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Clinical characteristics and treatment patterns in a real-world cohort of patients with advanced *HER2*-mutant NSCLC: Insights from the ESME database

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Objectives

To describe the demographic and clinical characteristics and real-world treatment patterns of patients with advanced *HER2*-mutant NSCLC who met the main eligibility criteria for the Beamion LUNG-2 trial, using data from the ESME LC database.

The Beamion LUNG-2 (NCT06151574) Phase III clinical trial compares the HER2-targeted tyrosine kinase inhibitor zongertinib with standard-of-care treatment in the first-line setting of advanced *HER2*-mutant NSCLC.

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Introduction

- The Épidémio-Stratégie Médico-Economique Lung Cancer (ESME LC) database is one of the largest real-world lung cancer databases in Europe, providing retrospective longitudinal data on patients treated in France.
- Characterizing patients with advanced *HER2*-mutant NSCLC and their treatment patterns provides real-world context to complement evidence from contemporary clinical trials, in particular the Beamion LUNG-2 trial (NCT06151574)[1].

Methods

Study design and data source

- This retrospective real-world study used data from the ESME LC database (NCT03848052)[2].
- Data were obtained from the October 2025 ESME LC data cut, which included 69,326 patients with lung cancer diagnosed between 2015 and 2025.

Key inclusion criteria for the study population:

- Advanced or metastatic, non-squamous NSCLC
- HER2 tyrosine kinase domain (TKD) mutation
- ECOG performance status (PS) 0 or 1 at initiation of first-line (1L) treatment

