Metastatic Non-Small Cell Lung Cancer (NSCLC) Without Driver Mutations: Projections by Line of Therapy (LOT) in Western Europe (WE), 2021–2026

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Background

- Lung cancer is the most prevalent cause of cancer-related mortality worldwide.[1] Approximately half a million new cases were diagnosed in Europe in 2020, and 384,176 people died of lung cancer.[2]
- Non-small cell lung cancer (NSCLC) comprises 85% of lung cancer cases. Nearly 70% of patients with lung cancer present with locally advanced or metastatic disease.[3]
- The treatment landscape of NSCLC has changed significantly since the introduction of targeted therapies that inhibit upregulated pathways in NSCLC, including epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), and ROS proto-oncogene 1 receptor tyrosine kinase (ROS1) genes.[4,5]
- The treatment landscape for patients with metastatic NSCLC without driver mutation is still evolving, and is being greatly influenced by immunotherapy, which further complicates the decision-making process.[5,6]
- Real-world data on clinical practice, such as the number of patients with metastatic NSCLC without driver mutations eligible for a given line of therapy (LOT) and the overall treatment duration within a specific LOT, are limited.[5,7]

Objectives

To report the results of an epidemiology model estimating the size of the stage IV NSCLC patient population in Western Europe (WE), including:

- The number of patients with prevalent stage IV NSCLC without driver mutations by histology and programmed death-ligand 1 (PD-L1) status.
- The number of prevalent patients treated with systemic therapy by line, from first line (1L) therapy through second line (2L) therapy, including 1L maintenance (1L MT).

Methods

- A retrospective data analysis of NSCLC in WE.

Data Sources

- Country-specific cancer registries
- Physician survey results from CancerMPact® (CMP)
- Targeted review of peer-reviewed literature

- Treatment by line data were extracted online from the CMP Treatment Architecture surveys 2019 and 2020, which recruited and surveyed 100 and 103 physicians, respectively.
- The total estimate of patients with metastatic NSCLC without driver mutations on a LOT among the prevalent patients was calculated using the following equation:

$$\frac{\text{Annual estimate of patients starting a LOT by year}}{\text{The total months per year}} \times \text{The average progression free survival in months for that LOT}$$

- Patient starts are not unique from line to line, it is possible for patients to start more than one line of therapy in the given year.

Incidence Calculation

- Recent country-, age-, and sex-specific incidence rates of NSCLC by histology were estimated and multiplied by respective projected country populations to estimate annual number of new cases for 2021–2026.
- Staging distribution (American Joint Committee on Cancer 8th edition) of NSCLC by histology from Surveillance Epidemiology and End Results (SEER) for 2018 was applied.

Methods (cont.)

Data Sources

- The 10-year prevalence measure of stage IV NSCLC by histology calculates stage-specific prevalence while accounting for progression from earlier stages to stage IV across the given timeframe (distant metastatic recurrence).
- The treated prevalence of patients with stage IV NSCLC without driver mutations on 1L, 1L MT, or 2L within a given year was calculated using data from the 2020 CMP physician survey.

Results

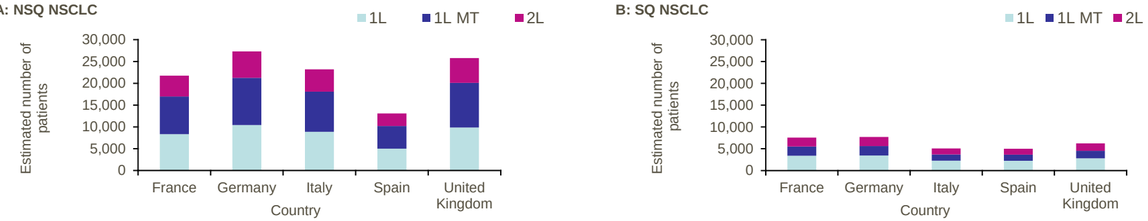
- The 10-year prevalence of patients with stage IV NSCLC without driver mutations in WE was estimated at 184,966 in 2021 and is projected to increase to 197,926 by 2026 (**Table 1**).

