Patient access to treatment in advanced NSCLC – Are European health systems ready to measure what matters?

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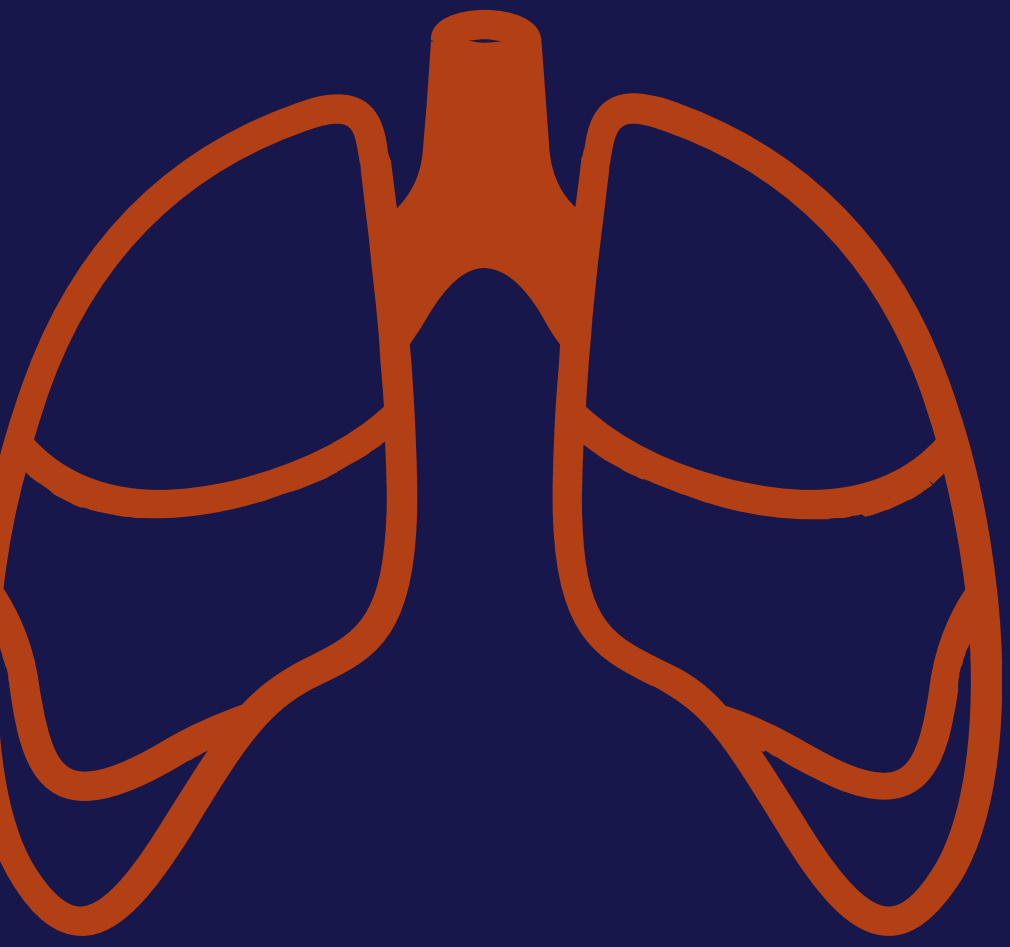

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Please cite this report as: Manxhuka B, Gustafsson A, Hofmarcher T. Patient access to treatment in advanced NSCLC – Are European health systems ready to measure what matters? IHE REPORT 2024:5. IHE: Lund, Sweden.

This report was commissioned and funded by MSD. The views and opinions of the authors are not necessarily those of MSD. The responsibility for the analysis and conclusions in this report lies solely with the authors.

IHE REPORT 2024:5
e-ISSN: 1651-8187
ISSN: 1651-7628

The report can be downloaded from IHE's website (www.ihe.se)

Foreword

Enhancing the quality of care is important to improve outcomes for cancer patients. This is especially true for lung cancer, which is characterized by comparatively low survival rates despite remarkable improvements achieved in the last ten years. However, not all lung cancer patients in Europe have access to adequate treatment. IHE has recently estimated and measured to what extent patients with advanced-stage non-small cell lung cancer (aNSCLC) have access to cancer medicines and how their access level differs from what clinical guidelines recommend. The results, covering 12 European countries, were published in an IHE report called "*Diagnosed but not treated: How to improve patient access to advanced NSCLC treatment in Europe*" as well as in a scientific article called "*Systemic anti-cancer therapy patterns in advanced non-small cell lung cancer in Europe*" in 2022.

The IHE research on the treatment of aNSCLC was used as a foundation to create a Call to Action by a broad group of stakeholders at the European level under the patronage of MEP Cristian-Silviu Buşoi. The Call to Action titled "*Fighting lung cancer together as equals*" was unveiled in December 2022 at the European Cancer Forum. One of the main asks in the Call to Action was to enhance data collection on treatment rates and their inclusion in the European Cancer Inequalities Registry.

This report is a continuation of the past work on treatment of aNSCLC in Europe and the Call to Action. It aims to explore if countries in Europe are ready to measure treatment patterns in aNSCLC. Unfortunately, the findings in this report paint a bleak picture. Nearly all of the 13 considered countries are not providing solid and relevant evidence on treatment patterns. However, it should be remembered that the data to make necessary measurements are usually available in medical records. The challenge for countries seems to be to interconnect data points, to analyze them, and to make them accessible.

Clearly, more efforts are needed by countries to measure what matters. Data and monitoring of treatment patterns are valuable and form the very basis to make informed decisions to improve care. Sweden and the UK are frontrunners in routinely analyzing and monitoring treatment data of aNSCLC and making them publicly accessible. Yet both of these countries currently only publish information on whether a patient receives treatment with cancer medicines or not, without providing information on the kind of treatment (the exact medicine or medicines belonging to a certain class of medicines) that patients receive. To enhance the quality of care and identify shortcomings in the current delivery of care, both who gets treated and the kind of treatment need to be measured.

Lund, March 2024

Peter Lindgren
Managing Director, IHE

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Summary

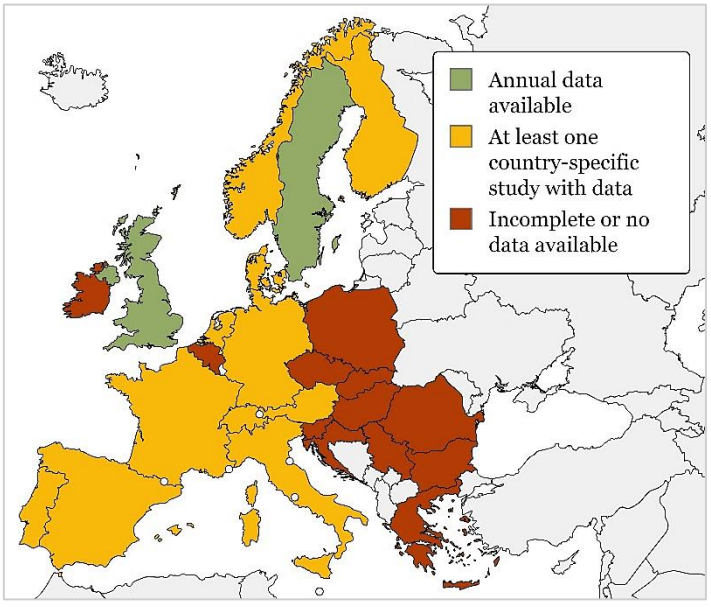
Lung cancer stands as the leading cause of cancer death in Europe, accounting for around 20% of cancer-related deaths and 12% of all newly diagnosed cancer cases in 2022. The launch of Europe's Beating Cancer Plan (EBCP) in February 2021 reignited the fight against cancer across Europe. For lung cancer, this includes efforts in the area of prevention to achieve a "Tobacco-Free Generation" by 2040. Early detection of lung cancer through screening of current and former smokers received a boost through the revised recommendation on cancer screening by the Council of the EU in December 2022. The treatment standards of lung cancer underwent considerable changes during the last two decades, moving towards a more personalized treatment approach following the introduction of targeted therapies and immunotherapies. The "Cancer Diagnostic and Treatment for All" initiative in the EBCP supports efforts to enable access to innovative and evidence-based personalized treatment.

In December 2022, a group of stakeholders under the patronage of MEP Cristian-Silviu Buşoi issued a Call to Action titled "*Fighting lung cancer together as equals*". It called for:

- Improving prevention, ensuring earlier diagnosis, and driving health literacy
- Ensuring faster patient access to modern diagnostic tests and treatments
- Enhancing data collection on treatment rates and their inclusion in the Cancer Inequalities Registry

This Call to Action was partly built on the IHE report "*Diagnosed but not treated: how to improve the patient access to advanced NSCLC treatment in Europe*". The report assessed to what extent patients with advanced-stage non-small cell lung cancer (aNSCLC) receive treatment with cancer medicines across 12 European countries between 2014 and 2020. It also compared differences in the estimated national treatment patterns with treatment patterns according to clinical guidelines. The report found that a considerable share of aNSCLC patients remains untreated in all countries, yet with huge variations (20–60%) between countries. This reflects various systemic barriers, including delayed diagnosis and stringent eligibility criteria for treatment with medicines. In addition, many patients received older types of cancer medicines (chemotherapy) instead of newer types of medicines (immunotherapy and targeted therapy), stemming from delayed reimbursement of medicines, budget limitations, resource constraints for diagnostic testing, and gaps in continuing medical education.

The objective of this report was to continue the research on treatment rates in aNSCLC in the spirit of the Call to Action. The aim was to explore whether European health systems capture and publish reliable, up-to-date real-world data on treatment rates in aNSCLC. 13 European countries were analyzed. The map to the right shows the data availability status for 25 countries (the 13 countries from this report and the 12 countries from the previous IHE report) in 2023.



The review of published data on treatment rates in aNSCLC for the 13 countries in this report highlights a pronounced absence of reliable, comprehensive, up-to-date data. The lack of published data undermines the ability to evaluate the quality of care and adherence to treatment standards defined in clinical guidelines. The report's critical observations are as follows:

- **Lack of data**: For two countries – Croatia and Slovakia – no data on treatment rates in aNSCLC were found. For an additional three countries – Czechia, Serbia, and Slovenia- only multi-country studies with aggregated information but no detailed per-country breakdowns were identified. This conceals national treatment patterns.
- **Representativeness of data**: Most identified studies do not necessarily present nationally representative treatment practices. They merely capture treatment practices at a single hospital or a network of hospitals within a region. Only two countries – Denmark and Sweden – have published data using national registry data.
- **Up-to-dateness of data**: Apart from Sweden, the latest available data in all countries are comparatively old. Many studies do not capture the introduction of immunotherapy and most targeted therapies in the first-line treatment setting.
- **Comparability of data**: Studies of aNSCLC are characterized by varying definitions of the patient group. This includes differing definitions of disease stage, oncogenic mutation status, functional status, and treatment lines. There are also differences in the definition of systemic therapies and other treatments that patients receive.

Among the 25 European countries assessed in the previous and current IHE report, only Sweden and the UK (England+Wales) regularly provide annual data on treatment rates in aNSCLC in public databases. These examples set a benchmark for best practices in data transparency and commitment to ongoing monitoring of lung cancer treatment practices. Yet, even in these countries, specific details regarding the types of systemic therapies administered to patients are not published. There is only data on whether a patient was treated with systemic therapies, but no data on the kind of systemic therapy (chemotherapy, immunotherapy, targeted therapy, or a combination of these). This suggests that European health care systems are currently by and large not adequately equipped to measure treatment rates in aNSCLC.

Another finding of this report is that recent advances in the medical treatment of aNSCLC may not be fully utilized in clinical settings. Indeed, several studies indicate an underuse of newer treatments options (immunotherapy and targeted therapy) and an overuse of older treatment options (chemotherapy) compared to recommendations in clinical guidelines. This finding confirms a key result from the previous IHE report.

Given the complexity and the significant inter-country variability in published treatment rate data across European countries, there is a pressing need for systematic monitoring and reporting. National clinical cancer registries should prioritize the analysis of treatment rates, with regular publication of findings to facilitate transparency and accountability. Systematic monitoring would enable health care providers and policymakers to measure and track progress of the quality of care, benchmark against best practices and clinical guidelines, and tailor interventions to specific national or regional needs.

List of abbreviations

aNSCLC	Advanced-stage non-small cell lung cancer
ECOG PS	Eastern Cooperative Oncology Group Performance Status
EBCP	Europe's Beating Cancer Plan
EMA	European Medicines Agency
ESMO	European Society for Medical Oncology
EU	European Union
GDP	Gross domestic product
LDCT	Low-dose computed tomography
NGS	Next-generation sequencing
NSCLC	Non-small cell lung cancer
SACT	Systemic anti-cancer therapy
WHO	World Health Organization

Country abbreviations

AT – Austria
BE - Belgium
BG - Bulgaria
HR – Croatia
FI - Finland
EL - Greece
CZ - Czechia
DK - Denmark
FR - France
DE - Germany
HU - Hungary
IE - Ireland
IT - Italy
NL – Netherlands
NO - Norway
PL - Poland
PT - Portugal
RO - Romania
RS - Serbia
SK - Slovakia
SI - Slovenia
ES - Spain
SE - Sweden
CH – Switzerland
UK – United Kingdom

1. Introduction

Epidemiology of lung cancer

Lung cancer, both globally and in Europe, stands as the leading cause of cancer-related deaths (1). In 2022, the estimated count of lung cancer-related deaths in the European Union (EU) reached 252,582 (20% of all cancer deaths) compared to 319,236 newly diagnosed cases (12% of all new cancer cases) (2). Men account for approximately 64% of the incidence numbers and 65% of the mortality numbers. In the EU, around 29% of lung cancer-related deaths occur before the age of 65, similar to global trends (2, 3). The substantial frequency of premature deaths within the working-age population causes a considerable loss in potential working life years and subsequent high indirect costs (4). This adds to the overall economic burden of lung cancer, which also includes health care expenditure and informal caregiving costs (5).

Policy developments

Recent policy developments have significantly influenced cancer control strategies at the European level, notably through the publication of Europe's Beating Cancer Plan (EBCP) in February 2021 and the EU Cancer Mission under Horizon Europe 2021–2027. The EBCP represents a holistic approach by the European Commission to tackle cancer across its full spectrum, from prevention to diagnosis, treatment, and the quality of life of patients and survivors (6). The plan also emphasizes the importance of research and innovation in cancer care, including the development of new technologies and treatments. By focusing on these areas, the EBCP aims to reduce the incidence of all cancers, improve survival rates, and ensure that cancer patients and their families receive the support they need.

Although not exclusively focused on lung cancer, the EBCP addresses several key aspects directly relevant to lung cancer care. In the area of prevention, the EBCP supports initiatives to establish a 'Tobacco-Free Generation' by 2040, with less than 5% of the population using tobacco (6). It also plans to evaluate current air quality legislation and revise the EU's air quality standards to align them more closely with recommendations from the World Health Organization (WHO).

In the area of early detection, the EBCP aims to evaluate the extension of the range of organized cancer screening programs to lung cancer alongside existing programs for breast, cervical, and colorectal cancer (6). This expanded scope is reflected in the Council's updated cancer screening recommendation from December 2022, which encourages member states to assess the feasibility of low-dose computed tomography (LDCT) for high-risk groups (e.g., current and former heavy smokers) and integrating screening services within prevention strategies (such as smoking cessation counseling) (7). The EU's commitment to this cause is further demonstrated by support for research aimed at identifying and engaging high-risk populations. In support of these initiatives, the SOLACE project, funded by the EU4Health Program, is progressing in several EU countries to refine LDCT screening protocols (8).

The "Cancer Diagnostic and Treatment for All" initiative in the EBCP supports efforts to enable equal access to innovative and evidence-based personalized treatment across the EU (6). This includes better access to diagnostic testing with next-generation sequencing (NGS) technology. This diagnostic technology of testing tumor samples for multiple predictive biomarkers in parallel rather than sequentially is fundamental for a personalized treatment approach, especially for lung cancer.

