



P3.289: Large Cell Neuroendocrine Carcinoma:
Real-World Evidence of Limited Survival and Unmet Therapeutic Need

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IASLC 2026 World
Conference on Lung Cancer
SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

- Large cell neuroendocrine carcinoma (LCNEC) is a rare and aggressive neoplasm of the lung accounting for approximately 3% of all lung cancers.
- Evidence guiding treatment remains limited and current treatment strategies are largely extrapolated from small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) treatment paradigms.
- We evaluated real-world treatment patterns and clinical outcomes of patients with LCNEC treated at a tertiary referral centre.

METHODS

- We conducted a retrospective study of patients with **histologically confirmed LCNEC** managed at the Royal Marsden Hospital **between 2015 and 2025**.
- Baseline demographic and clinical characteristics were summarised descriptively.
- Overall survival (OS), recurrence-free survival (RFS), and progression-free survival (PFS) were estimated using the Kaplan–Meier method, with 95% CI. Differences between groups were assessed using the log-rank test.
- The **advanced/recurrent cohort** comprised patients with either **de novo locally advanced or metastatic disease** or **recurrence following prior radical treatment**, all of whom were subsequently treated with palliative systemic anticancer therapy (SACT).
- All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant.
- This project was approved by the RM IRB (SE1528).

CONCLUSIONS

- LCNEC is associated with poor survival, with prognosis strongly influenced by stage at diagnosis.**
- Patients undergoing surgery and definitive CCRT achieved longer survival.**
- Adjuvant chemotherapy showed a non-significant trend towards improved OS.**
- Outcomes with systemic therapy remain poor in advanced disease.**
- Platinum-etoposide was the most commonly used 1st-line regimen.**
- These findings highlight the urgent need for more effective treatment strategies in LCNEC.**
- Genomic profiling may identify actionable alterations in LCNEC.**

RESULTS

Overall cohort

- 66 patients** were included. Median age was 66 years. Most patients had good PS (ECOG PS 0-1, 76%; Table 1).
- At a median follow-up of 71.4 months, **median OS for the overall cohort was 14.7 months (95% CI 9.6-19.7)**.
- OS differed significantly by stage ($p < 0.001$; Table 2, Figure 1).

Table 2. OS by initial stage

	Median OS, months (95% CI)	1-year OS, %
Stage I	29.9 (10.3-49.4)	66.7
Stage II	20.7*	80.0
Stage III	18.5 (10.0-27.0)	74.2
Stage IV	8.4 (4.3-12.5)	34.1

*Confidence intervals were not reported for stage II due to the small sample size (n=10)

Radical treatment outcomes

- 21 patients underwent surgery** as primary treatment (stage I, n=10; stage II, n=6; stage III, n=5). Median RFS and OS after surgery were 20.1 (95% CI 1.7-38.5) and 41.1 months (95% CI 39.1-43.1), respectively.
- 9 patients received adjuvant chemotherapy** (stage I, n=5; stage II, n=2; stage III, n=2; carbo-etoposide, n=7; carbo-vinorelbine, n=2); with a median OS of 41.2 months vs. 23.4 months in the non-adjuvant group ($p=0.305$).
- 6 patients underwent radical chemoradiotherapy** with a median OS of 15.6 months.

Palliative SACT outcomes

- 26 patients received palliative SACT as primary treatment and 8 received it after recurrence following radical treatment.** PFS was improved for those treated in the recurrent setting ($p=0.043$), while OS did not differ significantly ($p=0.232$; Table 3). Platinum-etoposide was the most commonly used regimen (Table 4, Figure 2).
- Genomic data were available for 12 patients:** 3 had targetable alterations (**KRAS G12C**, n=2; **NTRK fusion**, n=1), although none received targeted therapies. 9 had non-targetable alterations including *Rb1*, *TP53*, *STK11*, *EGFR* amplification, *BRAF* non-V600, and *KRAS* G12A.

Table 3. PFS and OS in patients receiving palliative SACT

	Median PFS, months (95% CI)	Median OS, months (95% CI)
De novo locally advanced or metastatic (n=26)	5.2 (3.6-6.8)	10.2 (6.0-14.4)
Recurrent disease (n=8)	12.1 (6.8-17.4)	12.8 (0-34.9)
Overall (n=34)	6.4 (2.8-10.0)	11.3 (7.8-14.8)

Table 4. Treatment efficacy according to first-line SACT

	ORR (%)	DCR (%)	Median PFS, months	Median OS, months
Platinum-etoposide (n=25)	48	88	8.9	11.5
Chemo-IO (n=5)	40	40	3.4	4.7
IO (n=1)	100	100	13.2	33.0
Other platinum regimens (n=3)	33	33	2.9	5.3

