Real-World Outcomes in Third-Line and Beyond in Patients with Small Cell Lung Cancer: A Systematic Literature Review

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INTRODUCTION

- Small cell lung cancer (SCLC) accounts for approximately 15% of all lung cancer cases.[1,2]
- Most patients with SCLC receive and respond to first-line platinum-based chemotherapy. However, the responses are short-lived, and these patients often experience progression within the first year of treatment.[1,2]
- Patients with disease progression or resistance to first-line therapy have limited treatment options and a poor prognosis.[3]
- There is currently no established treatment for the third line and beyond (3L+) setting.

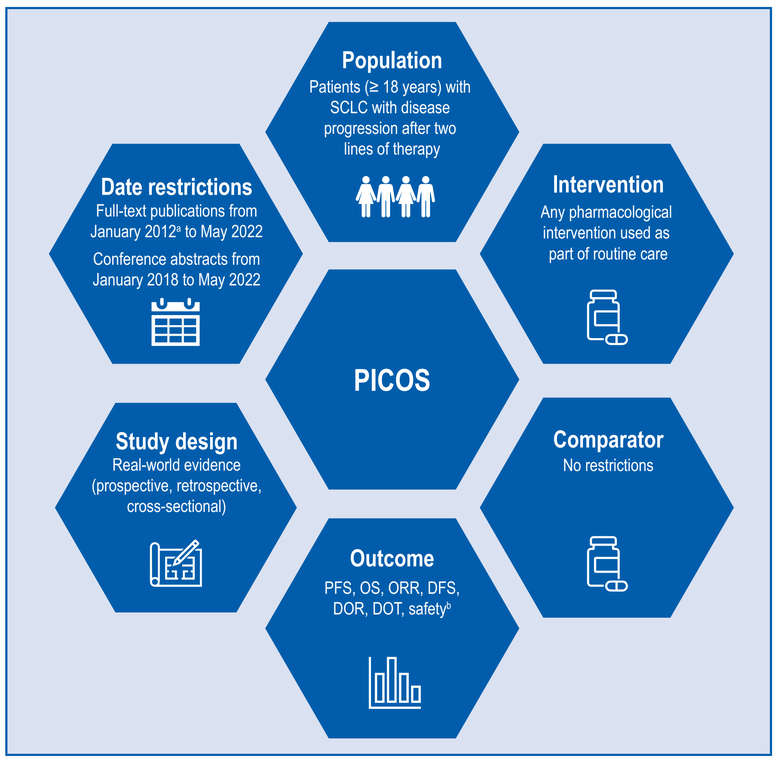
OBJECTIVE

- The objective of this systematic literature review (SLR) was to understand the clinical effectiveness of pharmacological treatments currently utilized in real-world clinical practice for patients with 3L+ SCLC, with a focus on North American and European populations.

METHODS

- The SLR was conducted following methodological guidance from the Centre for Reviews and Dissemination and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).
- Searches and study selection were performed according to predefined Population, Intervention, Comparison, Outcomes and Study design (PICOS) eligibility criteria (**Figure 1**).
- Searches were conducted on 9 May 2022 using the OVID platform in the Embase, MEDLINE, and Cochrane Library databases, complemented by hand searches to identify conference abstracts and other publications not indexed in the above databases.
- Eligible studies were selected by two independent researchers (double-blind) during both title and abstract screening and full-text review.
- Data were extracted by one researcher and validated by a second researcher.

Figure 1. PICOS Eligibility Criteria



[a] 10-year restriction was applied to promote the identification and selection of an evidence base that is relevant to the modern treatment context. [b] DFS, DOR, DOT, and safety were included in the scope of this SLR but are not reported here.
DFS, disease-free survival; DOR, duration of response; DOT, duration of treatment; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PICOS, Population, Intervention, Comparison, Outcomes and Study design; SCLC, small cell lung cancer; SLR, systematic literature review.