Potential for reducing the disease burden of lung cancer

There is great potential for the reduction of the disease burden of lung cancer. Firstly, prevention can substantially lower incidence rates, as tobacco smoking alone drives approximately 80% of newly diagnosed lung cancer cases (9). Secondly, survival rates are greatly influenced by the stage at diagnosis and the quality of medical care provided. For instance, the five-year survival rate in stage I lung cancer was 57% compared to only 3% in stage IV lung cancer in England in the diagnosis period 2013–2017 (10). This underlines the importance of early detection of lung cancer.

There is a great need for more effective treatments to bring survival rates closer to 100%. The current decade has a witnessed continuous influx of new medicines for NSCLC, contributing to the ongoing transformation of treatment standards. Between 2011 and 2023, the European Medicines Agency (EMA) approved 28 new medicines for patients in advanced stages of the subtype non-small cell lung cancer (NSCLC) which accounts for around 85% of all lung cancer cases. Most of these new medicines were targeted therapies that act on specific mutations involved in the growth of lung cancer tumors. Around 20–25% of Caucasian NSCLC patients in Europe have mutations that have become targetable by medicines approved in 2011-2020 (11). Five immunotherapies that help the body's immune system to recognize and attack cancer cells, were also approved for use in NSCLC during this period (12). Immunotherapies are primarily used in patients without targetable mutations. The introduction of these medicines over the past decade was accompanied by a rise in survival rates, e.g., five-year survival rates for lung cancer increased from 17% to 25% between the diagnosis periods 2005-2014 and 2015-2021 in the Netherlands (13). In addition, several immunotherapies and targeted therapies have recently been approved in early-stage NSCLC, signifying a similar progressive shift towards personalized and effective interventions that advanced-stage NSCLC went through in the previous decade. As medical research and innovation continue, it is anticipated that additional breakthroughs will shape the future of NSCLC care in the years to come, offering enhanced treatment options and improved outcomes for patients at various stages of the disease (14).

IHE's 2022 Report ("Phase 1 report")

Despite recent advancements in the treatment possibilities of lung cancer, many patients do not seem to be able to benefit from them. The IHE report *"Diagnosed but not treated: how to improve the patient access to advanced NSCLC treatment in Europe"* published in 2022 found noteworthy shortcomings in the care of advanced-stage NSCLC (aNSCLC) patients in 12 European countries in the period from 2014 to 2020 (11). The two main findings were the following:

- Many aNSCLC patients remain untreated with cancer medicines. In Belgium, Greece, Norway, and Portugal around 70-75% of patients received cancer medicines in 2019, close to what clinical guidelines by the European Society for Medical Oncology (ESMO) recommend. By contrast, Poland and the UK had the lowest treatment rates of around 40% in 2019, meaning that just around half of the eligible patient population according to ESMO guidelines received drug treatment.
- Many aNSCLC patients received older types of cancer medicines (chemotherapy) instead of newer types of medicines (immunotherapy and targeted therapy) as recommended by ESMO guidelines. The underuse of newer types of medicines was prevalent in all countries, irrespective of the magnitude of the overall treatment rate. This confirmed earlier research that highlighted limited patient access to newer lung cancer medicines despite regulatory approval by the EMA as a major challenge in many countries in Europe (12).

Barriers to high treatment rates include delayed diagnosis, stringent eligibility criteria for treatment with medicines, as well as treatment refusal by patients. Barriers to administering modern medicines encompass delayed local reimbursement of medicines, budget limitations, resource constraints for diagnostic testing, and gaps in continuing medical education. These findings underscore the complexity of achieving optimal care in aNSCLC and the necessity for targeted interventions to bridge the existing health care gap. Increasing the number of patients who receive timely and adequate state-of-the-art drug treatment could generate a significant and long-lasting positive impact on patients, their families, and society at large.

Call to Action – "Fighting lung cancer together as equals"

Building on the insights from the Phase 1 report by IHE, a group of stakeholders under the patronage of MEP Cristian-Silviu Buşoi issued a Call to Action titled "*Fighting lung cancer together as equals*" in December 2022 (15). It called for:

- Improving prevention, ensuring earlier diagnosis, and driving health literacy
- Ensuring faster patient access to modern diagnostic tests and treatments
- Enhancing data collection on treatment rates and their inclusion in the European Cancer Inequalities Registry

The Call to Action aligns with the ongoing implementation phase of the EBCP, emphasizing the urgency to act and reduce inequalities in lung cancer care across the EU.

1.1 Objective

This report builds on the insights from the Phase 1 report and centers specifically on the third area of the Call to Action about treatment rates. The objective of this report is to investigate whether European health systems capture and publish reliable, up-to-date real-world data on "drug treatment rates" in aNSCLC. The overview of the current data landscape is supposed to aid the inclusion of treatment rates as a quality indicator at national level as well as the European level. It also helps to gain insights into disparities in treatment rates between countries that were not covered in the Phase 1 report. The geographic scope of the current analysis encompasses most of the remaining EU countries as well as other populous countries in Europe. The 13 countries included are Austria, Croatia, Czechia, Denmark, France, Germany, Italy, Serbia, Slovakia, Slovenia, Spain, Sweden, and Switzerland.

1.2 Method

A pragmatic literature review was performed between March and October 2023 to gather published data on drug treatment rates in aNSCLC. This involved systematically searching published sources for information on the use of cancer medicines (systemic anti-cancer therapy, SACT) in aNSCLC in each of the 13 included European countries. The search strategy employed standard medical databases, PubMed and Google Scholar, using relevant keywords and MeSH terms specific to each country and NSCLC treatment; see Appendix. Reports and databases of national cancer registries (in cases these exist in a country) were also searched.

The study population of interest in the analysis of drug treatment rates included patients with aNSCLC (i.e., stage IIIB/C and stage IV). This patient group constitutes the target for virtually all medicines approved by the EMA in the 2010s. No strict time period was defined in the searches, and all studies up to the day of the search in 2023 were considered relevant, whereas studies published before 2005 were disregarded. Ultimately, only studies published between

2007 and 2023 were included, capturing the dynamic development surrounding the introduction of immunotherapies and targeted therapies in aNSCLC.

The Appendix contains a brief epidemiological overview of lung cancer in each country. The data for this overview were primarily sourced from national cancer registries. In countries without national cancer registries or missing information on specific details of lung cancer, a secondary search encompassed a review of relevant published articles and reports in PubMed and Google Scholar.

2. Previous findings

This section provides a summary of the main findings of the "Phase 1 report" published by IHE in 2022 (11). It recaps the results of the numerical estimation of drug treatment rates in aNSCLC as well as qualitative explanations for the observed treatment rates across the 12 studied countries.

2.1 Drug treatment rates in aNSCLC

The quantitative part of the Phase 1 report assessed the quality in cancer care by measuring whether eligible patients were (i) treated with any drug treatment and (ii) treated with modern guideline-recommended medicines. Drug treatment rates in aNSCLC were defined as the ratio of "the number of patients treated with systemic anti-cancer therapy (i.e., chemotherapy, immunotherapy, targeted therapy)" and "the number of potentially eligible patients for systemic anti-cancer therapy". Treated patients were estimated by combining national sales volume data of cancer medicines used in aNSCLC with estimations on average medicine use per aNSCLC patient. Potentially eligible patients were estimated from national epidemiological data and encompassed both first line (newly diagnosed cases at an advanced stage and recurrent cases from earlier stages), second line (progressing cases from first line), and third line (progressing cases from second line) patients.

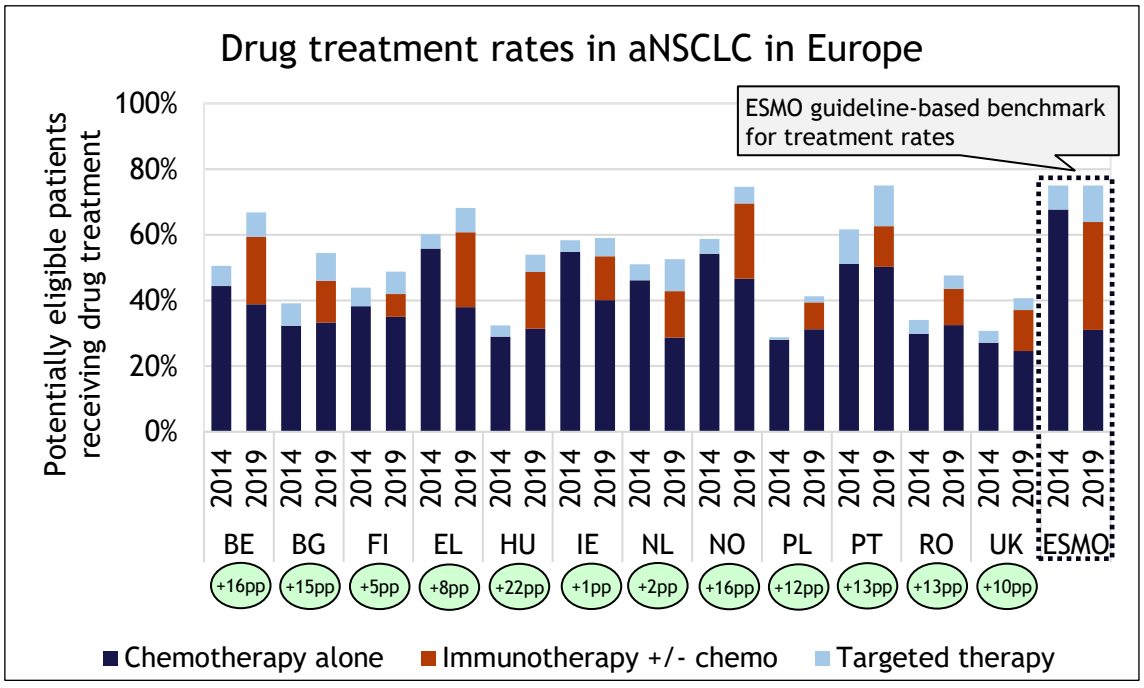


Figure 1: Drug treatment rates in aNSCLC in selected European countries and ESMO guidelines-based benchmark for optimal treatment in 2014 and 2019.

Notes: Drug treatment rates were estimated for all years between 2014 and 2020. 2020 data are not shown here because they were less robust due to the (back then) uncertain impact of COVID-19 on patient numbers (official cancer registry data are often published with a 2–3-year delay) and on medicine sales volume (stockpiling). It is also important to emphasize that this analysis is an approximation based on best available aggregated national data, and it should be viewed as a complement to registry-based studies with analysis of patient-level data.

Source: Hofmarcher et al. (2022) (11).

The results of the analysis of drug treatment rates in 12 European countries in 2014 and 2019 are shown in Figure 1. Several observations can be made:

(1) Overall treatment rates

a) The proportion of treated patients increased markedly over time in most countries, whereas in Finland, Ireland, and the Netherlands it remained stable. This increase coincided with the introduction of immunotherapy, a pattern also observed in the United States (16). The change in the standard-of-care might have sparked renewed interest in treating this patient group after almost two decades of only platinum-based chemotherapy, which was characterized by comparatively poor outcomes. Despite the improvements, most countries missed the approximate ESMO-guideline-based benchmark for the overall treatment rate of around 75% in all years between 2014 and 2020.

b) There were very large differences in treatment rates across countries. Belgium, Greece, Norway, and Portugal had the highest treatment rates in 2019. They also more or less met the approximate ESMO-guideline-based benchmark for the overall treatment rate that year. By contrast, Poland and the UK had the lowest treatment rates in both 2014 and 2019, and they only seemed to treat around half of the patients for which guidelines recommend drug treatment.

c) There seemed to be no correlation between the economic strength of a country and the magnitude of the overall treatment rates. For example, the country pairs of Portugal and Norway, Romania and Finland, and Poland and the UK all exhibit similar rates despite large differences in GDP per capita.

(2) Composition of the treatment rates

a) The entry of immunotherapy and new druggable targets for targeted therapy led to profound changes of the kind of drug treatment administered. The general pattern in nearly all countries between 2014 and 2020 was that the proportion of patients treated with targeted therapy increased slightly, the proportion of immunotherapy (given as monotherapy or combination with chemotherapy) increased considerably over time after initial reimbursement, while the proportion of chemotherapy (given as platinum-based combination or monotherapy) declined.

b) Far from all patients seemed to receive standard-of-care treatment compared to the approximate ESMO-guideline-based benchmark. Underuse of both immunotherapy and targeted therapy and overuse of chemotherapy was common. This was independent of whether a country had a high or low overall treatment rate. In fact, countries that (almost) met the ESMO-guideline-based benchmark for the overall treatment seemed to lag about 2–3 years behind the kind of treatment options that ESMO guidelines recommended.

2.2 Barriers to achieving optimal treatment rates

The qualitative part of the Phase 1 report drew on survey answers and input collected during workshops with local experts in each country. It identified barriers to achieving high overall drug treatment rates and barriers to using modern drug treatment options in each country. There was typically not just one single barrier preventing a country from achieving high drug

treatment rates; see Table 1. Similarly, several barriers were identified to prevent countries from administering modern drug treatment options to all eligible patients; see Table 2.

Table 1: Barriers to achieving high drug treatment rates

Barrier	Explanation
Poor functional status at the time of diagnosis	Many patients are diagnosed very late. Late diagnosis increases the proportion of frail patients with poor functional status (ECOG PS 3–4) and decreases the proportion of patients with good functional status (ECOG PS 0-2). Patients with poor functional status are generally not recommended to receive systemic therapy in clinical guidelines which is why a treatment rate of around 75% (and not 100%) is a realistic benchmark. In addition, co-morbidities (such as cardiovascular diseases or kidney problems) and old age might make it unfeasible to administer systemic therapy, although these patients are mostly the same as those with poor ECOG PS.
Delays in time from diagnosis to treatment	Long delays between diagnosis and start of treatment can make patients ineligible to systemic therapy because their functional status might deteriorate during this time. Delays in diagnostic testing (pathological analysis and genomic testing) are the main bottleneck. There can also be long delays in reaching a treatment decision and initiating treatment. These delays are caused by limited testing infrastructure, shortages in human resources (especially pathologists), and general capacity shortages of hospital beds and care places. Patients may also be "lost" when being referred from one hospital to another during the diagnostic process leading up to treatment start.
Narrow eligibility criteria for receiving drug treatment	Some national clinical guidelines and/or reimbursement guidelines might not be consistent with ESMO guidelines. For example, they might not recommend/cover administering systemic therapy to patients with fair functional status (ECOG PS 2). In addition, national clinical practices for treating patients diagnosed with stage IIIB and IIIC differ (either (i) treatment as metastasized disease with systemic therapy, (ii) surgery preceded by chemotherapy and/or radiotherapy, or (iii) chemoradiotherapy followed by maintenance immunotherapy) and might restrict receipt of systemic therapy.
Treatment refusal by patients	Some patients might refuse to receive systemic therapy, e.g., because of stigma (among current/former smokers), fear of treatment side effects, or low trust in health care professionals and/or the health care system.

Table 2: Barriers to administering modern drug treatment options

Barrier	Explanation
Delays in reimbursement of modern medicines	The local reimbursement of new medicines (or new indications of existing medicines) which are recommended as standard-of-care in ESMO guidelines might take several years after EMA approval. During this time most patients can only access older treatment options.
Limited public (medicine) budgets	Slow reimbursement of new medicines can be caused by constrained public health care budgets or constrained public (cancer) medicine budgets. In addition, even reimbursed medicines might not be available for all patients if hospital budgets are restricted.
Limited resources for diagnostic testing	Genomic testing and immunohistochemistry are prerequisites for selecting appropriate targeted therapies and immunotherapies in aNSCLC. Extensive genomic testing with NGS for less common genomic alterations (e.g., ROS1, NTRK) might not be done because of practical reasons (lack of high-quality tumor tissue), limited testing capacity (both infrastructure and human resources such as pathologists), or financial reasons (lack of reimbursement of testing).
Limited continuing medical education	The rapidly changing treatment landscape in aNSCLC poses a challenge for the fast diffusion of new treatment practices. In certain patient subgroups, health professionals faced a new treatment paradigm on a yearly basis in 2014-2020. A lack of continuous training of health professionals at all treating hospitals across the whole country delays the rapid and widespread adoption of new treatment options.