Figure 1. Overall survival by initial stage

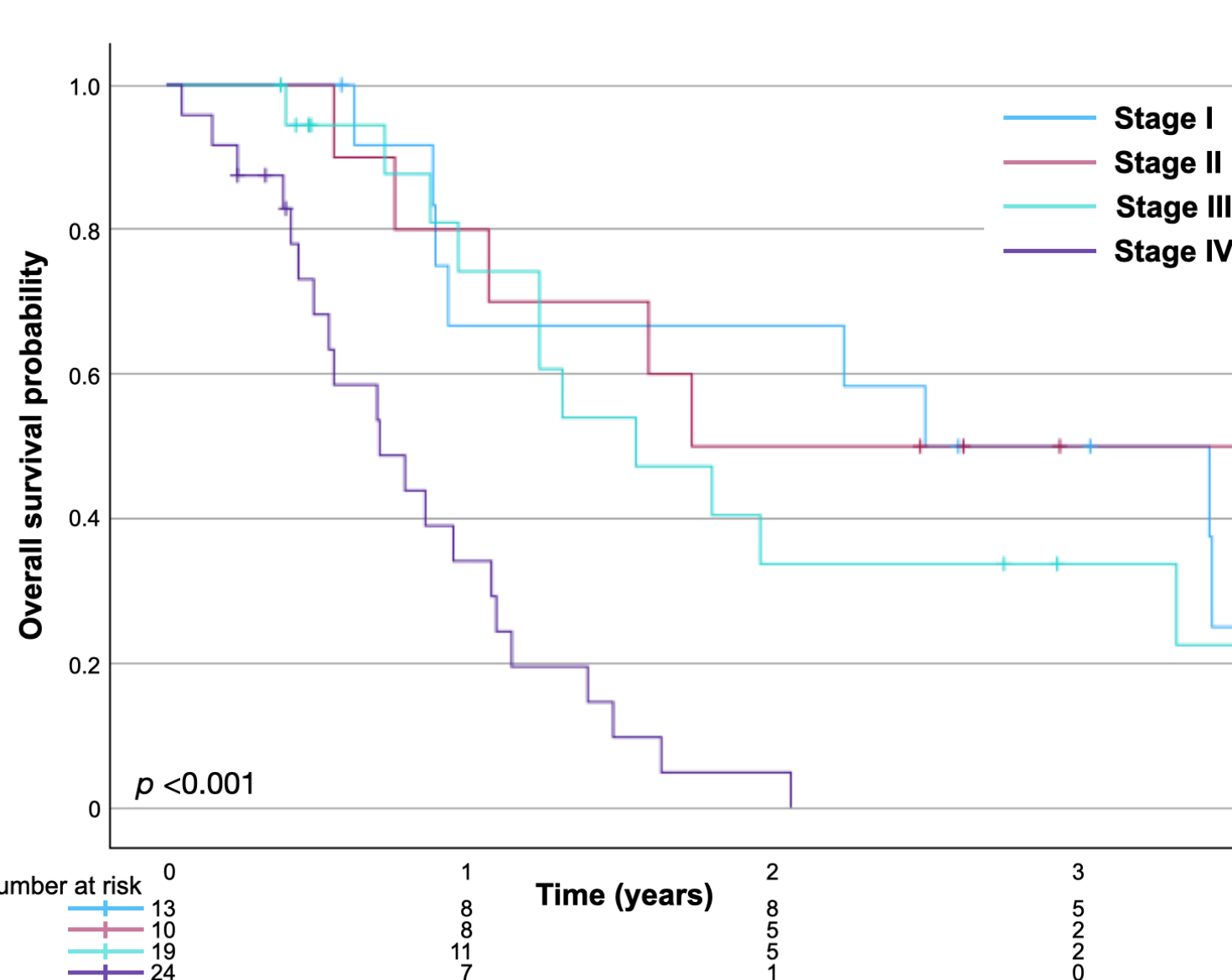


Table 1. Baseline characteristics

	LCNEC patients (N=66)
Age, years median (IQR)	66 (59-76)
Male, n (%)	39 (59)
ECOG PS 0/1/≥2, n (%)	13 (20)/ 37 (56)/ 16 (24)
Stage at diagnosis, n (%)	
I	13 (20)
II	10 (15)
III	19 (29)
IV	24 (36)
Primary treatment, n (%)	
Surgery	21 (32)
Concurrent chemoradiation (CCRT)	6 (9)
SACT	26 (39)
No treatment	13 (20)

Figure 2. First-line SACT regimens used