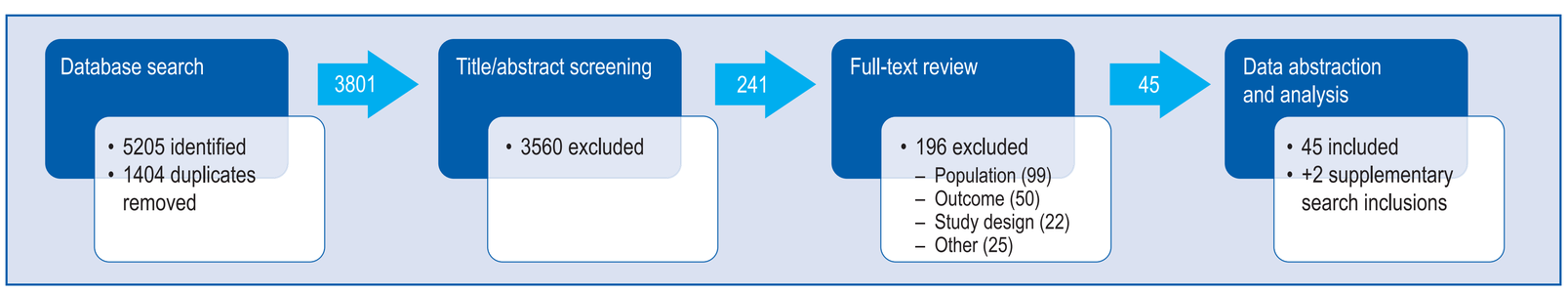
RESULTS

- Database searches returned 5205 records, of which 46 studies (47 publications) met the inclusion criteria and were included for data extraction (**Figure 2**).
- Most studies were conducted in Asia (n = 26, 57%), and other locations were as follows: Europe (n = 13, 28%), North America (n = 5, 11%), and international (n = 2, 4%).
- The focus of this poster is the 20 studies that were conducted in North America and Europe, including the 2 international studies. All studies apart from 1 report data from a 3L setting.

Characteristics of studies conducted in North America and Europe

- In 18 studies that reported prior treatment with platinum-based chemotherapy, most patients received it as first-line therapy (range, 68–100%).
  - In 1 study all patients were platinum-sensitive.[4]
- The study populations were generally small (range, 23–679 patients); 15 studies (75%) reported outcomes for fewer than 100 patients and 8 studies (40%) for fewer than 50 patients.
- Only 8 out of 20 studies reported baseline characteristics specifically for the 3L+ population, and a wide range for Eastern Cooperative Oncology Group performance status 0–1 was observed (58–91%). The presence of brain metastasis was reported in only 1 study.
- 3L+ treatments varied widely, with studies reporting data for patients receiving: topotecan or topotecan-based regimens (6 studies); platinum-based chemotherapy (6 studies); and cyclophosphamide, doxorubicin, and vincristine; adriamycin, cyclophosphamide, and vincristine; and lurbinectedin (1 study each). Two studies reported data on patients receiving best supportive care.

Figure 2. PRISMA Flow Diagram



PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Clinical outcomes for North American and European populations in the 3L+ setting

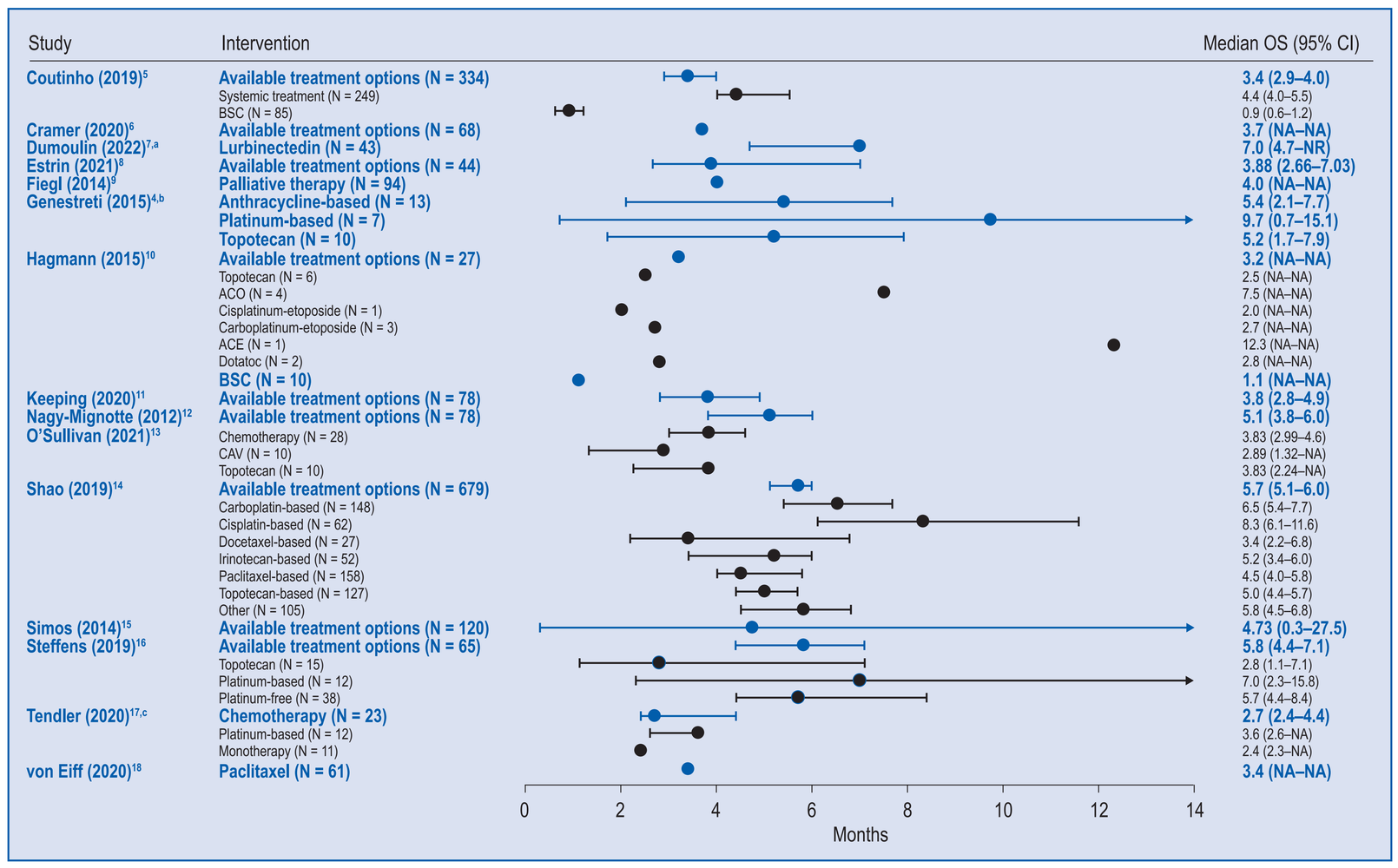
- On a study level, the median overall survival (OS) ranged from 2.7 to 7.0 months (14 studies)[5–18] for patients receiving active treatment. Median progression-free survival (PFS) ranged from 1.3 to 3.4 months (10 studies),[5–7,9,10,15–17,19,20] and objective response rate (ORR) from 7.7% to 21.3% (12 studies).[5,7,9,10,12,15,16,18,20–23]
- In the subgroup of patients with platinum-sensitive SCLC, outcomes were slightly numerically higher than the overall population with median OS ranging between 5.2 and 9.7 months and median PFS ranging between 1.7 and 5.0 months.[4] However, the results should be interpreted with caution owing to small population sizes (range, 7–13).
- OS, PFS, and ORR by specific treatment are shown in **Table 1**. The 15 studies reporting OS are shown in **Figure 3**.