2.3 Published studies on drug treatment rates

A side result of the Phase 1 report was the identification of previously published observational studies on drug treatment rates in aNSCLC in the included countries. These studies used patient-level data to estimate drug treatment rates. The following studies were identified:[1]

- **England+Wales**: 66% of patients with stage IIIB–IV NSCLC and ECOG PS 0–1 received systemic anti-cancer therapy in 2018, according to the National Lung Cancer Audit (17). Notably, the National Lung Cancer Audit publishes these statistics on an annual basis.
- **Finland**: Around 66% of patients with stage IV NSCLC diagnosed in 2014-2018 and treated in 2014-2019 received systemic anti-cancer therapy (including chemoradiotherapy), according to an analysis of patients with NSCLC diagnosed in four (out of five) university hospitals in Finland (18). An additional 1% of patients received only surgery, and 13% only radiation therapy (excluding palliative radiation therapy).
- **Netherlands**: Almost 90% of stage IV NSCLC patients with active tumor treatment (i.e., excluding those receiving best supportive care) received systemic therapy (including chemoradiotherapy) with cancer medicines as first-line treatment in 2019, according to the Dutch Lung Cancer Audit study (19)
- **Norway**: Around 50% of stage III–IV NSCLC patients diagnosed in January–October 2019 received systemic therapy (including chemoradiotherapy) with cancer medicines as first-line treatment in 2019, according to a nationwide analysis of three (out of four) health care regions (20)
- **Portugal 1**: 76% of patients with stage IIIB–IV NSCLC diagnosed in 2015–2016 received at least one line of systemic therapy with cancer medicines in IPO-Porto, Portugal's largest oncology hospital (21)
- **Portugal 2**: 50% of patients with metastatic lung cancer diagnosed in 2014–2015 received at least one line of chemotherapy and 6% received at least one line of immunotherapy, according to data from the regional cancer registry of Southern Portugal (22)

These studies have in common that they are based on data obtained from cancer registries and/or hospital records. However, they apply varying definitions to define the number of patients treated (the numerator of the treatment rate) and the number of patients eligible for treatment (the denominator of the treatment rate). These treatment rates are thus not comparable across countries and also not within countries in the case of the two studies for Portugal.

[1] The study for Finland was identified in the course of the literature search for this report.

3. Results

The evaluation of drug treatment rates is a critical component in understanding local treatment practices in aNSCLC. This is fundamental for the assessment of quality of care and disparities in access to care. Treatment rates reflect the proportion of patients who receive treatment compared to those patients who are considered eligible for treatment. They are defined as (in %):

$$\text{Drug treatment rate} = \frac{\text{Number of treated patients}}{\text{Number of eligible patients}}$$

A further refinement in the analysis of treatment rates is the type of treatment received. Both the overall size of the treatment rates and the composition of the treatment rates are required to assess the quality of treatment. It is also important to define who is considered eligible for treatment.

This section will first establish a common benchmark for optimal treatment of aNSCLC based on ESMO clinical guidelines. This helps to better gauge the size and the composition of the drug treatment rates that were found in the literature review for a specific country. These results are presented in the next section. The final section describes the availability of published data on treatment rates in aNSCLC and helps to understand to what extent European health systems are ready to measure treatment rates.

3.1 Recommended treatment in aNSCLC

The drug treatment rate in aNSCLC can theoretically range from 0% (no patients get treated) to 100% (all patients get treated). The upper limit of 100% is a hypothetical target. A certain proportion of patients will only receive “best supportive care” as first-line treatment, because factors such as poor ECOG PS, presence of certain co-morbidities (such as cardiovascular diseases or kidney problems), or old age limit the use of systemic anti-cancer therapy.

ESMO treatment guidelines for metastatic NSCLC recommend systemic anti-cancer therapy for patients with ECOG PS 0–2 but not for patients with ECOG PS 3–4 (except for EGFR-positive patients) (23). Surgery, radiotherapy, or chemoradiation therapy are not recommended as treatments in this patient group. Many countries lack public, nationally representative data on the distribution of ECOG PS in newly diagnosed aNSCLC patients; see Appendix in the Phase 1 report and Country summaries in the Appendix of this report. Based on the limited information available, around 75% of newly diagnosed aNSCLC patients in Europe might have ECOG PS 0-2. Therefore, the benchmark for the overall drug treatment rate in aNSCLC is 75% (and not 100%).

Figure 2 presents a benchmark for drug treatment rates, drawing on ESMO treatment guidelines for aNSCLC in its versions from 2014, 2016, 2018, 2019, 2020, and 2023 (23-28), as well as on the year of approval of ESMO-recommended cancer medicines by the EMA. The overall drug treatment rate amounts to 75% in all years from 2014–2023. The 75%-benchmark assumes that around 25% of newly diagnosed patients are not recommended to receive any first-line systemic anti-cancer therapy due to poor ECOG PS (3-4) and instead receive best supportive care. The same 75%-benchmark is also assumed to be applicable for patients receiving second-line treatment.

The landscape of medical treatment for aNSCLC has evolved significantly following the approval of numerous targeted therapies and immunotherapies in both first-line and second-line

treatment; see Appendix for a list of EMA-approved medicines. Figure 2 illustrates how these advancements altered the standard-of-care across lines of therapy according to ESMO guidelines. A pivotal shift was the introduction of immunotherapy. Initially recommended for second-line treatment of squamous NSCLC in 2015, immunotherapy as monotherapy gained prominence as a first-line option for PD-L1-high expressers in 2017, replacing chemotherapy alone and displacing it to the second-line setting. In 2018, immunotherapy in combination with chemotherapy started to become standard of care for non-PD-L1-high expressers. At the same time, targeted therapies began to replace chemotherapy in the first-line setting, starting with the approval of an ALK inhibitor in 2015, followed by ROS1, BRAF, NTRK, and RET inhibitors over the subsequent years. The scope of targeted therapies further expanded in the second-line setting with the approval of KRAS and MET inhibitors in 2022, and a HER2 inhibitor in 2023.

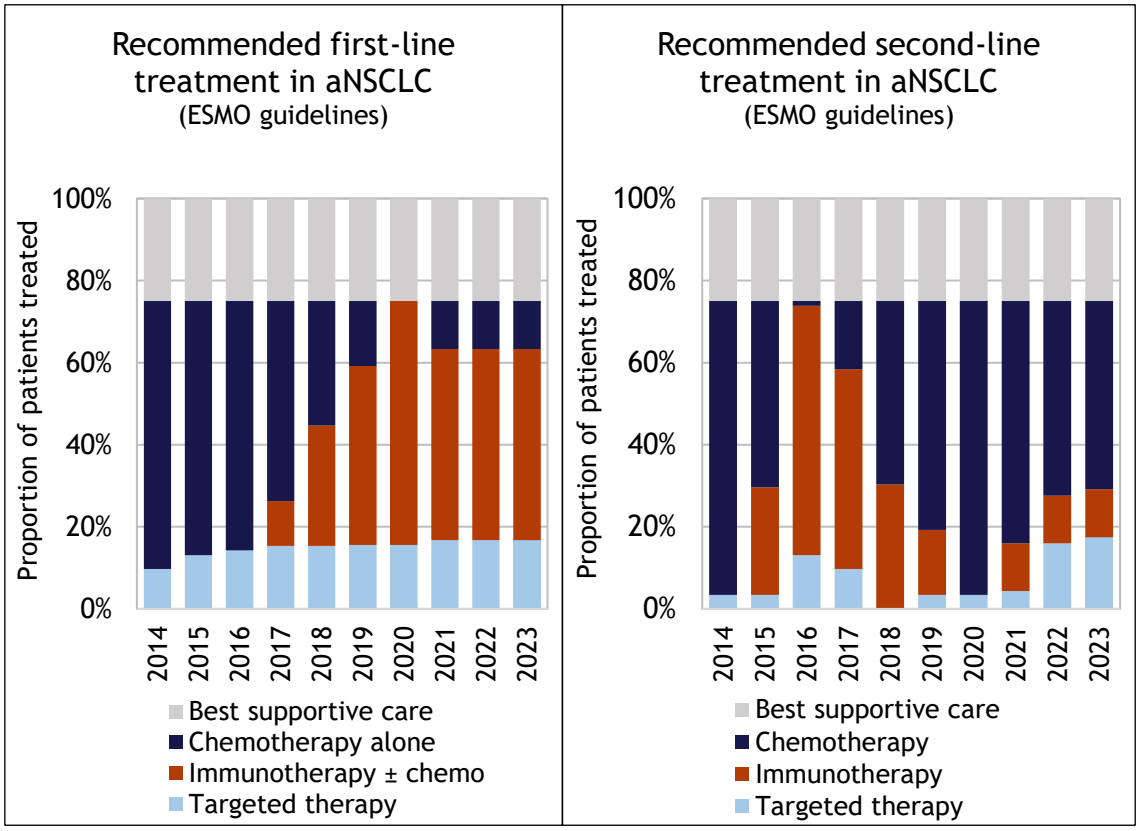


Figure 2: Recommended first-line and second-line treatment of aNSCLC based on ESMO guidelines, 2014-2023.

Notes: Best supportive care = no treatment with cancer medicines. Chemotherapy alone = platinum-based chemotherapy, Immunotherapy ± chemo = immunotherapy as monotherapy or in combination with platinum-based chemotherapy. 25% of newly diagnosed patients were assumed to have ECOG PS 3–4 and receive best supportive care. 55% of newly diagnosed patients were assumed to have ECOG PS 0–1 and 20% ECOG PS 2, and these patients were assumed to receive systemic therapy. The same ECOG PS distribution was also assumed for second-line treatment. Cancer histology was assumed to be 65% non-squamous disease (including all druggable mutations) and 35% squamous disease; the same histological proportions in first and second line were assumed. The proportion of druggable mutations was assumed to be EGFR 13%, ALK 4.5%, ROS1 1.5%, BRAF V600E 1.5%, NTRK 0.3%, RET 1.5%, MET ex14 3%, KRAS G12C 12.5%, EGFR Ex20Ins 1.3%, HER2 2%. The proportion of patients with PD-L1 ≥ 1% and PD-L1 ≥ 50% expression was assumed to be 54% and 25%, respectively, in both non-squamous disease (excluding all druggable mutations) and squamous disease, with the same proportions assumed in first and second line. The 2023 ESMO treatment guidelines for aNSCLC provide a more granular stratification of patient groups compared to the 2020 version, which clarifies that first-line immunotherapy had not entirely replaced the use of chemotherapy. Patients without druggable mutations with ECOG PS 2 and PD-L1 <50% should receive first-line chemotherapy. For those patients, immunotherapy is instead recommended as second-line treatment.

Source: ESMO guidelines (23-28), and assumptions for prevalence of histological subtypes and mutations (11, 29, 30).

3.2 Studies on drug treatment rates in aNSCLC

The pragmatic literature review identified numerous studies related to NSCLC drug treatment rates. A detailed summary for every country is provided in the Appendix. In total, published treatment rates in aNSCLC were found for 11 of the 13 European countries. No data points were identified for Croatia and Slovakia. The identified studies show a wide spectrum of drug treatment rates, ranging from 57% to 95%; see Figure 3. The overall treatment rates (i.e., describing whether diagnosed patients receive any cancer drug treatment) are relatively high in most observed countries. Only Denmark (57%), Switzerland (69%) and France (71%) are below the ESMO-benchmark drug treatment rate of 75%. Germany had the highest treatment rate (95%), yet these findings stem from a selective sample not representative on a national scale.

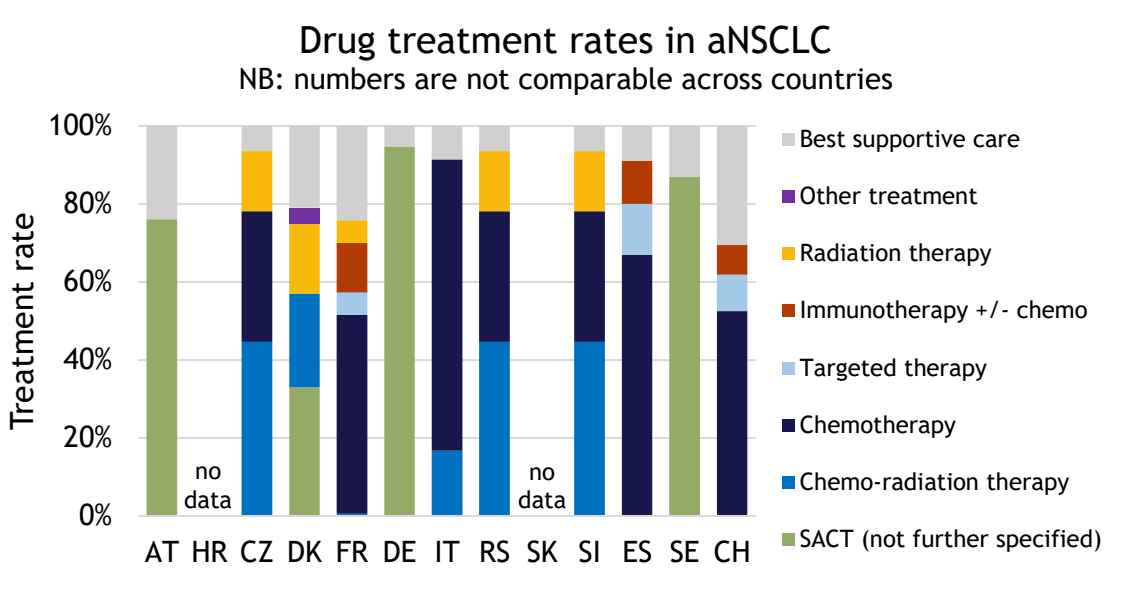


Figure 3: Drug treatment rates in aNSCLC in Europe from published studies covering the years 2007-2022.

Notes: SACT = systemic anti-cancer therapy, i.e., cancer medicines of any kind. Source: see Table 4.

The most important insight from Figure 3 is the fact that published drug treatment rates in aNSCLC are not comparable across countries. The research settings differ from study to study. Table 4 summarizes key characteristics of each study shown in Figure 3. The following challenges inhibit meaningful cross-country comparisons:

- **Lack of country-specific data.** There are no published treatment rate data for Croatia and Slovakia, creating a gap in the understanding of aNSCLC care in these countries. Additionally, the data from Czechia, Serbia, and Slovenia are aggregated from multi-country studies that do not offer detailed insights on a country-specific basis.

- **No national representativeness.** The extent to which data represents national treatment practices is often limited. Some studies are based on single institutions or regional data, potentially not reflecting the treatment landscape at a national level. Only two countries – Denmark and Sweden – have published treatment rates based on national registry data.

- **Up-to-dateness of data and variation in study periods.** Apart from Sweden, the latest available data in all countries are comparatively old. The time frames of the collected

data extend from 2007 to 2022. Most studies only capture the period before the introduction of immunotherapy and most targeted therapies in the first-line treatment setting.

- **Study population diversity.** The patient populations studied across the literature are diverse, covering different disease stages (III, IV, IIIB-IV, unresected cases), patients with different ECOG performance statuses (all, 0-2, 0-3), and patients with different mutation profiles (all or excluding EGFR/ALK mutations).

- **Inconsistencies in reporting of treatment.** The reviewed studies exhibit a lack of standardization in reporting treatment modalities and treatment lines. Many studies categorize treatments as systemic anti-cancer therapy without distinguishing between chemotherapy, immunotherapy, or targeted therapy. Additionally, treatment lines are variably reported, with some studies focusing exclusively on first-line treatment and others on any treatment use throughout the patient's course.

The variability of the identified studies renders it impossible to provide a coherent picture of disparities in aNSCLC care across EU countries. It is also difficult to provide more country-specific assessments of the quality of aNSCLC care based on a comparison with treatment standards defined in the ESMO guidelines (see section 3.1) due to the absence of detailed information on the type of cancer medicines received. Nevertheless, the findings from the following four studies summarized in Table 3 offer some perspectives on the adherence to ESMO guidelines. These insights are particularly relevant in light of the findings in the Phase 1 report (see section 2). They generally confirm that far from all patients seemed to receive standard-of-care treatment compared to the ESMO-guideline-based benchmark, with underuse of both immunotherapy and targeted therapy and overuse of chemotherapy being prevalent.