Table 1. 10-Year Prevalence of Patients with Stage IV Non-squamous (NSQ) and Squamous (SQ) NSCLC Without Known Driver Mutations

NSQ	2021	2022	2023	2024	2025	2026
France	26,717	27,232	27,708	28,154	28,581	28,971
Germany	34,051	34,302	34,571	34,859	35,155	35,483
Italy	28,755	29,127	29,505	29,892	30,290	30,689
Spain	16,125	16,426	16,733	17,045	17,359	17,675
United Kingdom	31,964	32,436	32,920	33,417	33,935	34,469
Total	137,612	139,523	141,437	143,367	145,320	147,287
SQ	**2021**	**2022**	**2023**	**2024**	**2025**	**2026**
France	11,282	11,499	11,708	11,912	12,111	12,297
Germany	11,640	11,670	11,723	11,798	11,893	12,002
Italy	7,610	7,686	7,770	7,864	7,967	8,070
Spain	7,471	7,612	7,761	7,917	8,079	8,239
United Kingdom	9,351	9,477	9,608	9,745	9,889	10,030
Total	47,354	47,944	48,570	49,236	49,939	50,638

- The treated prevalence of stage IV NSQ NSCLC by LOT in 2021 was estimated at 42,484 in 1L, 44,151 in 1L MT, and 24,516 in 2L (**Figure 1A**).
- The treated prevalence of stage IV SQ NSCLC by LOT in 2021 was estimated at 14,174 in 1L, 8,815 for 1L MT, and 8,595 in 2L (**Figure 1B**).

Figure 1. Estimated Treated Prevalence by LOT, Stratified by Country, 2021*



*Calculations were made using the mean time to progression by LOT. The same time to progression assumptions were applied across all WE countries.

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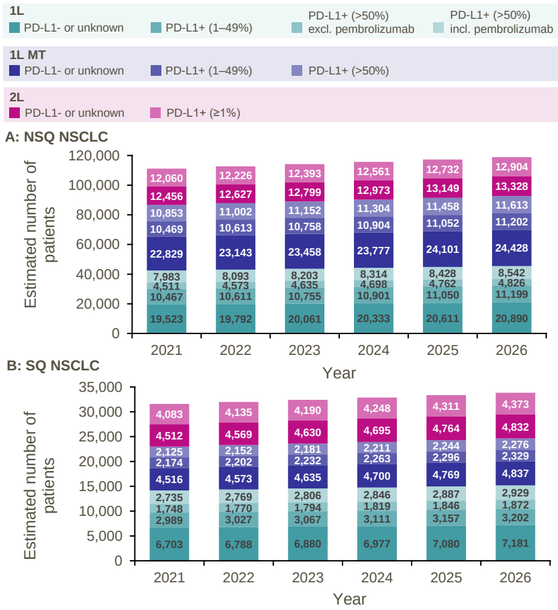
- **KK**, **GK**, **LD**, **OC**, and **KN** are employees of Cerner Enviza, a global consultancy company that acts in the healthcare market, and have as clients: pharmaceutical companies, health insurance companies and hospitals, including GlaxoSmithKline; **TJG**, and **CH** were employees of GlaxoSmithKline with stock options when research was conducted; **LK, JC**, **AA**, and **AS** are employees of GlaxoSmithKline.

Figure 2. Estimated Treated Prevalence of Patients Receiving 1L, 1L MT or 2L Therapy, Stratified by PD-L1 Status, 2021–2026

- The total increase in the treated prevalence over 2021–2026 varied by country (NSQ [range]: 4.5%–9.5%; SQ: 3.7%–10.4%).



- Estimated treated prevalence for NSQ and SQ across the studied time period in 1L excluded pembrolizumab treatment in ~50% of patients with PD-L1>50%.

Conclusions

- The 10-year prevalence of patients without driver mutations was estimated at 184,966 in 2021, with a projected increase to 197,926 by 2026.
- The estimated overall treated prevalence of stage IV NSQ NSCLC (including 1L, 1L MT, and 2L therapies) in 2021 was 111,151 and is expected to increase to 118,932 in 2026; the corresponding numbers for SQ NSCLC are 31,584 and 33,831, respectively.
- The highest estimated number of treated patients was observed in 1L MT for NSQ NSCLC and 1L for SQ.
- When stratified by PD-L1 status, the estimated proportion of treated patients with PD-L1 positive status ranged from 48.3% to 54.0% across LOTs for patients with NSQ NSCLC, and 47.5%–52.7% for patients with SQ NSCLC.

Discussion

- Ageing is a major contributing factor in the projected increase of patients with NSCLC in the future.[8]
- The 5-year overall survival for stage IV NSCLC remains ~7%,[9] highlighting the need for new treatments.

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