	58 (47–69)	52.6 (47–63)	65.3 (59–69)
Sex, <i>n</i> (%)			
Female	6 (67)	4 (80)	2 (50)
Male	3 (33)	1 (20)	2 (50)
Metastatic sites, <i>n</i> (%)			
Contralateral lung	4 (44)	4 (80)	–
Liver	1 (11)	1 (20)	–
Brain	1 (11)	1 (20)	–
Lymphatic system	1 (11)	1 (20)	–
Time since diagnosis, <i>n</i> (%)			
< 6 months	2 (22)	1 (20)	1 (25)
6–12 months	1 (11)	1 (20)	–
1–2 years	1 (11)	1 (20)	–
2–3 years	1 (11)	1 (20)	–
4–5 years	1 (11)	–	1 (25)
≥ 5 years	3 (33)	1 (20)	2 (50)
Current treatment, <i>n</i> (%)			
Chemotherapy	2 (22)	1 (20)	1 (25)
Chemotherapy + radiation	1 (11)	1 (20)	–
Chemotherapy + radiation + pembrolizumab	1 (11)	1 (20)	–
Atezolizumab (maintenance)	1 (11)	1 (20)	–
None	4 (44)	1 (20)	3 (75)
Prior treatment, <i>n</i> (%)			
Chemotherapy + atezolizumab	1 (11)	1 (20)	–
Chemotherapy + radiation + IO ^a	3 (33)	3 (60)	–
Surgery + chemotherapy then pembrolizumab ^b	1 (11)	–	1 (25)
Surgery + chemoradiotherapy ^c	2 (22)	–	2 (50)
None	1 (11)	1 (20)	–
Total lines of SCLC treatment received (prior plus current therapies), <i>n</i> (%)			
1	4 (44)	1 (20)	3 (75)
≥ 2	5 (56)	4 (80)	2 (50)

IO immuno-oncology drug, SCLC small cell lung cancer

^aPembrolizumab (*n* = 2), unconfirmed "IO" (*n* = 1)

^bPatient received pembrolizumab + unconfirmed therapy as second-line therapy

^c*n* = 1 patient subsequently received chemoradiotherapy as second-line therapy

and caregiver pair was scheduled to undertake this 90-min activity once.

Data Analysis

For qualitative analyses, a grounded theory approach was employed using open, axial, and selective coding [14, 15]. Interview transcripts were open coded and analyzed qualitatively using the Atlas.ti software. Two coders coded the first two transcripts and then compared and reconciled codes to ensure consistency. Throughout the analysis process, all codes were compared, discussed, and reconciled wherever there were differences. Coders maintained a catalog of codes used to ensure consistency while allowing for emergent codes to be added. An interim analysis of the first four video diaries/follow-up interviews was conducted and used to update and refine the discussion guide. Subsequently, increased focus was placed on exploring the most bothersome symptoms and the effects of these symptoms on daily life. Numerical data are presented descriptively and no statistical comparisons were undertaken.

RESULTS

The study included nine patients, five with ES and four with LS disease, and nine caregivers. Eight patients completed the 5-day online video diary and 60-min webcam interview, and all caregivers completed the 5-day community board. One patient/caregiver pairing participated in the web ethnographic exercise; this patient had LS disease and did not complete the video diary and webcam interview. All other patients and caregivers were unmatched.

Patients

As shown in Table 1, this study included a small sample of predominantly female (67%) patients with SCLC aged 47–69 years with either ES ($n = 5$) or LS ($n = 4$) disease. Four of five patients with ES disease had metastases in the contralateral lung; one patient each had metastases in the liver, brain, or lymphatic system.

Among the patients with ES disease, time since diagnosis ranged from < 6 months to ≥ 5 years, and most (4/5) were currently receiving treatment. Three of the five patients with ES disease were receiving chemotherapy, with or without concomitant palliative radiotherapy to symptomatic sites of metastasis; one was receiving a checkpoint inhibitor as maintenance therapy; the other was awaiting test results to determine whether they would undergo further immunotherapy or chemotherapy. By contrast, three of the four patients with LS disease had been diagnosed ≥ 4 years earlier and had responded successfully to therapy; these three patients were not receiving active treatment. Two of these three patients had previously received chemoradiotherapy, and the other patient chemotherapy alone. The fourth patient with LS disease had been diagnosed < 6 months earlier and was currently receiving chemotherapy (carboplatin plus etoposide).