Table 1. Clinical Outcomes Across Studies According to Selected Treatment Regimens

Treatment	Ranges across studies			
	N	Median OS, months	Median PFS, months	ORR, %
Topotecan or topotecan-based	6–127	2.5–5.2 (5 studies)[4,10,13,14,16]	1.4–3.2 (4 studies)[4,10,16,19]	0–6.7 (2 studies)[10,16]
Platinum-based	1–148	2.0–9.7 (5 studies)[4,10,14,16,17]	1.3–5.6 (5 studies)[4,10,16,17,20]	0–100 (3 studies)[10,16,20,a]
Lurbinectedin[b]	43	7.0 (1 study)[7]	1.5 (1 study)[7]	16.3 (1 study)[7]
CAV or ACO	4–10	2.9–7.5 (2 studies)[10,13]	1.3 (1 study)[10]	25 (1 study)[10]
BSC	10–85	0.9–1.1 (2 studies)[5,10]	Not reported	Not reported

[a] ORR of 100% was reported in the study in which only 1 patient was treated with the therapy. [b] 3L+ setting.
3L+, third line and beyond; ACO, adriamycin, cyclophosphamide, and vincristine; BSC, best supportive care; CAV, cyclophosphamide, doxorubicin, and vincristine; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SCLC, small cell lung cancer.

Figure 3. Median OS According to Treatment(s)



[a] 3L+ setting. [b] Included only platinum-sensitive SCLC patients. [c] Reports also on patients with limited stage SCLC (data not shown here).
Rows in bold represent the overall study cohort in the 3L setting, except Dumoulin (2022) which is in the 3L+ setting.
3L, third line; 3L+, third line and beyond; ACE, adriamycin, cyclophosphamide, and etoposide; ACO, adriamycin, cyclophosphamide, and vincristine; BSC, best supportive care; CAV, cyclophosphamide, doxorubicin, and vincristine; CI, confidence interval; NA, not applicable; NR, not reached; OS, overall survival; SCLC, small cell lung cancer.

CONCLUSIONS

- Patients with SCLC with disease progression after 2 or more lines of therapy have a poor prognosis and a high unmet need for new treatment options; however, results of this SLR highlight one of the challenges of conducting a randomized trial, given the lack of established therapies in this setting.
- Population size and patient characteristics varied greatly between studies, with patient characteristics not always well defined.
- Direct comparisons of the studies were difficult because the treatment regimens varied widely, and some studies reported only clinical outcomes for groups of treatments without specifying drugs names.

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DISCLOSURES

F Dirnberger and G Suri are employees of Amgen and hold Amgen stocks. K Appiah, M Rizzo, and B Mayer are employees of Cytel, a consulting company that has provided paid consulting services to Amgen, which funded the development and conduct of this study and abstract.

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