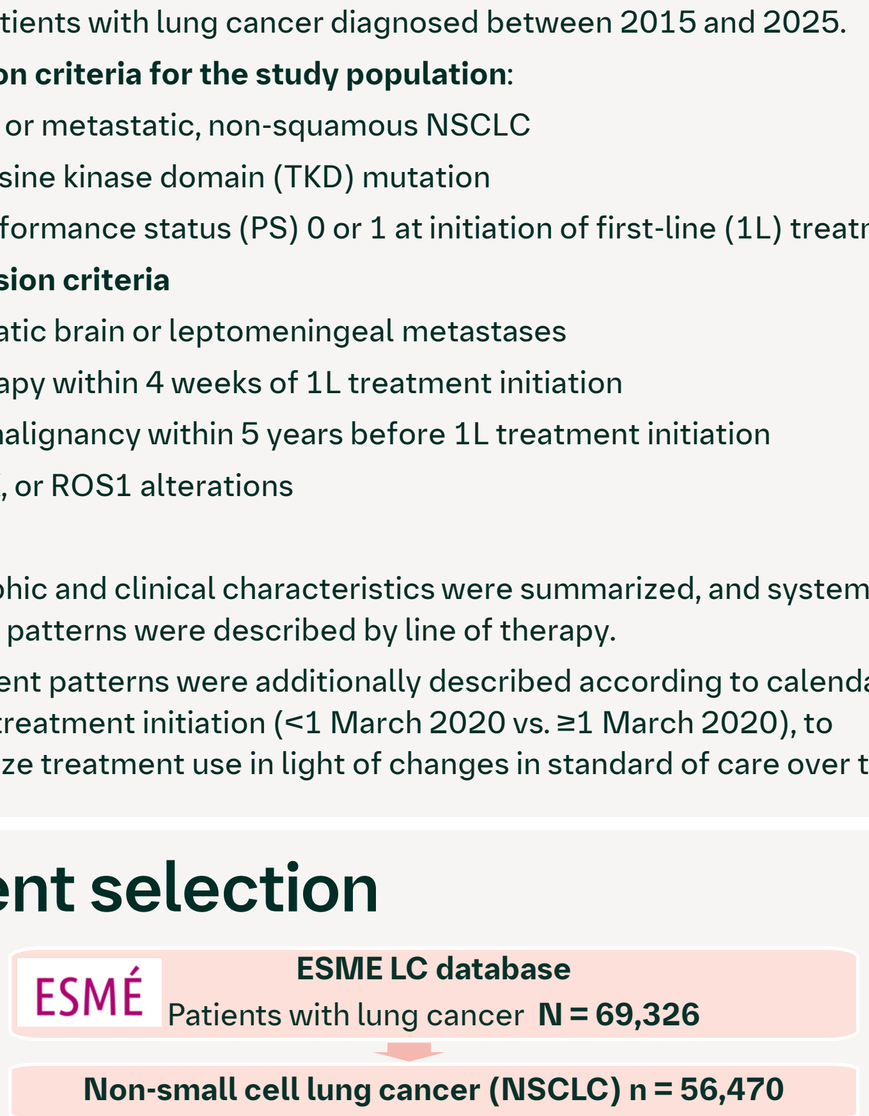
Main exclusion criteria

- Symptomatic brain or leptomeningeal metastases
- Radiotherapy within 4 weeks of 1L treatment initiation
- Another malignancy within 5 years before 1L treatment initiation
- EGFR, ALK, or ROS1 alterations

Analyses

- Demographic and clinical characteristics were summarized, and systemic treatment patterns were described by line of therapy.
- 1L treatment patterns were additionally described according to calendar period of treatment initiation (<1 March 2020 vs. ≥1 March 2020), to characterize treatment use in light of changes in standard of care over time.

Patient selection



Abbreviations
1L, first-line; 2L, second-line; ALK, anaplastic lymphoma kinase; carbo, carboplatin; CI, confidence interval; cis, cisplatin; CT, chemotherapy; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; ESME LC, Épidémio-Stratégie Médico-Economique Lung Cancer; HER2, human epidermal growth factor receptor 2; IO, immunotherapy; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; PS, performance status; ROS1, ROS proto-oncogene 1; T-DXd, trastuzumab deruxtecan; TKD, tyrosine kinase domain.

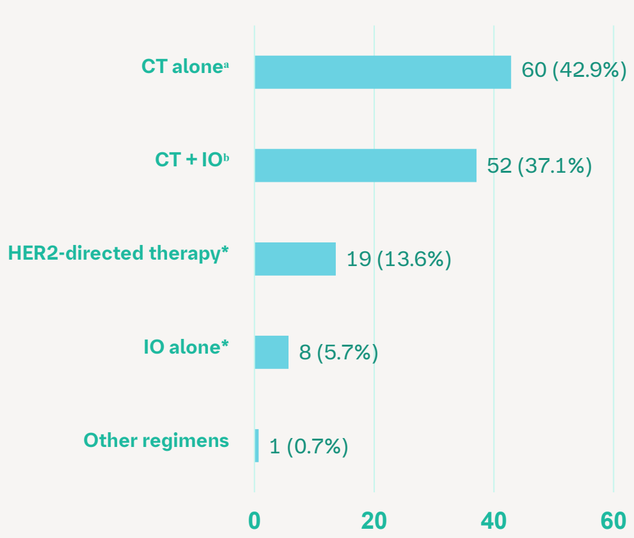
Patient and disease characteristics

Characteristic		N = 140
Age at 1L initiation, years		
Median (min–max)		64.0 (37–86)
Female, n (%)		**87 (62.1)**
Smoking status at initial cancer diagnosis, n (%)		
Never-smoker		74 (52.9)
Former/current smoker		63 (45.0)
Missing		3 (2.1)
ECOG PS at 1L initiation, n (%)		
0		62 (44.3)
1		78 (55.7)
Adenocarcinoma, n (%)		**135 (96.4)**
De novo metastatic disease, n (%)		**117 (83.6)**
Metastatic sites at 1L initiation, n (%)†		
Non-symptomatic brain metastases		44 (31.4)
Bone metastases		76 (54.3)
Liver metastases		38 (27.1)
≥3 metastatic sites		48 (34.3)
PD-L1 screening before 1L initiation		**106 (75.7)**
Of screened,	PD-L1 <50%	83 (78.3)
	PD-L1 ≥50%	21 (19.8)
	Missing	2 (1.9)

†Multiple categories possible per patient.