Symptoms

The most common patient-reported symptoms are presented in Fig. 1. The patients considered shortness of breath, coughing, and chest pain as disease symptoms, while nausea, vomiting, and diarrhea were perceived as treatment-related adverse events. Fatigue was regarded as either a disease symptom or a treatment-related adverse event.

The most common impactful symptoms in patients with ES disease were shortness of breath, fatigue, coughing, chest pain, and nausea/vomiting. Shortness of breath was a fairly constant symptom, although it worsened with exertion and could be exacerbated by coughing. Patients described trouble getting enough oxygen, difficulty taking deep breaths, and impaired mobility. Two patients reported using oxygen tanks. Patients with ES disease commented on their shortness of breath as follows:

“The shortness of breath is always, always, always there with any type of exertion at all (sometimes accompanied by coughing)... even though it’s very bothersome, it’s something I can relieve more easily than the coughing: I can sit down and rest.”

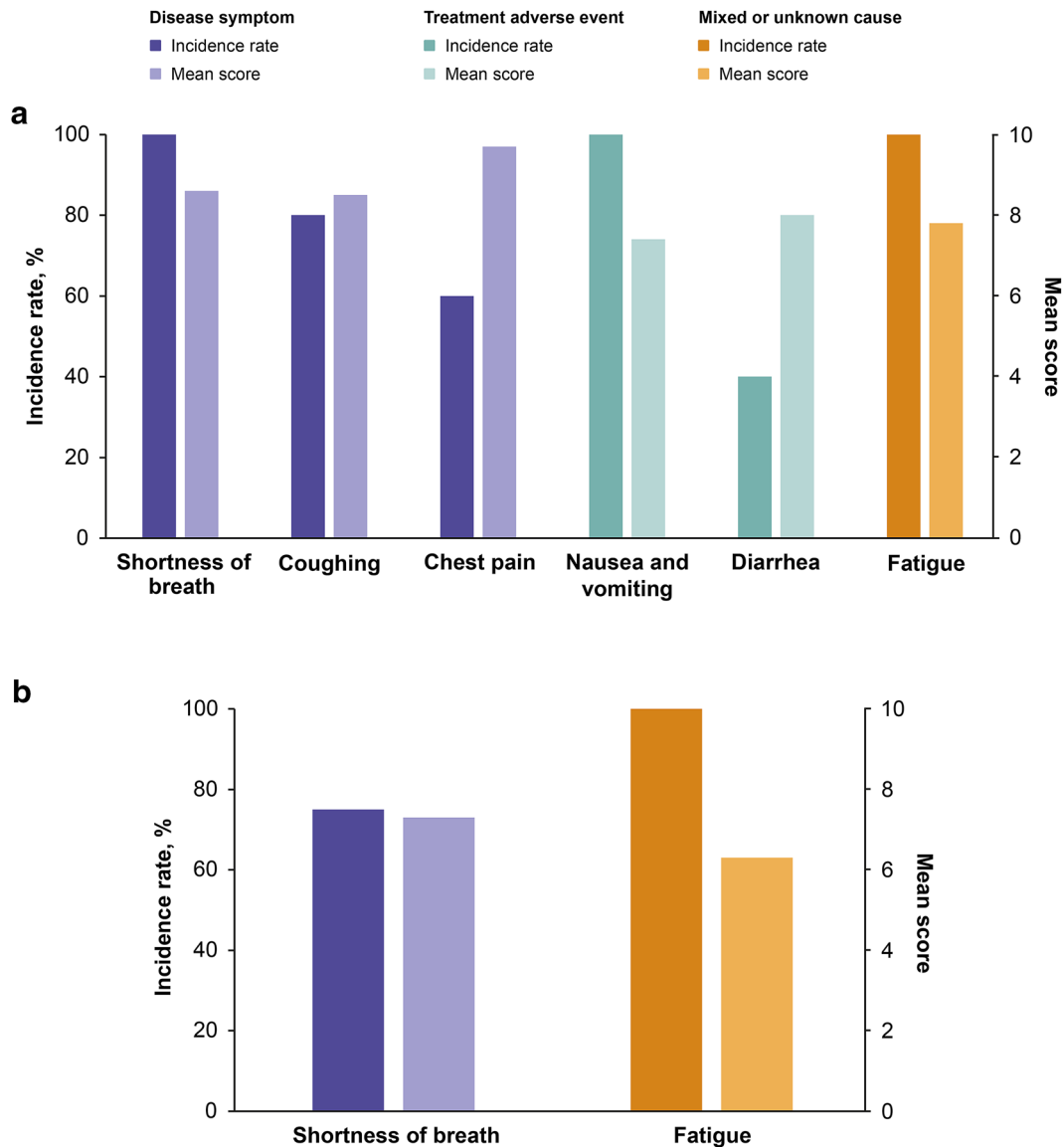


Fig. 1 Patient-reported symptoms: extensive-stage disease (a) and limited-stage disease (b). Mean scores are for patients reporting the symptom; scale from 1 to 10 (10 being most bothersome). All symptoms reported by > 1 patient are shown. Note that data are subjective; a standardized scale was not used and patients were all at different points in their journey (i.e., on different treatments and with varying time since diagnosis). Additional symptoms (reported by one patient with extensive-stage disease each) comprised: disease symptoms—pain

swallowing, coughing blood; treatment adverse events—hot flashes, cold extremities, toileting difficulties (constipation, trouble urinating), hair loss, port area pain and discomfort, change in taste; and symptoms of mixed or unknown cause—hazy/drugged feeling, pain in bones, dizziness, jerking and cramping of muscles, lack/loss of appetite, back pain. Additional symptoms (reported by one patient with limited-stage disease each) comprised: disease symptoms—difficulty swallowing, voice loss/change; and treatment adverse event—neuropathy

“I’m always feeling like suffocating. [My mobility is] very restricted. Around the house, it’s a very long walk from my bedroom to the kitchen.”