Table 3: Utilization of ESMO-recommended treatment options in selected countries

Country	Description
Denmark	A registry analysis examining the entire Danish NSCLC patient population from 2005 to 2015 revealed an increase in the use of SACT among aNSCLC patients prior to the introduction of immunotherapy and most targeted treatments (31). This correlated with an improvement in 1- and 2-year overall survival rates for stage IIIB patients, yet stage IV patients did not experience improved overall survival during the study period. This situation may be explained by the observation that, even in 2015, a notable 22% of stage IV patients received a treatment other than SACT (mostly radiation therapy) and a further 21% of patients received no treatment at all. This suggests a distinct deviation from the therapeutic approach set out in ESMO guidelines.
France, Germany, Italy, Spain, and UK (Multi-country analysis)	A multi-country analysis of survey data from 2020 from France, Germany, Italy, Spain, and the UK indicated a considerable use of immunotherapy as a first-line treatment in 63% of patients with aNSCLC without EGFR and ALK mutations (32). Yet, 35% of patients received chemotherapy as a first-line treatment. Targeted therapy was only used in 1% of patients. This pattern suggests a divergence from ESMO guideline-based benchmarks, with an apparent underutilization of both immunotherapy and targeted therapy. The findings imply that the adoption of recommended treatment options in the big European countries may lag, on average, by approximately two years behind ESMO guidelines.
France - Centre-Val de Loire region	In a French regional retrospective cohort study from 2018, a majority of patients (76%) with unresectable NSCLC were treated with SACT as their first-line treatment (33). Chemotherapy was the predominant treatment modality (51% of patients), while immunotherapy (13%) and targeted therapy (6%) were less frequently administered. This treatment patterns diverges from ESMO benchmarks, which recommended a greater use of both immunotherapy and targeted therapy and a lower use of chemotherapy in 2018.

Country	Description
Spain – The Thoracic Tumors Registry (RTT)	In a retrospective study based on data from the Thoracic Tumors Registry (RTT) from August 2016 to January 2020, 91% of metastatic NSCLC patients were treated with SACT as their first-line treatment (34). Chemotherapy was administered to 67% of patients, followed by targeted therapy (13%), and immunotherapy alone or in combination with chemotherapy (11%). The findings indicate that treatment patterns in Spain diverge from ESMO benchmarks. While the use of targeted therapy aligns quite closely with these benchmarks, the underutilization of immunotherapy at the expense of chemotherapy suggests a significant lag in the adoption of new treatment standards in clinical practice.
Switzerland - Community hospital in Basel	In a retrospective study of data from a Swiss community hospital from 2007 to 2018, the introduction of targeted therapies and immunotherapy influenced first-line and second-line treatment regimens for aNSCLC (35). A majority of patients (69%) were treated with SACT as their first-line treatment between 2015 and 2018. However, the adoption rates of immunotherapy (8%) and especially targeted therapy (9%) remained below average values defined in ESMO guidelines for 2015-2018, with chemotherapy (53%) persisting as the predominant first-line therapy. The indicated underutilization of recommended immunotherapy and targeted therapy highlights a lag in aligning clinical practice with evolving clinical guidelines.

Table 4: Published studies of drug treatment rates in aNSCLC across 13 European countries

Country	Time period	Patient group			Setting/population coverage	Treatment rate	Comments (source)
		Disease stage	ECOG PS	Line of therapy			
Austria	2013-2015	IIIB-IV	All (0-2: 90%)	First line	17 hospital departments	76%	Pilot study including 50% of all newly diagnosed cases in Austria in 2013 (36)
Croatia	–	–	–	–	–	–	No data
Czechia	2014-2017	III	0-3 (0-2: 95%)	First line	7 countries, 16 medical centers	78%	No country-specific data. Full sample n=583 (Czechia n=269 [46%]) (37). Treatment rate is based on non-surgical patients (n=448)
Denmark	2015	IV	Not specified	First line	National registry data	57%	The Danish SCAN-LEAF cohort: all adult NSCLC patients from Jan 2005 to Dec 2015 (31)
France	2018	Mostly III+IV	All (0-2: 94%)	First line	Centre-Val de Loire region	71%	Retrospective cohort study. 466 patients with unresectable NSCLC (33).
Germany	2011-2016	IIIB-IV	All	All: 1L to 2L=38% 1L to 3L=14%	Statutory German Sickness fund AOK PLUS covering Saxony/Thuringia (>50% of the overall population in these states)	95%	Full sample n=15,871. Included non-representative sample n=1,741 (38)
Italy	2007-2008	IIIB-IV	All	First line	74 centers throughout Italy	92%	1-year longitudinal multicenter study (SUN): 987 NSCLC patients from Jan 2007 to Mar 2008 (39)
Serbia	2014-2017	III	0-3 (0-2: 95%)	First line	7 countries, 16 medical centers	78%	No country-specific data. Full sample n=583 (Serbia n=109 [19%]) (37). Treatment rate is based on non-surgical patients (n=448)
Slovakia	–	–	–		–	–	No data
Slovenia	2014-2017	III	0-3 (0-2: 95%)	First line	7 countries, 16 medical centers	78%	No country-specific data. Full sample n=583 (Slovenia n=53 [9%]) (37). Treatment rate is based on non-surgical patients (n=448)
Spain	2016-2020	Metastatic	Not specified	First line	The Thoracic Tumors Registry (RTT) including data of patients diagnosed with NSCLC in hospitals across Spain.	91%	Patients included in the RTT (Aug 2016- Jan 2020) = 12,897. Patients included in this retrospective analysis = 5,049 (34)
Sweden	2022	IIIB-IV	0-2	Not specified	National registry data	87%	Annual drug treatment rate data with full national coverage since 2009 (40)
Switzerland	2015-2018	IV	Not specified	First line	One community hospital in Basel	69%	Hospital-specific data from all consecutive patients diagnosed with stage IV NSCLC between 2007 and 2018 (35)

Notes: This table presents the most pertinent studies on drug treatment rates in aNSCLC for each country included in our literature review conducted from March to October 2023. Detailed summaries of all identified publications by country can be found in the Appendix. No data were identified for Croatia and Slovakia. No country-specific data were found for Czechia, Serbia, and Slovenia.

3.3 Availability of published data on drug treatment rates

The previous section highlighted significant gaps in the availability of published data on drug treatment rates in aNSCLC in the 13 countries included in the literature review of this report. The Phase 1 report described the availability of published data for 12 additional countries, albeit not based on an equally systematic literature review (see section 2.3). Figure 4 draws together information for all 25 countries studied in the previous and current IHE report and illustrates the landscape of published data availability for aNSCLC drug treatment rates. All countries are categorized into three distinct groups based on the comprehensiveness of published data.

Green category: Sweden (via the National Quality Registry for Lung Cancer)[2] and the UK (via the UK Lung Cancer Audit and the National Disease Registration Service)[3] are the only countries regularly providing annual drug treatment rates data publicly. They set a benchmark for best practices in data transparency and commitment to ongoing monitoring of lung cancer treatment practices. However, even in these two leading examples, granular published information regarding the types of cancer medicines administered is missing. There is only data published on whether a patient was treated with systemic therapies, but no data on the kind of systemic therapy (chemotherapy, immunotherapy, targeted therapy, or a combination of these).

Yellow category: 11 countries have at least one published country-specific study contributing data, offering a fragmented picture of drug treatment rates in aNSCLC. Such snapshots, albeit useful, cannot replace the continuous data stream necessary for monitoring trends to inform timely policy decisions. Most of the available studies are outdated and do not provide insights into current clinical practices, in particular the use of modern treatment options.

Red category: About half of the countries (12 out of 25) have no published data at all or only non-country specific data from multi-national studies. Most of these countries are located in Central and Eastern Europe and represent a significant blind spot in the understanding of aNSCLC treatment patterns in the European context.

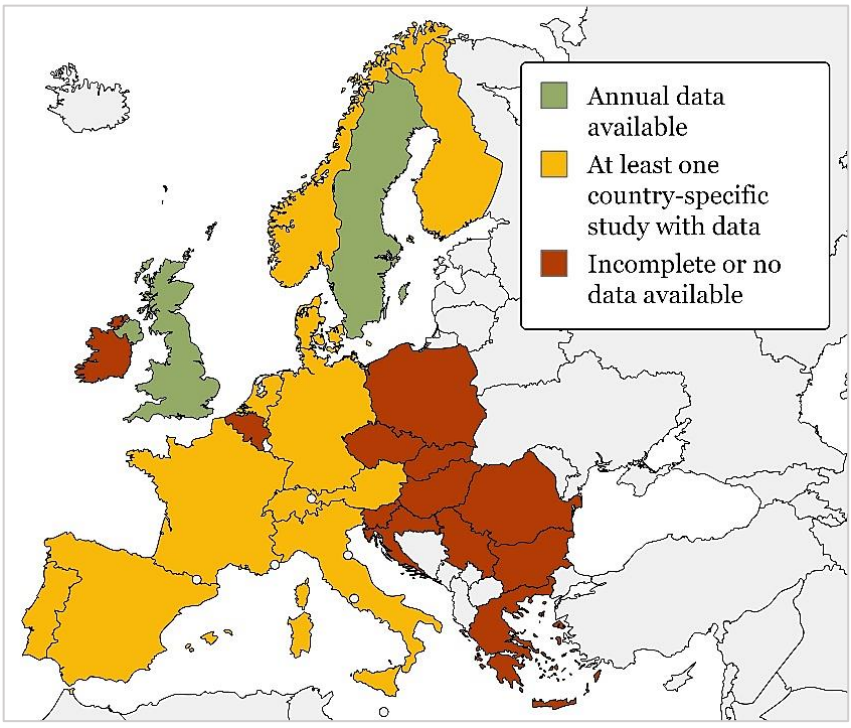


Figure 4: Availability of published drug treatment rate data in aNSCLC in Europe.

Source: see Table 4 and section 2.3.

[2] https://statistik.incanet.se/Lunga/
[3] https://www.lungcanceraudit.org.uk/ and https://digital.nhs.uk/ndrs/data/data-outputs/cancer-data-hub/cancer-treatments

4. Discussion and conclusion

Lung cancer persists as a critical health concern, as it accounts for a substantial proportion of the burden of cancer responsible for 20% of all cancer deaths in the EU in 2022. The EBCP by the European Commission presents an unprecedented opportunity to improve lung cancer care. To help seize this opportunity, a group of stakeholders under the patronage of MEP Cristian-Silviu Buşoi issued a Call to Action titled "*Fighting lung cancer together as equals*" in December 2022. It underscores the need to combat this disease through comprehensive strategies, aiming at fortifying prevention, enhancing early detection, driving health literacy, and ensuring faster patient access to modern diagnostic tests and treatments. It also calls for enhancing data collection on treatment rates and their inclusion in the European Cancer Inequalities Registry. The latter point was the rationale for the objective of this report to investigate whether European health systems capture and publish reliable, up-to-date real-world data on drug treatment rates in aNSCLC.

Measuring drug treatment rates transcends a mere statistical exercise; it is a quality indicator reflective of a health care system's capacity to translate clinical recommendations and scientific advances into clinical practice. A diagnosis of aNSCLC is no guarantee to receive guideline-recommended treatment with cancer medicines, because of delays in the diagnostic process or stringent eligibility criteria for treatment. Although reimbursement of novel medicines is essential for patient access, it does not guarantee their actual use. Various barriers, such as limited hospital budgets, lack of diagnostic testing infrastructure and personnel, and slow adoption of new treatment options, can hinder the delivery of guideline-recommended care. Therefore, measuring drug treatment rates is vital to identify these barriers, assess the impact of interventions, and ultimately elevate the standard of care.

The main result of this report is the apparent lack of reliable and relevant published data on aNSCLC drug treatment rates across European countries. This gap in published data underscores a systemic challenge in health care systems: the absence of robust and standardized systems for processing and utilizing data from medical records and to report aggregated data publicly. Drug treatment rates are just one example of a quality indicator that is reliant on the utilization of data that are registered and collected throughout the patient journey. The variability in published treatment rates data in scientific studies is problematic and renders it difficult to compare treatment practices across countries and to benchmark treatment patterns against ESMO guidelines. In sum, European health care systems are currently not ready to measure treatment rates in aNSCLC, which would offer a possibility to effectively monitor and optimize the delivery of aNSCLC care.

Given the complexity and the significant cross-country variability in published treatment rates, there is a pressing need for systematic monitoring and reporting. This report recommends the incorporation of drug treatment rates into national clinical cancer registries, with regular publication of findings to facilitate transparency and accountability. Systematic monitoring would enable health care providers and policymakers to track progress, benchmark against best practices and clinical guidelines, and tailor interventions to specific national or regional needs. The Swedish National Quality Registry for Lung Cancer and the UK Lung Cancer Audit serve as prime examples of how systematic data collection and analysis can be made publicly available and inform quality improvement initiatives and policy decisions. Such registries not only provide invaluable insights into national treatment patterns but also empower international comparisons and collaborative efforts to address disparities in aNSCLC care.

While acknowledging Sweden and the UK as leading examples in monitoring lung cancer treatment in Europe, it is evident that best practice requires further enhancements in data

collection and transparency. Specifically, this report recommends that national clinical cancer registries are established in places where they do not yet exist. Furthermore, they should detail therapeutic interventions with more precision, categorizing systemic therapies at least by type — chemotherapy, immunotherapy, and targeted therapy — and documenting their combinations and sequences across treatment lines. These registries should also incorporate a benchmark based on national or international clinical guidelines. A more granular approach to data collection and data provision would facilitate comprehensive analyses, enabling health care providers and policymakers to tailor interventions more precisely and benchmark real-world treatment practices against clinical guidelines with greater accuracy.

In conclusion, the fight against lung cancer in Europe requires a sustained commitment to data-driven policymaking and health care delivery. The integration of drug treatment rates into national cancer registries would be a critical step towards achieving the goals set forth by the EBCP. This report's findings reinforce the need for a concerted effort to ensure that all patients across Europe receive timely and effective treatments, and for a commitment to close the gap between clinical guidelines and real-world treatment practices.

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Appendix

Search strategy

The following search strategy to identify relevant studies about drug treatment rates in aNSCLC was applied.

PubMed: ("country"[MeSH Terms] OR "country"[Title/Abstract]) AND ("nsclc"[Title/Abstract] OR "non-small cell lung cancer"[Title/Abstract] OR "carcinoma, non-small cell lung"[MeSH Terms])

PubMed: ("country"[MeSH Terms] OR "country"[Title/Abstract]) AND ("nsclc"[Title/Abstract] OR "non-small cell lung cancer"[Title/Abstract] OR "carcinoma, non-small cell lung"[MeSH Terms]) AND ("systemic treatment"[Title/Abstract] OR "immunotherapy"[Title/Abstract] OR "targeted therapies"[Title/Abstract] OR "target therapy"[Title/Abstract] OR "target therapy"[Title/Abstract] OR "targeted therapy"[Title/Abstract])

Google Scholar: nsclc "country" systemic "treatment" rates "lung"

The word "country" was replaced with the specific country name of interest for the searches.