Median follow-up: 39.8 months (95% CI, 33.8-44.7)

Treatment patterns in 1L (2015-2025)



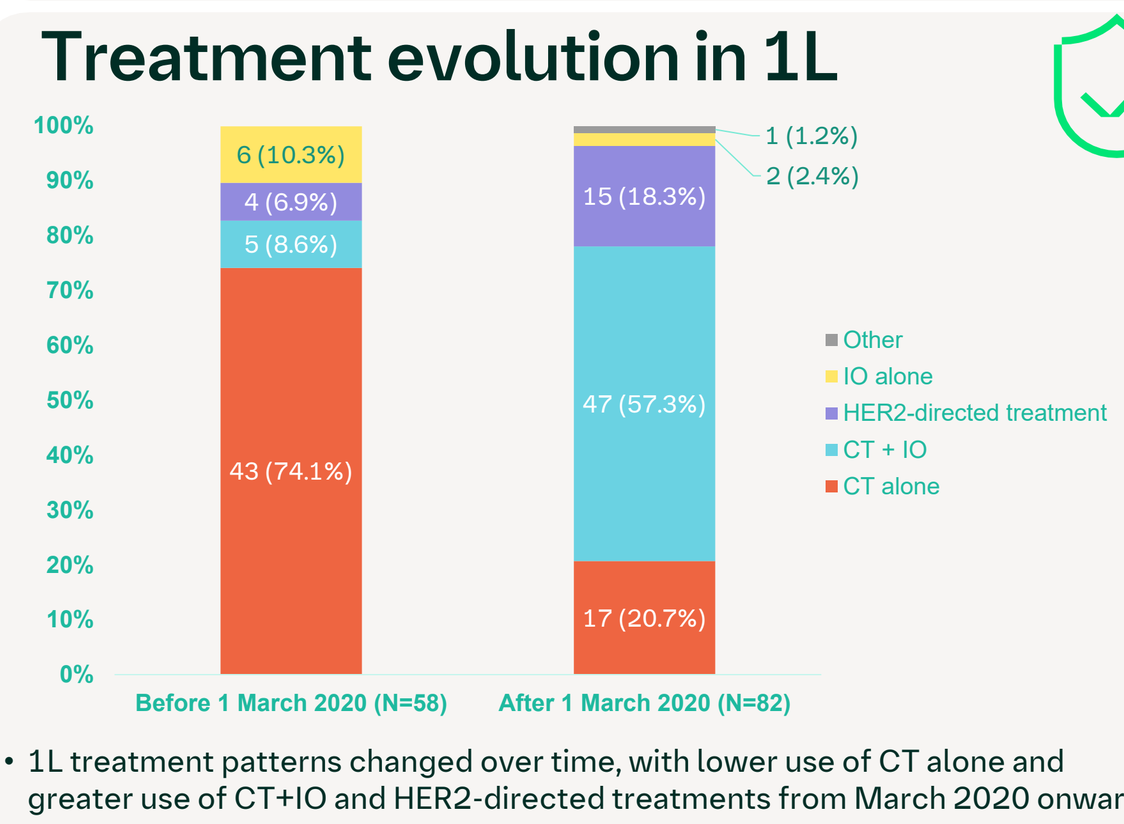
[a]Details of CT alone regimens	N=60
Carbo/cis, pemetrexed	29 (48.3%)
Carbo/cis, pemetrexed, bevacizumab	15 (25.0%)
Carbo/cis, Paclitaxel	12 (20.0%)
Other CT regimen	4 (6.7%)

[b]Details of CT+IO regimens	N=52
Carbo/cis, pemetrexed, pembrolizumab	44 (84.6%)
Other CT+IO regimen	8 (15.4%)

*HER2-directed therapy, mainly T-DXd (52.6%, all treated as part of a clinical trial); IO alone, mainly pembrolizumab (62.5%).

- 104/140 (74.3%) patients received 2L treatment.
- HER2-directed therapy was the most common 2L treatment: 41/104 (39.4%).

Treatment evolution in 1L



- 1L treatment patterns changed over time, with lower use of CT alone and greater use of CT+IO and HER2-directed treatments from March 2020 onwards.

Conclusions

1. In this French real-world cohort, patients with advanced *HER2*-mutant NSCLC who met the main Beamion LUNG-2 eligibility criteria predominantly received CT alone or CT+IO as first-line treatment between 2015 and 2025.
2. First-line treatment patterns changed over time, with decreased use of CT alone and increased use of CT + IO from March 2020 onward (74.1% to 20.7% and 8.6% to 57.3%, respectively).

References
1. Johnson ML, et al. *J Clin Oncol*. 2024;42(16_suppl). doi:10.1200/JCO.2024.42.16_suppl.TPS8654.
2. Girard N, et al. *Lung Cancer*. 2026;220:109585. doi:10.1016/j.lungcan.2026.109585.

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