Fatigue was experienced by all patients with ES disease and was generally very bothersome and a daily occurrence. Patients described two different types of fatigue that could co-exist: body/bone tired and drowsiness/sleepy feeling. The major impacts of fatigue were lack of willpower, inability to do simple things, and changed self-perception. Other symptoms/side effects (e.g., coughing, vomiting, diarrhea) could worsen fatigue. Examples of comments from patients with ES disease on fatigue are:

“Never having energy to do the things you want to do. When planning to do something on a certain day, meet somebody for lunch or something, it sounds like a really good idea, and then when the time comes, you’re simply too tired to do it.”

“I just don’t have the energy to do anything that normally I love doing.”

“It just kills your spirit and your motivation in life.”

Coughing was experienced by four patients with ES disease and was highly bothersome and a daily occurrence. Patients described how coughing disturbed their sleep, caused pain or soreness, and worsened fatigue and shortness of breath. Half of patients reported coughing up blood, while in some patients coughing led to urinary incontinence and vomiting. Patients also found coughing not socially acceptable, especially during the COVID-19 pandemic. Examples of patients’ comments on coughing are:

“(Coughing) always takes, it seems, like every bit of energy you even have left, so yes, it reflects on your life in such a direct drastic way because it just takes the life itself from your body.”

“This symptom happens daily. I cough a lot, but to this extreme varies. To cough this much is very bothersome. It causes me a lot of pain and discomfort, shortness of breath. It causes me urinary incontinence. I would say it happens every day, several times a day. It’s one of my more bothersome symptoms... You know,

it prevents me from sometimes stepping outside... from completing a shopping trip... I have to stop phone calls, phone conversations have to end sometimes.”

Chest pain was experienced by three patients with ES disease who found it extremely bothersome; for two patients, chest pain was their most bothersome symptom. Patients described chest pain as very acute and could feel like they were being stabbed in the chest or having a heart attack. Chest pain could be exacerbated by coughing. An example of a patient’s description of chest pain:

“When you’re in pain you can’t worry about your energy or anything when you are in pain. That’s what you are concentrating on. You are in pain. Nothing else basically matters.”