Country summaries

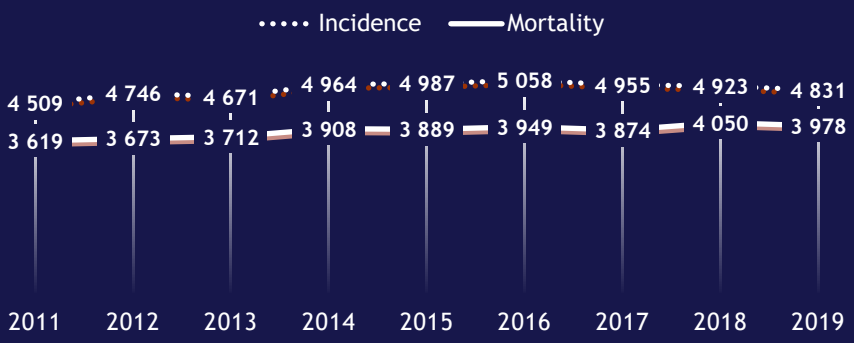
Austria

Epidemiology of NSCLC / lung cancer

Population (2022)	9.1 million
Health expenditure (2022)	
in % of GDP	11.4%
per capita in €	€ 5 659

Source: OECD (41, 42)

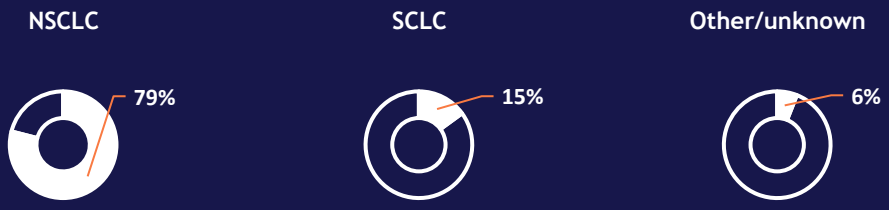
LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2019



DEATH CERTIFICATE ONLY (DCO) CASES: 12% of all diagnosed cases

Source: Statistik Austria (43)

SHARE OF SCLC VS. NSCLC



Source: Onkopedia (44)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF LUNG CANCER

PS 0	PS 1	PS 2	PS 3	PS 4	Unknown
38%	38%	14%	8%	2%	1%

Source: Burghuber et al. (2020) (36)

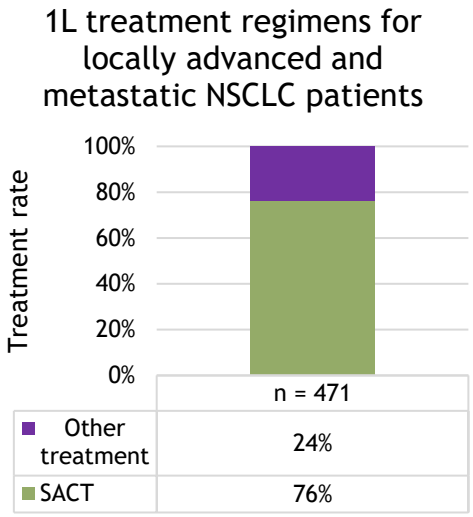
STAGE DISTRIBUTION OF LUNG CANCER

Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV
16%	8%	16%	12%	48%

Source: Burghuber et al. (2020) (36)

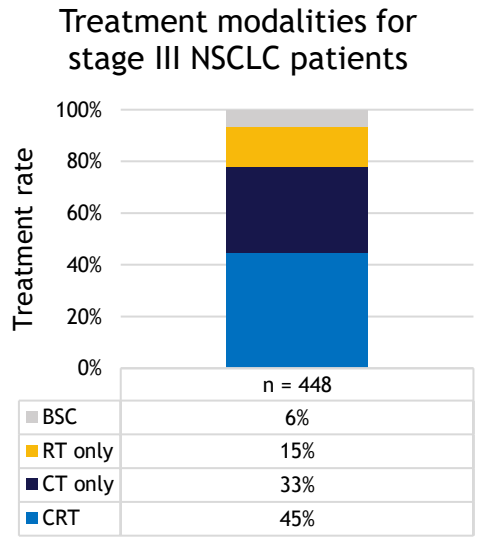
Drug treatment rates

The Austrian Lung Cancer Audit (ALCA) was a prospective pilot study conducted from 2013 to 2015. One of the purposes was to assess clinical factors related to lung cancer care in Austria. This study included 745 patients newly diagnosed with lung cancer, including 619 with NSCLC and 126 with SCLC, from 17 hospital departments in Austria (36). The demographic profile showed a majority (61%) of male patients, with an average age of 66 years. About 90% of these patients had an ECOG performance status of 0-2. Among those with advanced and metastatic NSCLC not undergoing surgical intervention (n=471), 76% received first-line systemic anti-cancer therapy (SACT).



Notes: 1L = first-line, NSCLC = non-small-cell lung cancer, SACT = systemic anti-cancer therapy. Source: (36)

A multinational study was conducted to investigate diagnostic and therapeutic approaches for stage III NSCLC in Central European countries and identify areas for improvement. Data were gathered between March 2014 and March 2017, involving 583 patients from 16 medical centers across seven Central European countries: 8 centers in Czechia, 2 in Serbia, 2 in Hungary, and one in each of Slovenia, Latvia, Lithuania, and Austria (37). Among the patient cohort, 68% were male, and 95% exhibited an ECOG performance status of 0-2. Findings indicated that over half of the patients (56%) received combined treatment modalities, with 80% receiving chemotherapy in combination with other modalities. Among the patients undergoing non-surgical therapy (n = 448), 78% received drug therapy. The most common approach was chemo-radiation therapy (45%) followed by chemotherapy alone (33%), radiation therapy alone (15%), and best supportive care (6%).



Notes: NSCLC = non-small-cell lung cancer, CRT = chemo-radiation therapy, CT = chemotherapy, RT = radiation therapy, BSC = best supportive care. Full sample including surgical patients: n = 583 (Czechia: n =269 [46.1%], Serbia: n = 109 [18.7%], Hungary: n = 48 [8.2%], Slovenia: n = 53 [9.1%], Latvia: n = 43 [7.4%], Lithuania: n = 38 [6.5%], Austria: n = 23 [4%]). Source: (37)

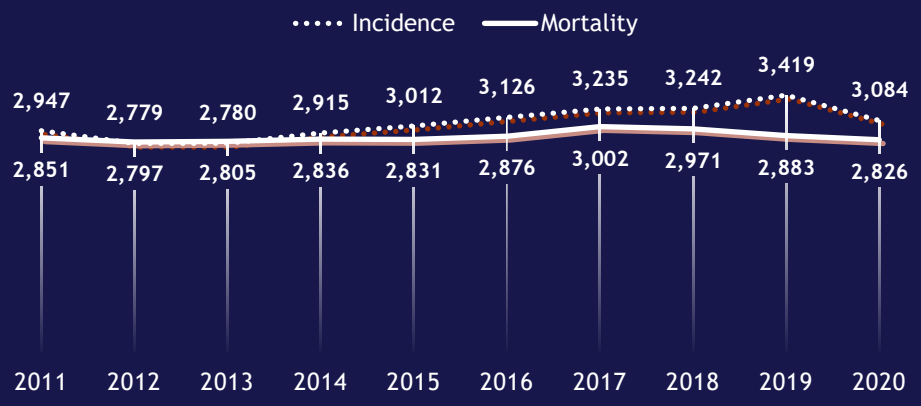
Croatia

Epidemiology of NSCLC / lung cancer

Population (2022)	3.9 million
Health expenditure (2021)	
in % of GDP	8.1%
per capita in €	€ 1 194

Source: OECD (41, 42)

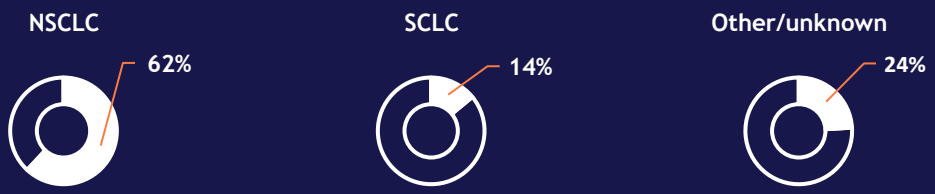
LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2020



DEATH CERTIFICATE ONLY (DCO) CASES: 7.3% of all diagnosed cases

Source: Incidence and DCO from Croatian National Cancer Registry (45-51). Mortality from Eurostat (52)

SHARE OF SCLC VS. NSCLC



Note: Assuming 2020 Croatian incidence data mirrors the SCLC vs. NSCLC distribution seen in Central and Eastern Europe during the same year. Source: (51, 53)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC / LUNG CANCER

PS 0	PS 1	PS 2	PS 3	PS 4

No information available

STAGE DISTRIBUTION OF NSCLC / LUNG CANCER

Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV

No information available

Drug treatment rates

No relevant publication on aNSCLC drug treatment rates in Slovakia were identified during the research period from March to October 2023.

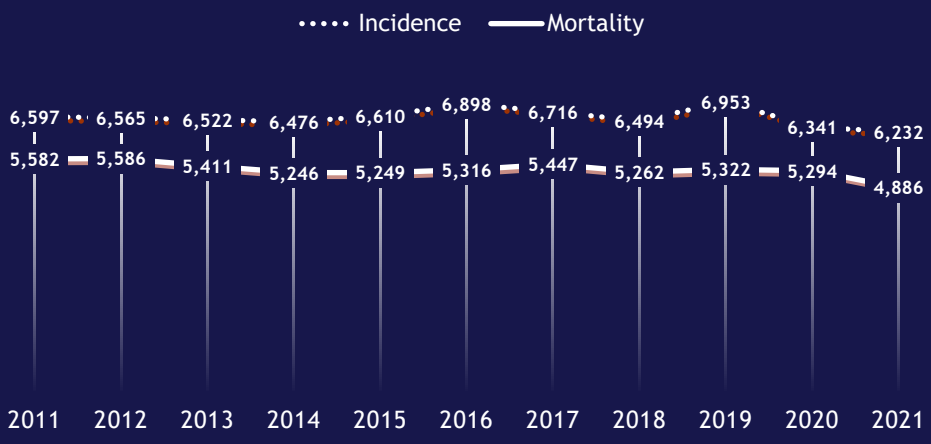
Czechia

Epidemiology of NSCLC / lung cancer

Population (2022)	10.8 million
Health expenditure (2022)	
in % of GDP	9.1%
per capita in €	€ 2 403

Source: OECD (41, 42)

LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2021



DEATH CERTIFICATE ONLY (DCO) CASES: No information available

Source: SVOD web portal (54)

SHARE OF SCLC VS. NSCLC

Note: SCLC is diagnosed in 15% to 18% yearly. Source: (55)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC / LUNG CANCER

PS 0	PS 1	PS 2	PS 3	PS 4
No available information				

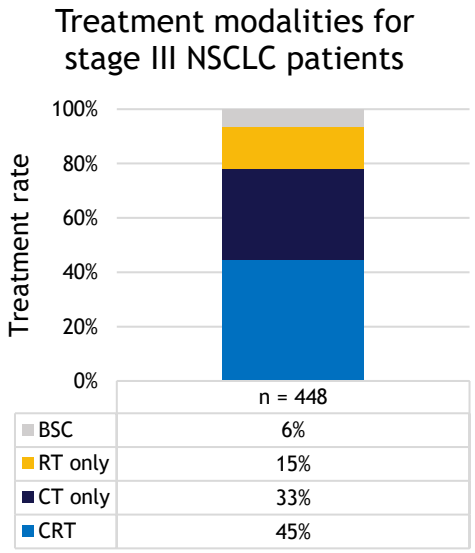
STAGE DISTRIBUTION OF LUNG CANCER

Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV	Unknown
10%	6%	17%		48%	19%

Source: SVOD web portal (54)

Drug treatment rates

A multinational study was conducted to investigate diagnostic and therapeutic approaches for stage III NSCLC in Central European countries and identify areas for improvement. Data were gathered between March 2014 and March 2017, involving 583 patients from 16 medical centers across seven Central European countries: 8 centers in Czechia, 2 in Serbia, 2 in Hungary, and one in each of Slovenia, Latvia, Lithuania, and Austria (37). Among the patient cohort, 68% were male, and 95% exhibited an ECOG performance status of 0-2. Findings indicated that over half of the patients (56%) received combined treatment modalities, with 80% receiving chemotherapy in combination with other modalities. Among the patients undergoing non-surgical therapy (n = 448), 78% received drug therapy. The most common approach was chemo-radiation therapy (45%) followed by chemotherapy alone (33%), radiation therapy alone (15%), and best supportive care (6%).



Notes: NSCLC = non-small-cell lung cancer, CRT = chemo-radiation therapy, CT = chemotherapy, RT = radiation therapy, BSC = best supportive care. Full sample including surgical patients: n = 583 (Czechia: n =269 [46.1%], Serbia: n = 109 [18.7%], Hungary: n = 48 [8.2%], Slovenia: n = 53 [9.1%], Latvia: n = 43 [7.4%], Lithuania: n = 38 [6.5%], Austria: n = 23 [4%]). Source: (37)

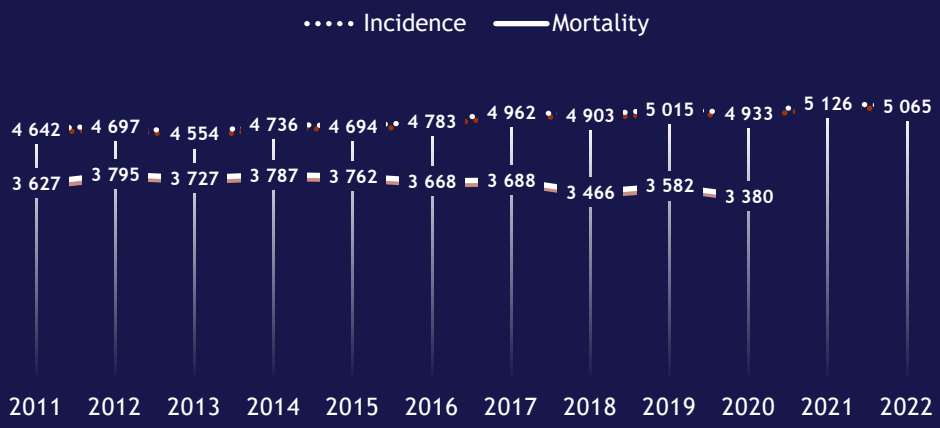
Denmark

Epidemiology of NSCLC / lung cancer

Population (2022)	5.9 million
Health expenditure (2022)	
in % of GDP	9.5%
per capita in €	€ 6 083

Source: OECD (41, 42)

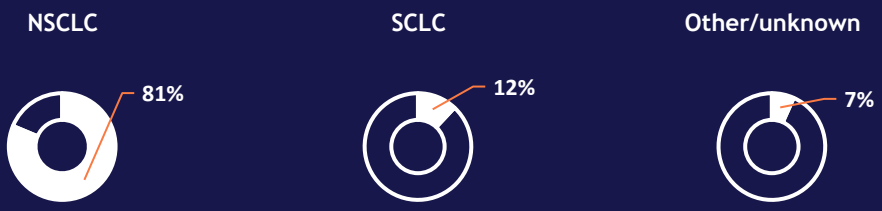
LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2022



DEATH CERTIFICATE ONLY (DCO) CASES: No information available

Source: Incidence from DLCR (56). Mortality from NORDCAN (57).

SHARE OF SCLC VS. NSCLC



Source: DLCR (56)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF LUNG CANCER

PS 0	PS 1	PS 2	PS 3	PS 4	Other/unknown
35%	30%	16%	8%	3%	5%

Source: DLCR (56)

STAGE DISTRIBUTION OF LUNG CANCER

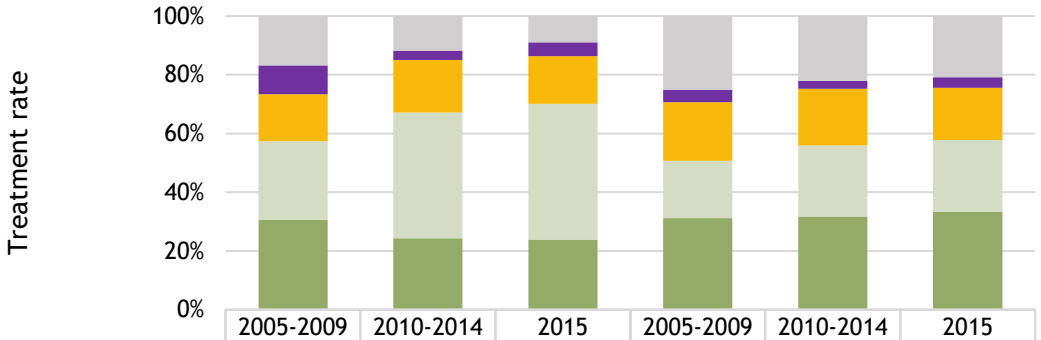
Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV	Unknown
27%	8%	9%	10%	45%	2%

Source: DLCR (56)

Drug treatment rates

The SCAN-LEAF study aimed at describing the evolution of first-line treatment patterns and overall survival of NSCLC patients in Scandinavia before the introduction of immunotherapy and novel targeted therapies. In Denmark, a total of 35,383 patients were diagnosed with NSCLC between 2005 and 2015. The median age at time of diagnosis was 69 years and 52% of these patients were male. A majority (51.6%) had developed stage IV disease at time of diagnosis. Overall, 54.4% of patients had Non-squamous NSCLC and 26.5% had Squamous NSCLC (31). In total, 31,939 NSCLC patients were analyzed. The findings for patients with advanced NSCLC showed that SACT + radiation therapy was the predominant first-line treatment option for both stage IIIB (46%) and stage IV (33%) in 2015, followed by SACT alone and radiation therapy alone. Notably, a large share (21%) of stage IV NSCLC patients remained untreated in the same year and instead received best supportive care.