Nausea, with or without vomiting, was experienced by all patients with ES disease who were receiving treatment (as described above, treatment was mostly chemotherapy). Diarrhea was experienced by two patients, both of whom were on treatment. Descriptions of gastrointestinal symptoms reported by patients with ES disease included:

“I had some nausea [when on chemotherapy]. The nausea was very uncomfortable. They gave me medicine for it, but the medicine made me sleepy, so it was a toss-up.”

“In the 2 days after I get chemotherapy, [the diarrhea is] constant. Now I have diapers that I wear when we go outside to appointments, especially if it is more than an hour. It’s embarrassing.”

In patients with LS disease, fatigue and shortness of breath were the most common impactful symptoms. Fatigue, experienced by all LS respondents, was generally very bothersome and was often a daily occurrence. This was particularly difficult for this patient group as fatigue impacted their ability to continue to work; it was frustrating and impacted them financially and emotionally. Patients with LS disease said the following about their fatigue:

“I had no energy to walk. I almost needed a wheelchair to help me get to a chemotherapy

appointment, and it wasn't a long walk either."

A patient not currently receiving treatment described their fatigue while on chemotherapy/radiation as follows:

"The [lack of] energy bothers me because I feel useless and that I can't do as much as I would like. It just puts everything behind and builds anxiety about not being able to get things done."

Three of the four patients with LS disease underwent surgery as part of their curative intent treatment and this resulted in shortness of breath. All three of these patients reported difficulty bending over, saying this would cause them to lose their breath:

"The inability to breathe deeply disturbs me a lot. Breathing is important to me for meditation, Tai Chi, and when I'm gardening. It seems like I have this issue more when I'm bending down."

"I'm more comfortable sitting or kneeling than bending over, it constricts your diaphragm and makes it a little more difficult to breathe."

Physical, Social, and Emotional Impact of the Disease

SCLC had a high physical, social, and emotional impact in patients with ES disease (Fig. 2). It also had a substantial impact in patients with LS disease, but the nature of that impact was different. With a longer life expectancy at diagnosis, patients with LS disease were concerned with matters such as the long-term effects of treatment on their bodies and the impact of the disease on their finances. By contrast, patients with ES disease—who knew that their prognosis was poor—instead missed simple everyday activities like playing with their grandchildren or going to the grocery store. The inability to participate in hobbies was also particularly bothersome for patients with ES disease as they wanted to spend the time they had left doing the activities they enjoyed, particularly outdoor activities that allowed them to get out in nature.

In all, five physical aspects were impacted substantially in patients with ES disease (i.e., impaired in ≥ 2 patients): leisure and hobbies,

work, sleep, ability to do household chores, and ability to complete daily errands and responsibilities outside home. Fatigue and shortness of breath generally prevented patients with ES disease from participating in these activities, as they had impaired mobility and decreased motivation/willpower. Disrupted sleep was another bothersome impact. Most patients with ES disease did not get a full night's sleep, potentially affecting their activities the next day. Symptoms such as coughing and chest pain or treatment side effects (e.g., hot flashes) kept them up at night; anxiety could also keep them awake.

Two social aspects were impacted substantially among patients with ES disease: family dynamics and extrafamilial social interaction. Respondents felt they were not able to participate in family activities like playing with grandchildren or being a good parent/grandparent/partner. They also felt they sometimes had to pretend to their families that they were fine. Outside of their families, respondents tended to retreat socially because of lack of energy and willpower or embarrassment at appearing in their current state (e.g., someone with low energy, who coughs all the time, or who has to wear diapers).

All ES respondents experienced emotional effects, and these effects were amplified in patients who had not achieved success with treatment. Mental health in particular was impacted substantially among ES respondents. The patients were afraid of dying and reported difficulties coming to terms with this. They understood that treatments were not curative, and most just hoped to go into remission as a means of gaining more time. They also expressed sadness and aggravation about the quality of their lives. The impact of treatment was considered worthwhile by the majority of patients if it gave them more time, although they also wanted to be independent.