First-line treatment of advanced NSCLC patients



	Stage IIIB			Stage IV		
	2005-2009 (n=1478)	2010-2014 (n=1255)	2015 (n=234)	2005-2009 (n=4888)	2010-2014 (n=6456)	2015 (n=1255)
BSC	17%	12%	9%	25%	22%	21%
Other treatment	10%	3%	5%	4%	3%	4%
RT alone	16%	18%	16%	20%	19%	18%
SACT + RT	27%	43%	46%	20%	24%	24%
SACT alone	31%	24%	24%	31%	32%	33%

Notes: ECOG performance status of patients was not specified in this study. SACT = systemic anti-cancer treatment, RT = radiation therapy, BSC = best supportive care, NSQ = non-squamous. Untreated = no SACT, RT or surgery reported. Source: (31)

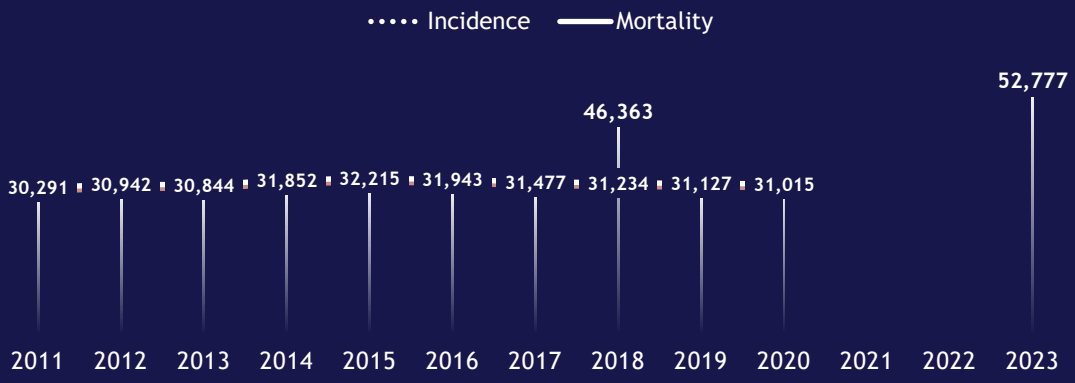
France

Epidemiology of NSCLC / lung cancer

Population (2022)	67.9 million
Health expenditure (2022)	
in % of GDP	11.9%
per capita in €	€ 4 632

Source: OECD (41, 42)

LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2023



DEATH CERTIFICATE ONLY (DCO) CASES: No information available

Source: Incidence (58, 59). Mortality (52)

SHARE OF SCLC VS. NSCLC

Source: Riviere et al. (2022) (33)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF ADVANCED NSCLC

PS 0-1	PS 2	PS 3-4
80%	14%	6%

Source: Riviere et al. (2022) (33)

STAGE DISTRIBUTION OF LUNG CANCER

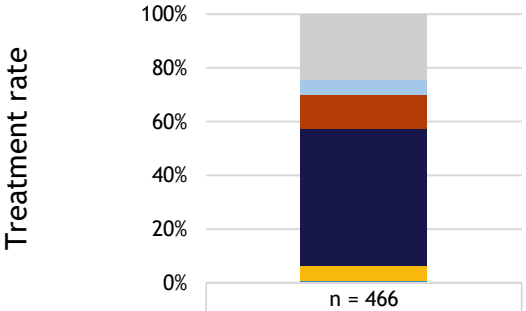
Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV
5%	5%	14%		76%

Source: Riviere et al. (2022) (33)

Drug treatment rates

A retrospective cohort study aimed to describe the care pathway of patients diagnosed with lung cancer in the Centre-Val de Loire region in France and covered the year 2018 (33). The median age of the study population was 66 years, 72% were males, and 94% exhibited an ECOG performance status of 0-2. The analysis presents that 353 (76%) of 466 patients diagnosed with unresectable NSCLC received SACT as their first-line treatment. The predominant first-line treatment consisted of chemotherapy (51%), trailed by immunotherapy (13%), radiation therapy (6%), targeted therapy (6%), and chemo-radiation therapy (1%). The remaining 113 patients (24%) received pallaiative care or therapeutic abstention.

First-line treatment rates for unresectable NSCLC patients

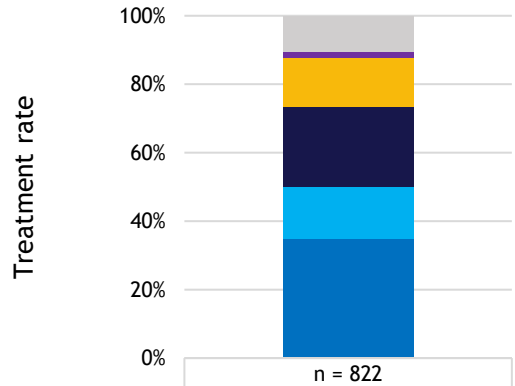


	n = 466
Untreated	24%
Targeted therapy	6%
Immunotherapy	13%
Chemotherapy	51%
Radiation therapy	6%
Chemo-radiation therapy	1%

Notes: Unresectable NSCLC = mostly stage IIIB+IV. Source: (33)

A French study investigated the management of patients with locally advanced NSCLC at a time when emerging immunotherapy was challenging the traditional approach of platinum-based chemo-radiation therapy (CRT). The study analyzed data from 8,514 lung cancer patients treated between 2015 and 2016 (60). Among the 822 patients diagnosed with unresectable locally advanced NSCLC, treatment initiation occurred for 736 patients. About 73% of all patients received drug therapy. The most common treatment modality was concurrent CRT (35%), followed by chemotherapy alone (23%), sequential CRT (15%), radiation therapy alone (14%), and other therapy (2%). The remaining 10% were untreated.

Treatment rates for locally advanced NSCLC patients

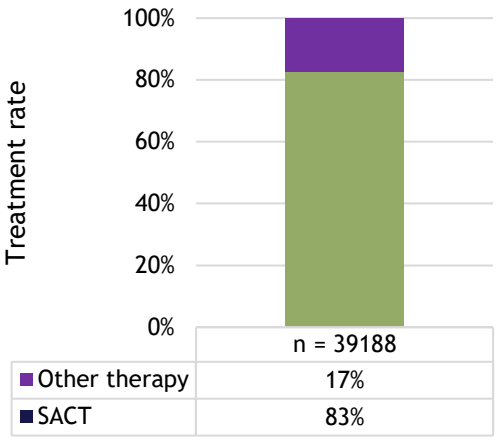


	n = 822
Untreated	10%
Other therapy	2%
RT alone	14%
CT alone	23%
sCRT	15%
cCRT	35%

Notes: cCRT = concurrent chemo-radiation therapy, sCRT = sequential chemo-radiation therapy, CT = chemotherapy, RT = radiation therapy, NSCLC = non-small cell lung cancer. Source: (60)

A study aimed to investigate the treatment approaches and patient characteristics in real-world settings for French individuals with advanced non-small cell lung cancer (NSCLC) at stages IIIB/IV. Data were extracted from case report forms (CRFs) collected by French physicians in 2015 (61). The study focused exclusively on treated, non-clinical trial participants. Results revealed a cohort of 39,188 patients, mostly male (69.3%) and averaging 64.2 years in age. The majority received first-line treatment (63.3%) and had an Eastern Cooperative Oncology Group (ECOG) score of 1 (61.1%). The predominant treatment approach was SACT (83%), with very few receiving additional treatments like surgery or radiotherapy alongside these therapies.

Type of therapy for treated stage IIIB/IV NSCLC patients

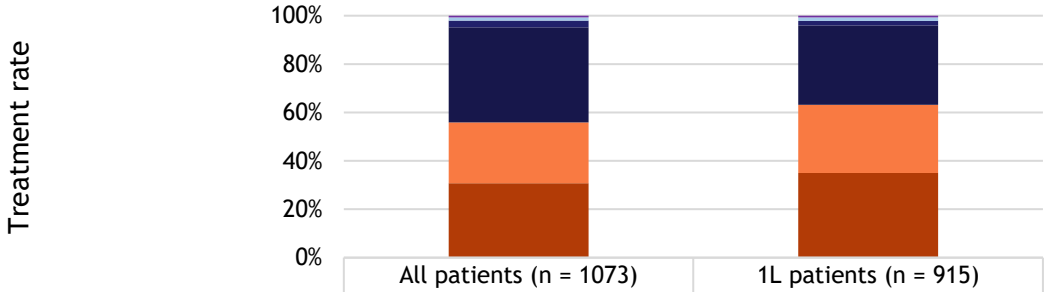


	n = 39188
Other therapy	17%
SACT	83%

Notes: SACT = systemic anti-cancer therapy (chemotherapy / targeted therapy / immunotherapy), Other therapy = not specified. Both first-line (63%) and second-line (37%) treatments are included. Source: (61)

A multi-country analysis examined the treatment patterns of patients with metastatic NSCLC without EGFR and ALK mutation (*EGFR*-WT/*ALK*-WT). Data were collected from July 2020 to November 2020, and the sample consisted of patients from France, Germany, Italy, Spain, and UK. The findings showed that, for both current first-line patients (n=915) and the entire population (n=1073), the predominant first-line treatment modality consisted of chemotherapy, trailed by immune-oncology with or without chemotherapy, and targeted therapy (32). The relevant findings are presented below.

First-line treatment rates for metastatic NSCLC patients



	All patients (n = 1073)	1L patients (n = 915)
Other	1%	1%
Targeted therapy	1%	1%
Chemotherapy combination	3%	2%
Chemotherapy only	39%	33%
IO + chemotherapy	25%	28%
IO monotherapy	31%	35%

Notes: 1L = first line, metatistic non-small cell lung cancer (NSCLC) = stage IIIB-IV , EGFR = epidermal growth factor receptor, ALK = anaplastic lymphoma kinase, IO = immuno-oncology. Main sample: n = 1073 (France: n = 264 [24.6%], Germany: n =152 [14.2%], Italy: n = 201 [18.7%], Spain: n = 226 [21.1%], UK: n = 230 [21.4%]). 1L patients = patients who did not progress beyond 1L therapy. All patients = 1L patients (n=915) + patients who progressed beyond 1L therapy (n=158). Source: (32)

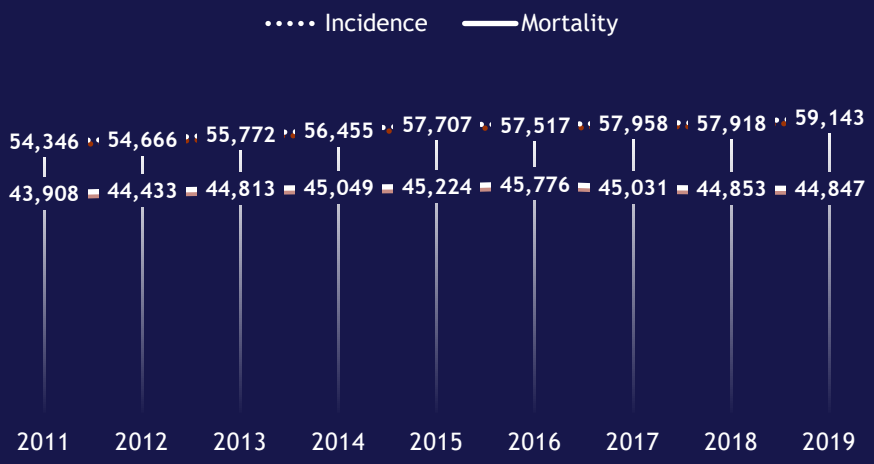
Germany

Epidemiology of NSCLC / lung cancer

Population (2022)	83.8 million
Health expenditure (2022)	
in % of GDP	12.8%
per capita in €	€ 5 879

OECD, 2023

LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2019



DEATH CERTIFICATE ONLY (DCO) CASES: 10% of all diagnosed cases

Source: Incidence and mortality from ZfKD (62). DCO from ZfKD (63)

SHARE OF SCLC VS. NSCLC

Note: Assuming 2019 German incidence data mirrors the SCLC vs. NSCLC distribution seen in Western Europe 2020. Source: (53, 62)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC

PS 0	PS 1	PS 2-4	Unknown
24%	49%	15%	12%

Source: (64)

STAGE DISTRIBUTION OF LUNG CANCER

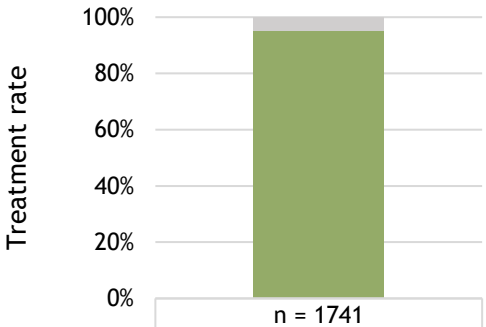
Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV
16%	9%	24%		52%

Source: ZfKD (63)

Drug treatment rates

A study attempts to describe the real-world treatment of German advanced NSCLC patient. The analysis covers the period from January 1, 2011, to December 31, 2016, and focuses on patients residing in the regions of Saxony/Thuringia in Germany. They find that approximately 95% of their observed advanced NSCLC patients received a SACT (38). Compared to previous literature, this is quite high. It should be noted, however, that the full sample had more than 15,000 patients, but only 1,741 patients were included in the analysis of the study. Thus, the sample does not seem to be representative of advanced NSCLC treatment in the studied regions of Germany.

Type of therapy advanced NSCLC patients

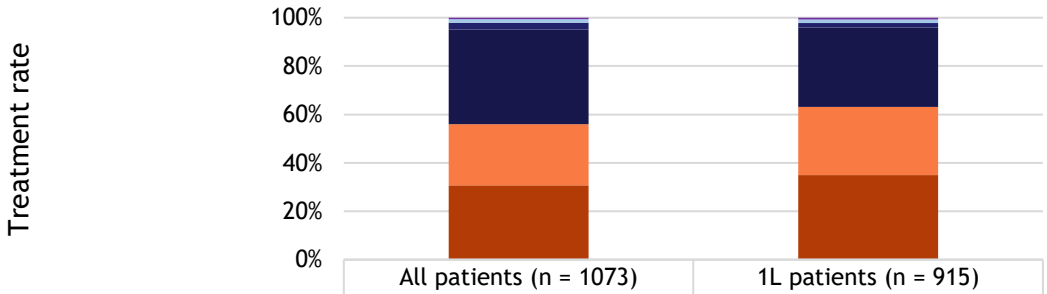


	n = 1741
No/other treatment	5%
SACT	95%

Notes: SACT: systemic anti-cancer therapy, other treatment = not specified. Source: (38)

A multi-country analysis examined the treatment patterns of patients with metastatic NSCLC without EGFR and ALK mutation (*EGFR*-WT/*ALK*-WT). Data were collected from July 2020 to November 2020, and the sample consisted of patients from France, Germany, Italy, Spain, and UK. The findings showed that, for both current first-line patients (n=915) and the entire population (n=1073), the predominant first-line treatment modality consisted of chemotherapy, trailed by immune-oncology with or without chemotherapy, and targeted therapy (32). The relevant findings are presented below.