With longer life expectancy at diagnosis, patients with LS disease face different challenges. These include long-term physical effects of treatment, the financial impact of the disease, and the emotional toll of an uncertain prognosis (e.g., if in remission, there remains a risk of the cancer returning). Most LS respondents struggled with being unable to work at

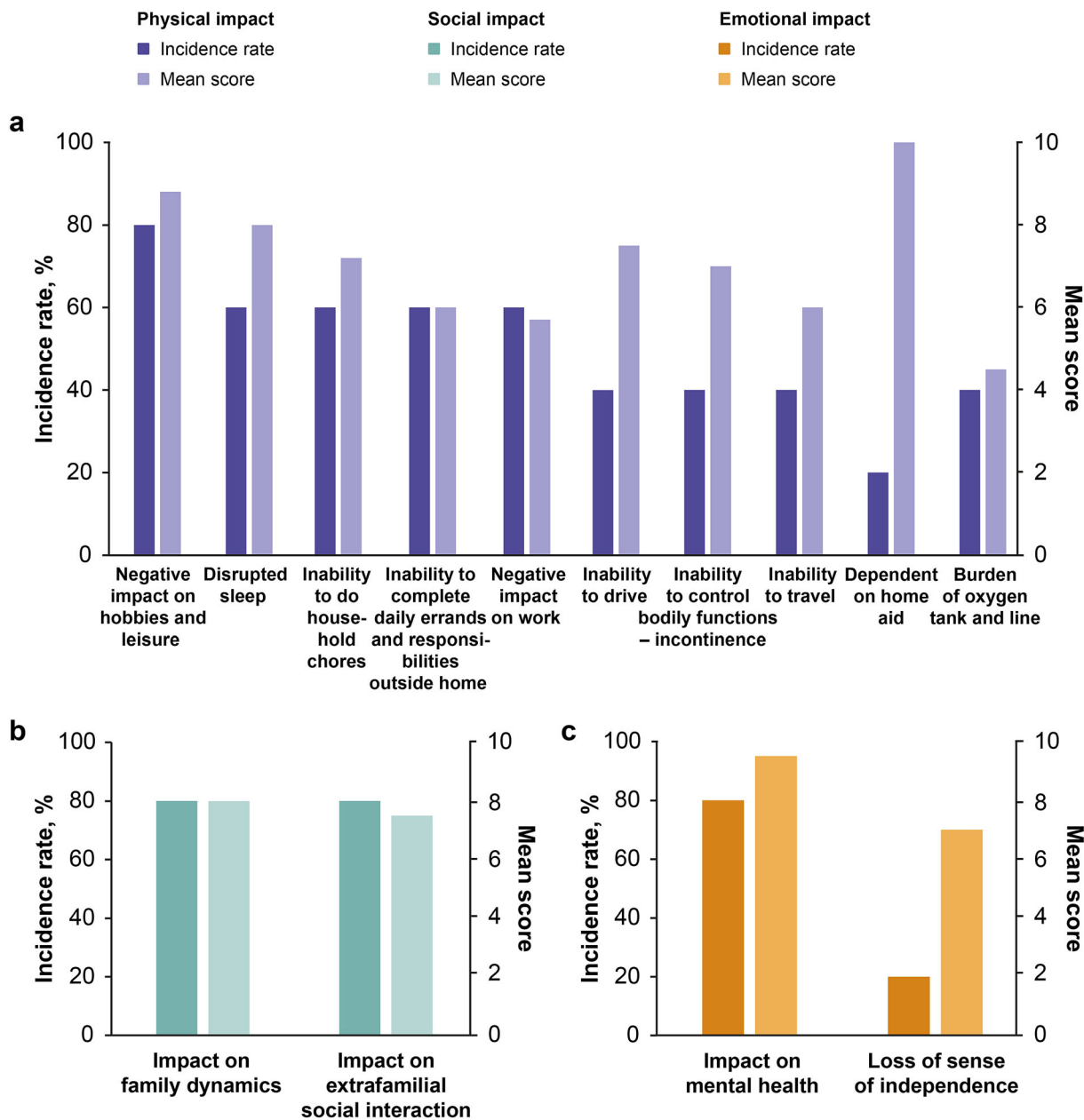


Fig. 2 Impacts on patients with extensive-stage disease: physical (a), social (b), and emotional (c). Mean scores are for patients reporting the impact; scale from 1 to 10 (10 being high impact)

the same capacity as they did before their diagnosis. Some were forced to resign from their jobs because of symptoms they experienced. This presented particular difficulties as they often did not know how long a future they needed to plan for. The social impact of their condition was mentioned by the majority of LS respondents who reported that the diagnosis of

SCLC caused them to lose friends, resulting in feelings of isolation and loneliness.