First-line treatment rates for metastatic NSCLC patients



	All patients (n = 1073)	1L patients (n = 915)
Other	1%	1%
Targeted therapy	1%	1%
Chemotherapy combination	3%	2%
Chemotherapy only	39%	33%
IO + chemotherapy	25%	28%
IO monotherapy	31%	35%

Notes: 1L = first line, metatistic non-small cell lung cancer (NSCLC) = stage IIIB-IV , EGFR = epidermal growth factor receptor, ALK = anaplastic lymphoma kinase, IO = immuno-oncology. Main sample: n = 1073 (France: n = 264 [24.6%], Germany: n =152 [14.2%], Italy: n = 201 [18.7%], Spain: n = 226 [21.1%], UK: n = 230 [21.4%]). 1L patients = patients who did not progress beyond 1L therapy. All patients = 1L patients (n=915) + patients who progressed beyond 1L therapy (n=158). Source: (32)

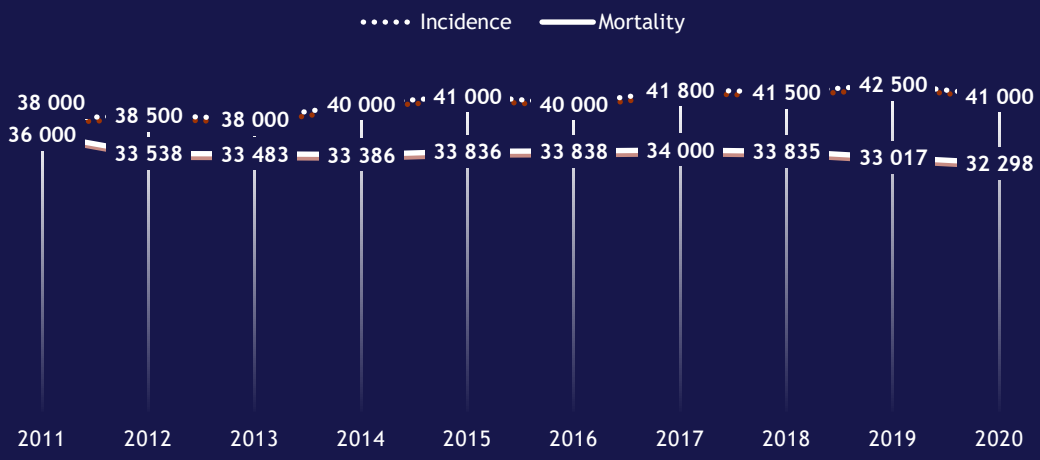
Italy

Epidemiology of NSCLC / lung cancer

Population (2022)	58.9 million
Health expenditure (2022)	
in % of GDP	9.0%
per capita in €	€ 2 912

Source: OECD (41, 42)

LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2020



DEATH CERTIFICATE ONLY (DCO) CASES: No information available

Source: Incidence (65). Mortality 2011-2017 (65) and 2018-2020 (52)

SHARE OF SCLC VS. NSCLC

Note: Data unavailable for Italy. We present the SCLC vs. NSCLC distribution seen in Southern Europe in 2020.
Source: (53)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC

PS 0-1	PS 2-4
87%	13%

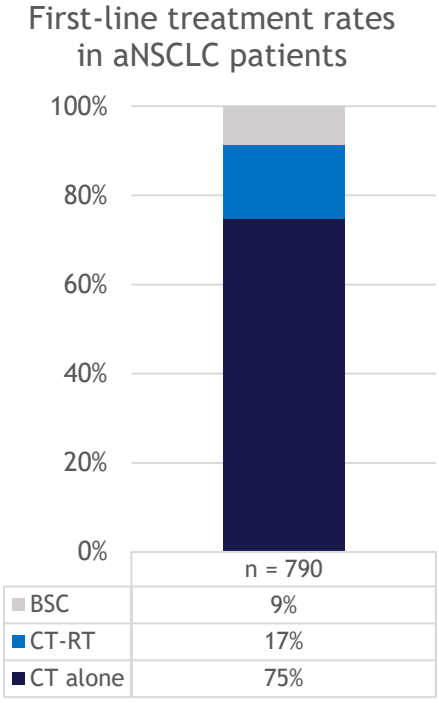
Source: Gobbini et al. (2017) (66)

STAGE DISTRIBUTION OF NSCLC / LUNG CANCER

Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV	Unknown
No information avilable					

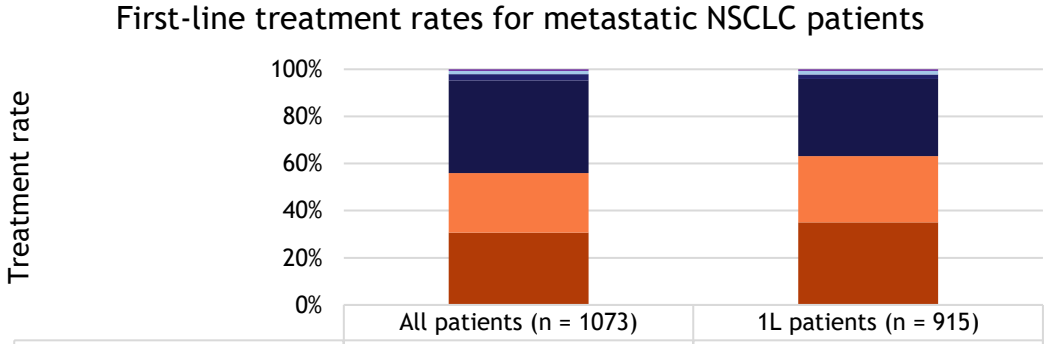
Drug treatment rates

In an observational in Italy, the care patterns for 987 patients diagnosed with advanced non-small cell lung cancer (NSCLC), during the timeframe of 2007 to 2008, were investigated. This comprehensive assessment encompassed 74 participating health care centers across Italy. Within the entire sample, the majority, accounting for 91.4%, received first-line medical treatment, while 8.6% exclusively received supportive care. For detailed analysis, the focus was solely on the subset of first-line patients who were not enrolled in clinical trials and received either chemotherapy or targeted therapies, amounting to a total of 790 individuals. The patient demographic profile revealed a median age of 66 years, with males constituting 75% of the cohort. Moreover, 78% of patients presented with stage IV NSCLC, and an equally substantial proportion, 78%, exhibited an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0-1 (39). The predominant first-line treatment was chemotherapy alone (75%) followed by chemo-radiation therapy (17%). Best supportive care alone was given to 9% of the patients.



Notes: aNSCLC = advanced non-small cell lung cancer, CT = chemotherapy, RT = radiation therapy, BSC = best supportive care. Source: (39)

A multi-country analysis examined the treatment patterns of patients with metastatic NSCLC without EGFR and ALK mutation (*EGFR*-WT/*ALK*-WT). Data were collected from July 2020 to November 2020, and the sample consisted of patients from France, Germany, Italy, Spain, and UK. The findings showed that, for both current first-line patients (n=915) and the entire population (n=1073), the predominant first-line treatment modality consisted of chemotherapy, trailed by immune-oncology with or without chemotherapy, and targeted therapy (32). The relevant findings are presented below.



	All patients (n = 1073)	1L patients (n = 915)
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Targeted therapy	1%	1%
Chemotherapy combination	3%	2%
Chemotherapy only	39%	33%
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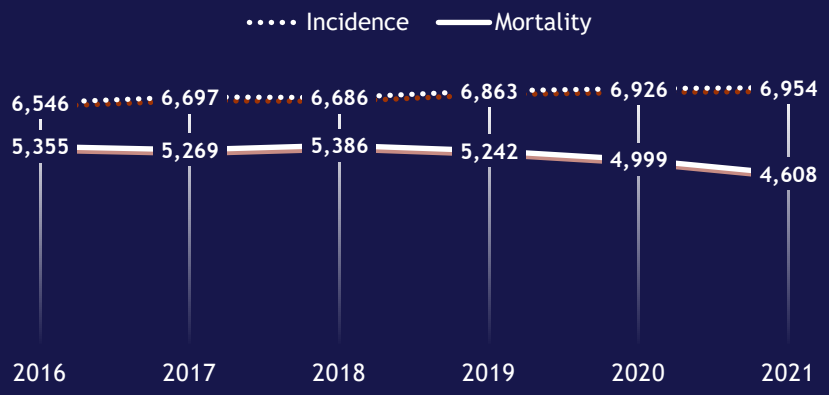
Serbia

Epidemiology of NSCLC / lung cancer

Population (2022)	6.8 million
Health expenditure (2022)	
in % of GDP	10.0%
per capita in €	€ 781

Source: Eurostat (67, 68)

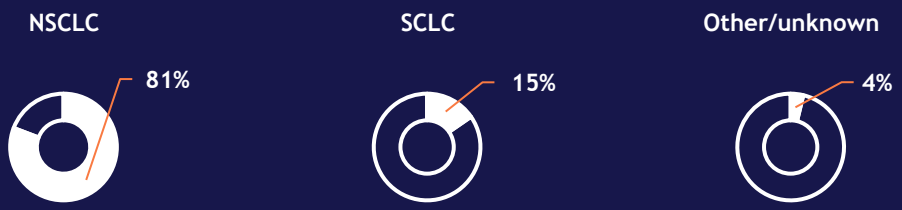
LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2016-2021



DEATH CERTIFICATE ONLY (DCO) CASES: 7% of all diagnosed cases

Source: Serbian cancer registry (69-74)

SHARE OF SCLC VS. NSCLC



Source: JD Malbasa et al. (2023) (75)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC / LUNG CANCER

PS 0	PS 1	PS 2	PS 3	PS 4
No information available				

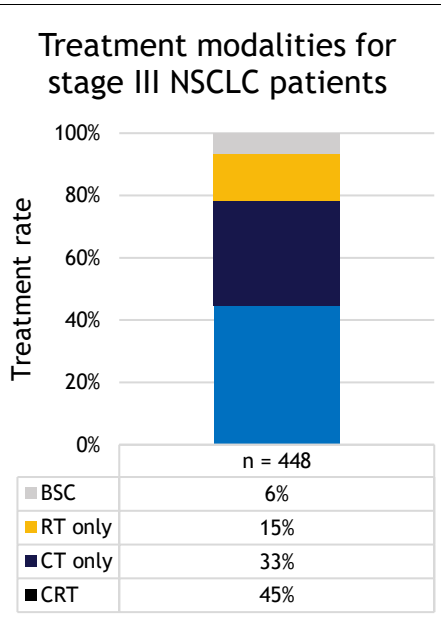
STAGE DISTRIBUTION OF LUNG CANCER

Stage I	Stage II	Stage III	Stage IV	Unknown
7%	8%	38%	41%	6%

Source: JD Malbasa et al. (2023) (75)

Drug treatment rates

A multinational study was conducted to investigate diagnostic and therapeutic approaches for stage III NSCLC in Central European countries and identify areas for improvement. Data were gathered between March 2014 and March 2017, involving 583 patients from 16 medical centers across seven Central European countries: 8 centers in Czechia, 2 in Serbia, 2 in Hungary, and one in each of Slovenia, Latvia, Lithuania, and Austria (37). Among the patient cohort, 68% were male, and 95% exhibited an ECOG performance status of 0-2. Findings indicated that over half of the patients (56%) received combined treatment modalities, with 80% receiving chemotherapy in combination with other modalities. Among the patients undergoing non-surgical therapy (n = 448), 78% received drug therapy. The most common approach was chemo-radiation therapy (45%) followed by chemotherapy alone (33%), radiation therapy alone (15%), and best supportive care (6%).



Notes: NSCLC = non-small-cell lung cancer, CRT = chemo-radiation therapy, CT = chemotherapy, RT = radiation therapy, BSC = best supportive care. Full sample including surgical patients: n = 583 (Czechia: n =269 [46.1%], Serbia: n = 109 [18.7%], Hungary: n = 48 [8.2%], Slovenia: n = 53 [9.1%], Latvia: n = 43 [7.4%], Lithuania: n = 38 [6.5%], Austria: n = 23 [4%]). Source: (37)

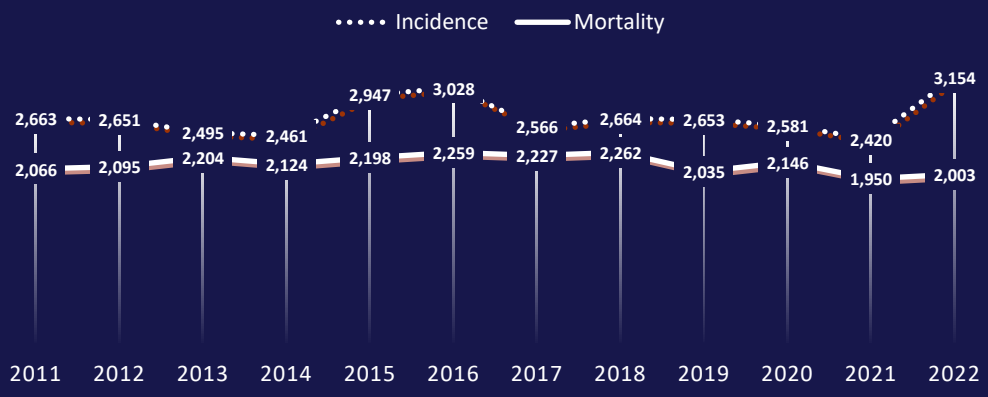
Slovakia

Epidemiology of NSCLC / lung cancer

Population (2022)	5.4 million
Health expenditure (2022)	
in % of GDP	7.6%
per capita in €	€ 1 527

Source: OECD (41, 42)

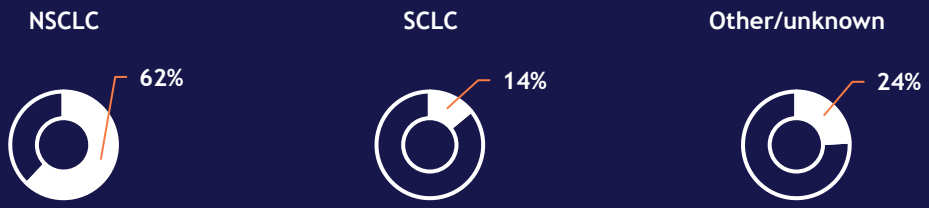
LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2022



DEATH CERTIFICATE ONLY (DCO) CASES: 2.1% of all diagnosed cases

Source: NCZI (76-78)

SHARE OF SCLC VS. NSCLC



Note: Assuming 2020 Slovakian incidence data mirrors the SCLC vs. NSCLC distribution seen in Central and Eastern Europe during the same year. Source: (53, 79)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC / LUNG CANCER

PS 0	PS 1	PS 2	PS 3	PS 4

No information available

STAGE DISTRIBUTION OF LUNG CANCER

Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV	Unknown
11%	6%	21%		60%	2%

Source: NCZI (79)

Drug treatment rates

No relevant publications on aNSCLC drug treatment rates in Slovakia were identified during the research period from March to October 2023.

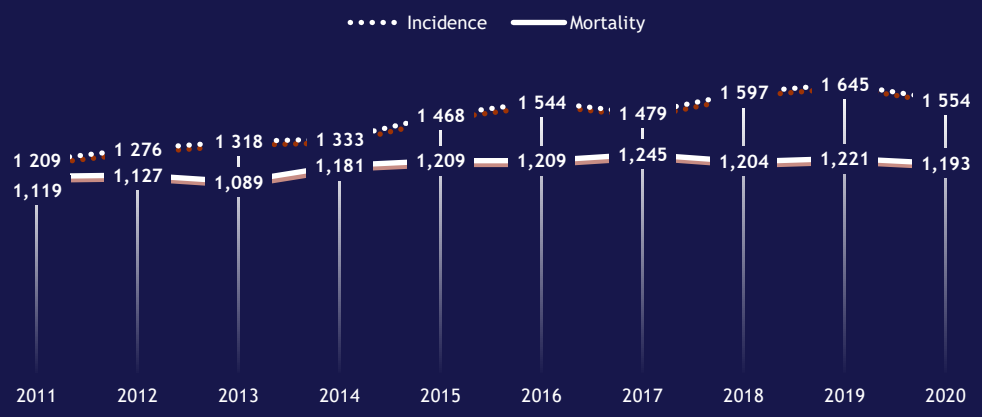
Slovenia

Epidemiology of NSCLC / lung cancer

Population (2022)	2.1 million
Health expenditure (2022)	
in % of GDP	8.8%
per capita in €	€ 2 477

Source: OECD (41, 42)

LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
SLOVENIA, 2011-2020



DEATH CERTIFICATE ONLY (DCO) CASES: 0.2% of all diagnosed cases

Source: CRS (80, 81)

SHARE OF SCLC VS. NSCLC

Source: CRS (81)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC / LUNG CANCER

PS 0	PS 1	PS 2	PS 3	PS 4

No information available

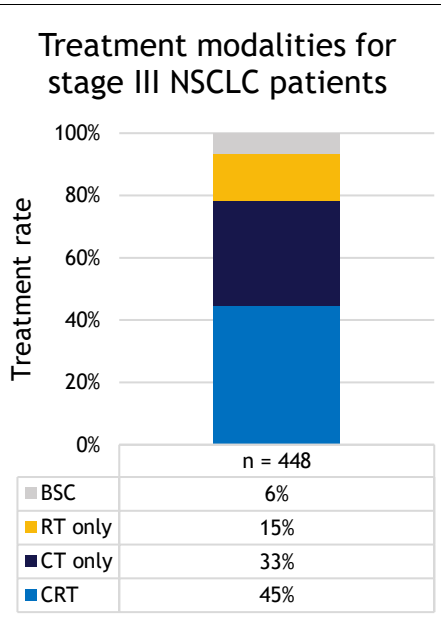
STAGE DISTRIBUTION OF LUNG CANCER

Localized	Regional	Distant	Unknown
18%	28%	53%	1%

Source: CRS (81)

Drug treatment rates

A multinational study was conducted to investigate diagnostic and therapeutic approaches for stage III NSCLC in Central European countries and identify areas for improvement. Data were gathered between March 2014 and March 2017, involving 583 patients from 16 medical centers across seven Central European countries: 8 centers in Czechia, 2 in Serbia, 2 in Hungary, and one in each of Slovenia, Latvia, Lithuania, and Austria (37). Among the patient cohort, 68% were male, and 95% exhibited an ECOG performance status of 0-2. Findings indicated that over half of the patients (56%) received combined treatment modalities, with 80% receiving chemotherapy in combination with other modalities. Among the patients undergoing non-surgical therapy (n = 448), 78% received drug therapy. The most common approach was chemo-radiation therapy (45%) followed by chemotherapy alone (33%), radiation therapy alone (15%), and best supportive care (6%).