Caregivers

Caregivers included in the study were mostly female (7/9; 78%), aged 28–67 years; all were unpaid relatives of the patients (Table 2). Six of

Table 2 Caregivers' baseline characteristics

Characteristic	Value (<i>N</i> = 9)
Sex, <i>n</i> (%)	
Female	7 (78)
Male	2 (22)
Relationship, <i>n</i> (%)	
Husband or wife of patient	3 (33)
Son or daughter of patient	6 (67)
Disease stage of the patient, <i>n</i> (%)	
Extensive	5 (56)
Limited	4 (44)
Time since diagnosis for the patient, <i>n</i> (%)	
< 6 months	3 (33)
6–12 months	2 (22)
1–2 years	2 (22)
2–3 years	0
4–5 years	1 (11)
≥ 5 years	1 (11)

the nine individuals were the son or daughter of the patient, and the remaining three were the patient's spouse. The caregivers' roles differed by SCLC stage. Those caring for patients with ES disease had an active role, often living with the patient. Those caring for patients with LS disease had a more supportive role, only living with the patient if they were their spouse.

SCLC carried a high personal and psychologic burden among the caregivers. Caregiving duties (particularly for patients with ES disease) were sometimes overwhelming, and although none of the interviewed caregivers left employment specifically to care for their patient, they wished they had more time for their careers, families, and hobbies. This

triggered feelings of hidden resentment and associated guilt. Specific comments included:

"My emotional well-being and social life have been hit hard by the diagnosis and caring duties. I try to always be there, but I have a life and kids of my own so it can be very challenging to juggle everything."

"Sometimes I'm frustrated about how much time and effort I have to put into being a caregiver and the sacrifices I have to make with my immediate family, my children, and my friends. This secret makes me feel guilty because I'm not the one fighting for my life with a cancer diagnosis."

Caregivers of patients with ES disease observed similar symptoms and impacts of SCLC on the patients as those reported by the patients themselves. Observed symptoms included shortness of breath, fatigue, and weakness. The caregivers commented on disease symptoms and impacts as follows:

"Every day is a challenge and a reminder that his situation is serious. Getting out of breath, feeling weak, fatigued, and sometimes hopeless."

"Lung cancer has taken away my loved one's ability to be independent. They isolate themselves and experience a lot of shame and guilt."

"It was extremely difficult for him to walk. Not only were his feet very swollen, but he was also very out of breath and couldn't go more than a few steps without becoming out of breath. He was very frustrated."

The greatest physical impacts of fatigue and shortness of breath experienced by patients with LS disease were corroborated by all caregivers. Fatigue was considered one of the biggest impacts of the disease, and shortness of breath affected their loved one's ability to perform simple activities such as climbing stairs, doing chores, and showering. The caregivers also commented on a reduced ability to participate in their own social lives and their emotional impact, such as anger, frustration, and being unable to do the things they wanted/needed to do.

Cancer-Focused Patient-Reported Outcome Instruments

Many of the core concepts identified in this study are captured by existing cancer-focused patient-reported outcome (PRO) instruments, such as the European Organization for Research and Treatment of Cancer 30-item Quality of Life Core Questionnaire (EORTC QLQ-C30) and European Organization for Research and Treatment of Cancer 13-item Quality of Life Questionnaire-Lung Cancer Module (EORTC QLQ-LC13; Table 3).

DISCUSSION

This study shows that, for patients with SCLC, the symptomatic burden of disease (particularly ES disease) is significant, with a number of highly bothersome symptoms that impact them physically, emotionally, and socially. The principal goal in SCLC management should be to allow patients to do more of what is important to them in the time they have left. Differences were observed between patients with LS and ES disease regarding the most burdensome symptoms and impacts on well-being; this may be attributable to differences in disease extent at diagnosis, the longer life expectancy of patients with LS disease, and the differences in treatment approaches. SCLC also had a high personal and psychologic burden among caregivers, whose duties consumed much of their time. Caregivers observed similar symptoms and impacts of both ES- and LS-SCLC as those reported by patients.

At the time of the study, two of the four patients with LS disease had completed chemoradiotherapy and one patient had completed chemotherapy. One patient with LS disease and three of the five patients with ES disease were receiving chemotherapy. One patient with ES disease was receiving atezolizumab maintenance therapy and the other was not receiving any treatment (awaiting test results). Most study participants thought that the impact of treatment would be worthwhile if it gave them more time. This is an important consideration when making

treatment decisions in SCLC. Determining the effect on survival is a priority when developing new treatments for SCLC and, consequently, overall survival is commonly chosen as the primary endpoint in clinical trials. However, patients also expressed a desire for regaining a level of independence and the ability to continue their life as close to normal as possible. A range of specific (sometimes seemingly mundane) activities and tasks are fundamental to patients' lives (e.g., playing with grandchildren, walking a dog, going to a grocery store independently), and these may be more meaningful for maintaining stability than clinicians would expect. The majority of patients, whether they had LS or ES disease, hoped that the treatments they received would improve not only their survival but also their QoL and ability to do the things that they enjoyed most. This is an important insight of this study, indicating that time in remission also matters to patients and suggesting that duration-of-response data from clinical trials should be a key consideration when making patient-centric treatment decisions. Furthermore, treatment toxicity and potential adverse events that most often impact patients' QoL should also be considered when making treatment decisions.

The overall symptom profiles and treatment methods encountered in this study are similar to those identified for non-small cell lung cancer (NSCLC) [16], despite differences in disease course between the two lung cancer subtypes that can translate into differences in disease severity and QoL [17, 18]. As a result, some similarities in disease burden and the perspectives of patients with SCLC and NSCLC may be expected.

The overall burden of SCLC reported in our study appears comparable to that reported for NSCLC. French, German, and US patients with advanced NSCLC reported symptom burden characterized by fatigue, loss of appetite, shortness of breath, cough, and pain [19, 20]. These symptoms were significant predictors of impairment in QoL, as assessed by the Functional Assessment of Cancer Therapy-Lung (FACT-L) total score. The importance of symptoms as an influence on QoL (physical and mental dimensions) in NSCLC was confirmed in

Table 3 Inclusion of core concepts identified in this study within existing cancer-focused PRO instruments

PRO instrument	Disease symptoms			Treatment adverse events			Physical function	
	Shortness of breath	Coughing	Chest pain ^a	Fatigue	Nausea/vomiting	Diarrhea	Disrupted sleep	Inability to participate in hobbies
EORTC QLQ-C30	✓	×	×	✓	✓	✓	✓	✓
EORTC QLQ-LC13	✓	✓	✓	×	×	×	×	×
FACT-L	✓	✓	×	✓	✓	×	✓	✓
LCSS	✓	✓	×	✓	×	×	×	✓
MDASI-LC	✓	✓	×	✓	✓	×	✓	×

EORTC QLQ-C30 European Organization for Research and Treatment of Cancer 30-item Quality of Life Core Questionnaire, *EORTC QLQ-LC13* European Organization for Research and Treatment of Cancer 13-item Quality of Life Questionnaire-Lung Cancer Module, *FACT-L* Functional Assessment of Cancer Therapy-Lung, *LCSS* Lung Cancer Symptom Scale, *MDASI-LC* MD Anderson Symptom Inventory for Lung Cancer, *PRO* patient-reported outcome

^aMost PRO instruments measure “pain” rather than “chest pain”

a Korean study [21]. A European NSCLC study published in 2019 showed that patients’ health utility, work productivity, activity, and health-related QoL deteriorated in line with their functionality, as measured by the Eastern Cooperative Group Performance Status [22]. Caregivers were also included in this study; they too reported QoL impairment (including reduced work-related activity) that was influenced by their patients’ functional status [22]. In 2015, LeBlanc et al. reported that functional concerns (physical movement or functioning) were most bothersome among patients with NSCLC and that the overall symptom burden increased with patients’ proximity to death [23]. A more recent survey of the patient-perceived burden of NSCLC showed that fear, anxiety, and depression had prevalence rates of 20–44% and that professional status and household finances were affected [24]. In a Chinese study of patients with NSCLC, efficacy was identified as the most important treatment attribute [25]. However, this study and others also show that treatment preferences among patients with NSCLC are influenced by other treatment attributes as well, such as toxicity/side effects, cost, and dosing regimen/mode of

administration [25–30]. Treatment preferences among patients with NSCLC have been reported to be also influenced by the severity of disease symptoms and prior treatment experience [28–30]. These data from studies in patients with NSCLC thus appear consistent with the findings of our study, supporting the existence of parallels between the two diseases. Patients may consider several trade-offs before making a treatment decision, and patients’ perspectives may differ according to clinical circumstances.

The parallels between the two diseases in terms of symptom burden as suggested by the existing literature are supported by our study. This provides additional confirmation that the use of validated, established PRO questionnaires common in NSCLC continues to be relevant in capturing the QoL in patients with SCLC. Of interest is the emerging paradigm of SCLC that has developed from epidermal growth factor receptor (*EGFR*)-positive NSCLC. Such transformation accounts for *EGFR* tyrosine kinase inhibitor resistance in 4–15% of *EGFR*-positive NSCLC cases [31, 32]. It may be that the biggest difference in patient experience will, in future, lie between those with driver mutation-positive disease that can be managed with well-tolerated

oral agents and those with driver mutation-negative disease whose only current option is more toxic chemotherapy or radiation therapy.

As shown in Table 3, existing lung cancer PRO instruments capture many of the core concepts identified in this study. Combined use of the EORTC QLQ-C30 and EORTC QLQ-LC13 may enable the best assessment of the main symptoms and adverse events while also measuring QoL. Notably, both of these instruments have been validated in SCLC [33–35].

We acknowledge that this study has several limitations. First, the research was mostly qualitative in nature, and this limits the scope for statistical robustness. Second, the sample was small, meaning that some patient characteristics (e.g., three of the four patients with LS disease undergoing surgery) may not reflect the majority of patients' experience in the wider population. Recruitment into studies such as this can be challenging, potentially because many patients with SCLC are at an advanced stage of disease, with overall survival rates measured in months; these patients are less likely to participate in the activities that would lead to their identification (e.g., via advocacy organizations), or they may be too ill or unwilling to participate. Except for one pair, the caregivers in our study were not caring for the patients who were included. Also, the symptom scores were subjective and therefore may not accurately reflect the true intensity of symptoms experienced by the patients. Likewise, the classification of symptoms as being disease related versus treatment related was based on patient opinion as opposed to any standardized scale. In addition, patients with LS disease may have completed treatment several years prior to participating in the study, meaning that recall bias may have affected the data on treatment-related symptoms; similarly, the overall outlook in patients surviving for many years may potentially influence their responses. Finally, since follow-up interviews were not performed with caregivers, numerical data (i.e., rating scores) were not available for this sample. Despite the limitations, consistencies and logic within the data (e.g., alignment in the symptoms and impacts of SCLC reported by caregivers and patients) lend confidence to the

findings. Importantly, the long-term consequences of curative treatment are captured in the experience of patients with LS disease who, despite the cure, continue to describe disease- and treatment-related limitations. Further confidence arises from the consistency of our findings with previous studies conducted in patients with both SCLC and NSCLC (described above).

CONCLUSION

This study provides valuable insights into the patient-perceived burden of SCLC as well as caregiver perspectives on the burden of SCLC on patients and themselves, which may help shape studies of novel therapies. In clinical practice, clinicians must invest time to understand the views of each patient to ensure that interventions are selected appropriately. A patient-centered approach will enable the overall management of SCLC to be optimized.

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requirements, ethics approval was obtained prior to the administration of study procedures. The protocol was reviewed and approved by the Western Copernicus Group Institutional Review Board as well as the Amgen internal Observational Research Review Group, and the study was conducted in accordance with Good Clinical Practice. All study participants provided informed consent to participate in the study; they were provided with a consent information sheet that clearly stated which data were being collected and that data may be published. Patients also voiced their consent before participating in the study interviews.

Data Availability. The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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