Notes: NSCLC = non-small-cell lung cancer, CRT = chemo-radiation therapy, CT = chemotherapy, RT = radiation therapy, BSC = best supportive care. Full sample including surgical patients: n = 583 (Czechia: n =269 [46.1%], Serbia: n = 109 [18.7%], Hungary: n = 48 [8.2%], Slovenia: n = 53 [9.1%], Latvia: n = 43 [7.4%], Lithuania: n = 38 [6.5%], Austria: n = 23 [4%]). Source: (37)

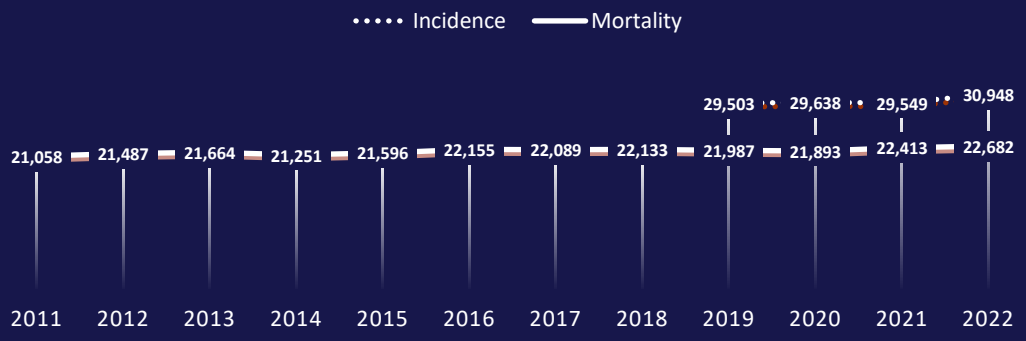
Spain

Epidemiology of NSCLC / lung cancer

Population (2022)	47.6 million
Health expenditure (2022)	
in % of GDP	10.5%
per capita in €	€ 2 926

Source: OECD (41, 42)

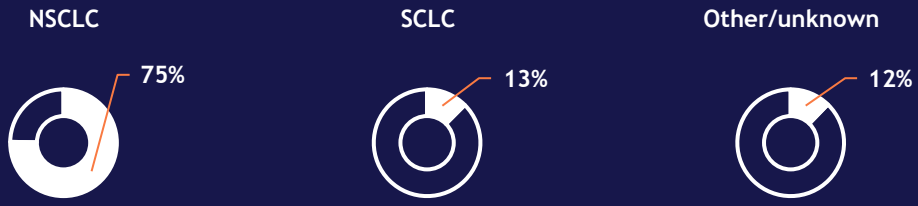
LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2021



DEATH CERTIFICATE ONLY (DCO) CASES: No information available

Source: Incidence (82, 83). Mortality (84)

SHARE OF SCLC VS. NSCLC



Notes: Assuming 2020 Spanish incidence data mirrors the SCLC vs. NSCLC distribution seen in Southern Europe during the same year. Source: (53, 83)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC

PS 0	PS 1	PS 2	PS 3	PS 4	Other/unknown
36.3%	50.6%	9.9%	2.4%	0.3%	0.5%

Source: Provencio et al. (2019) (85)

STAGE DISTRIBUTION OF NSCLC

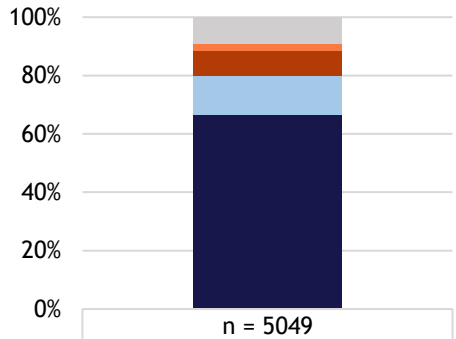
Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV	Unknown
10.0%	9.0%	15.8%	12.6%	52.2%	0.4%

Source: Provencio et al. (2019) (85)

Drug treatment rates

A study analyzed the clinical and epidemiological aspects of NSCLC in the Spanish population. The analysis is based on 5,049 patients with metastatic NSCLC and covers the time period from August 2016 to January 2020. Data were collected from the Thoracic Tumors Registry (RTT) of the Spanish Lung Cancer Group. The findings indicate that about 91% of metastatic NSCLC patients received systemic anti-cancer therapy. The most common approach was chemotherapy (67%), followed by target therapy (13%), immunotherapy (9%) and chemotherapy in combination with immunotherapy (2%). The remaining patients received no systemic anti-cancer therapy (34).

First-line treatment rates for metastatic NSCLC patients

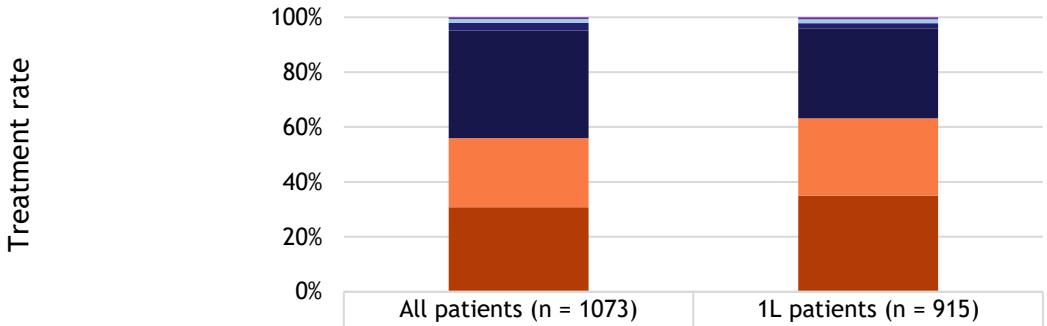


	n = 5049
No/other treatment	9%
CT+IO	2%
IO	9%
TT	13%
CT	67%

Notes: CT = chemotherapy, TT = targeted therapy, IO = immuno-oncology. Source: (34)

A multi-country analysis examined the treatment patterns of patients with metastatic NSCLC without EGFR and ALK mutation (*EGFR*-WT/*ALK*-WT). Data were collected from July 2020 to November 2020, and the sample consisted of patients from France, Germany, Italy, Spain, and UK. The findings showed that, for both current first-line patients (n=915) and the entire population (n=1073), the predominant first-line treatment modality consisted of chemotherapy, trailed by immune-oncology with or without chemotherapy, and targeted therapy (32). The relevant findings are presented below.

First-line treatment rates for metastatic NSCLC patients



	All patients (n = 1073)	1L patients (n = 915)
Other	1%	1%
Targeted therapy	1%	1%
Chemotherapy combination	3%	2%
Chemotherapy only	39%	33%
IO + chemotherapy	25%	28%
IO monotherapy	31%	35%

Notes: 1L = first line, metatistic non-small cell lung cancer (NSCLC) = stage IIIB-IV , EGFR = epidermal growth factor receptor, ALK = anaplastic lymphoma kinase, IO = immuno-oncology. Main sample: n = 1073 (France: n = 264 [24.6%], Germany: n =152 [14.2%], Italy: n = 201 [18.7%], Spain: n = 226 [21.1%], UK: n = 230 [21.4%]). 1L patients = patients who did not progress beyond 1L therapy. All patients = 1L patients (n=915) + patients who progressed beyond 1L therapy (n=158). Source: (32)

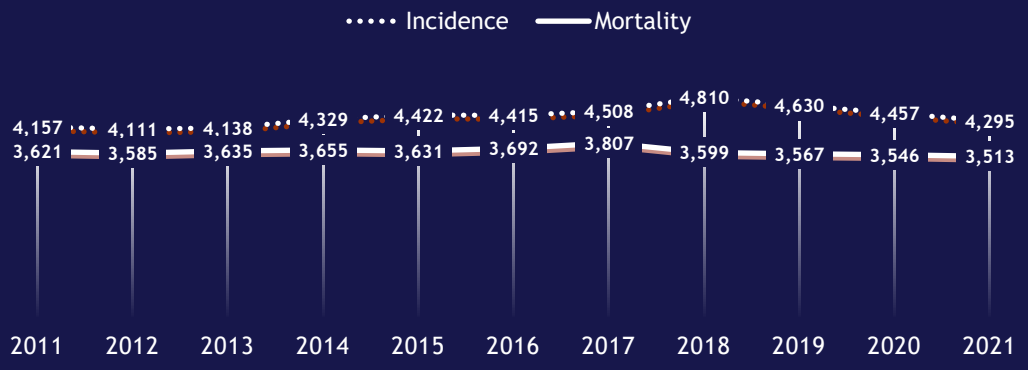
Sweden

Epidemiology of NSCLC / lung cancer

Population (2022)	10.5 million
Health expenditure (2022)	
in % of GDP	10.7%
per capita in €	€ 5 550

Source: OECD (41, 42)

LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2021

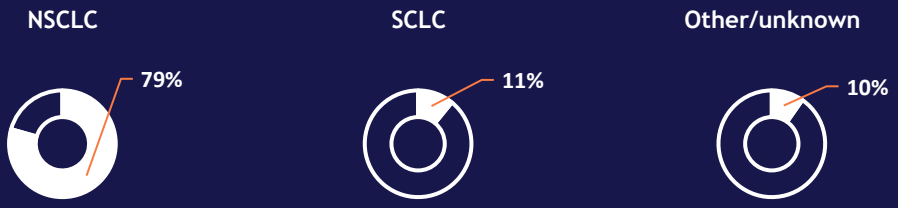


DEATH CERTIFICATE ONLY (DCO) CASES:

The Swedish Cancer Registry does not search for and perform follow-back in other registers for cancer cases identified from death certificates.

Source: Socialstyrelsen (86, 87)

SHARE OF SCLC VS. NSCLC



Source NLCR (40)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC BY STAGE

All stages (stage IIIB-IV)

PS 0	PS 1	PS 2	PS 3	PS 4	Unknown
23% (14%)	41% (37%)	20% (25%)	9% (14%)	3% (4%)	4% (6%)

Source: NLCR (40)

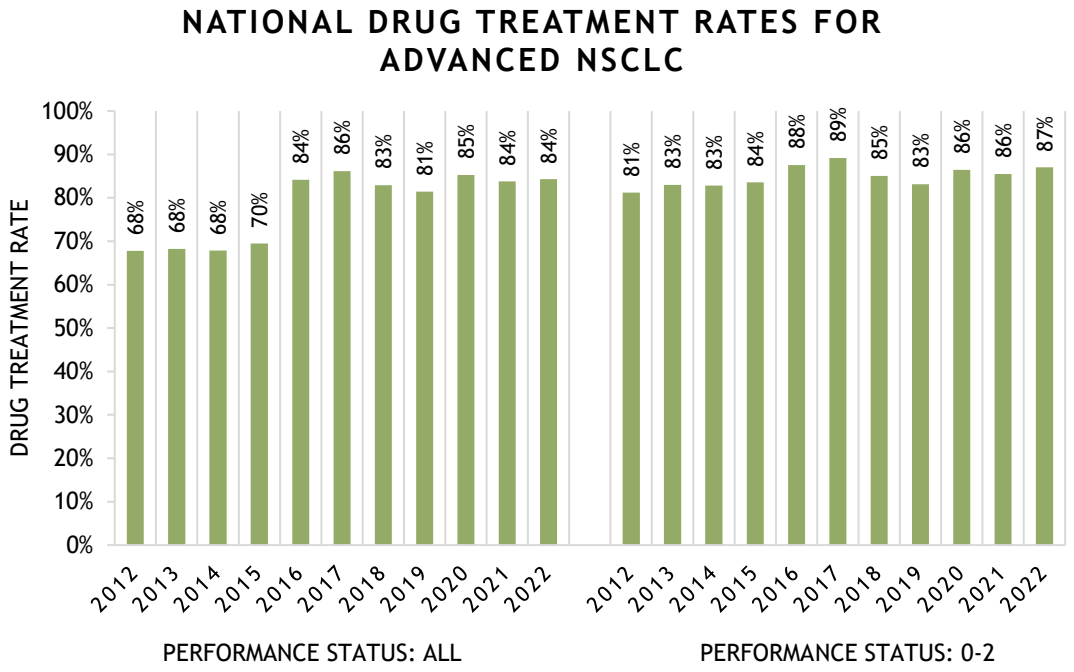
STAGE DISTRIBUTION OF NSCLC

Stage I	Stage II	Stage IIIA	Stage IIIB/IIIC	Stage IV	Unknown
25%	7%	9%	10%	48%	1%

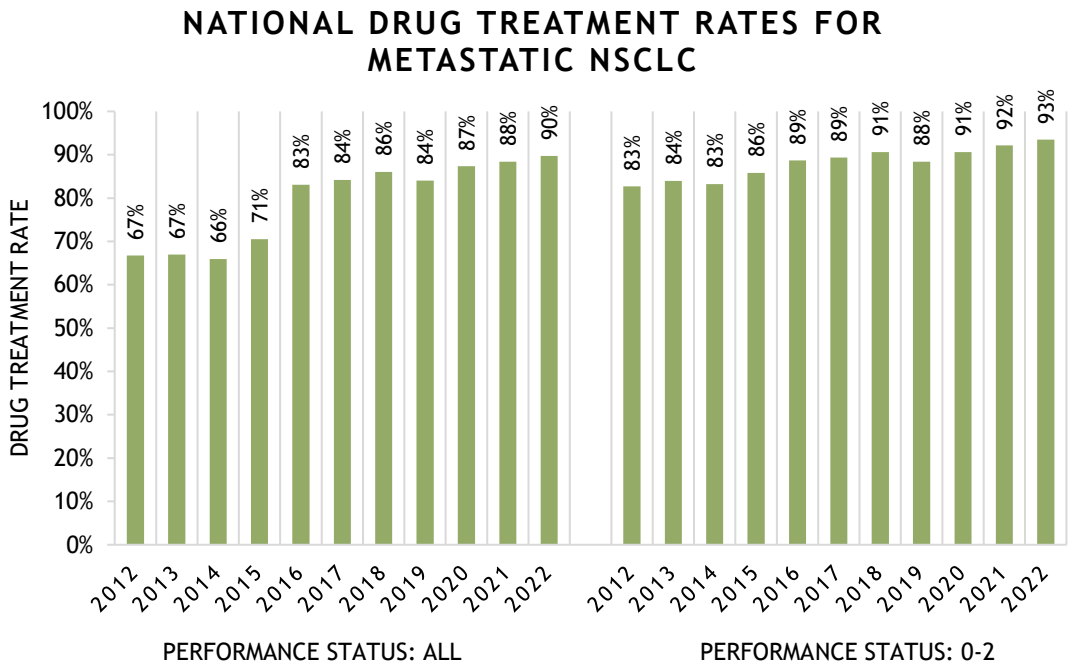
Source: NLCR (40)

Drug treatment rates

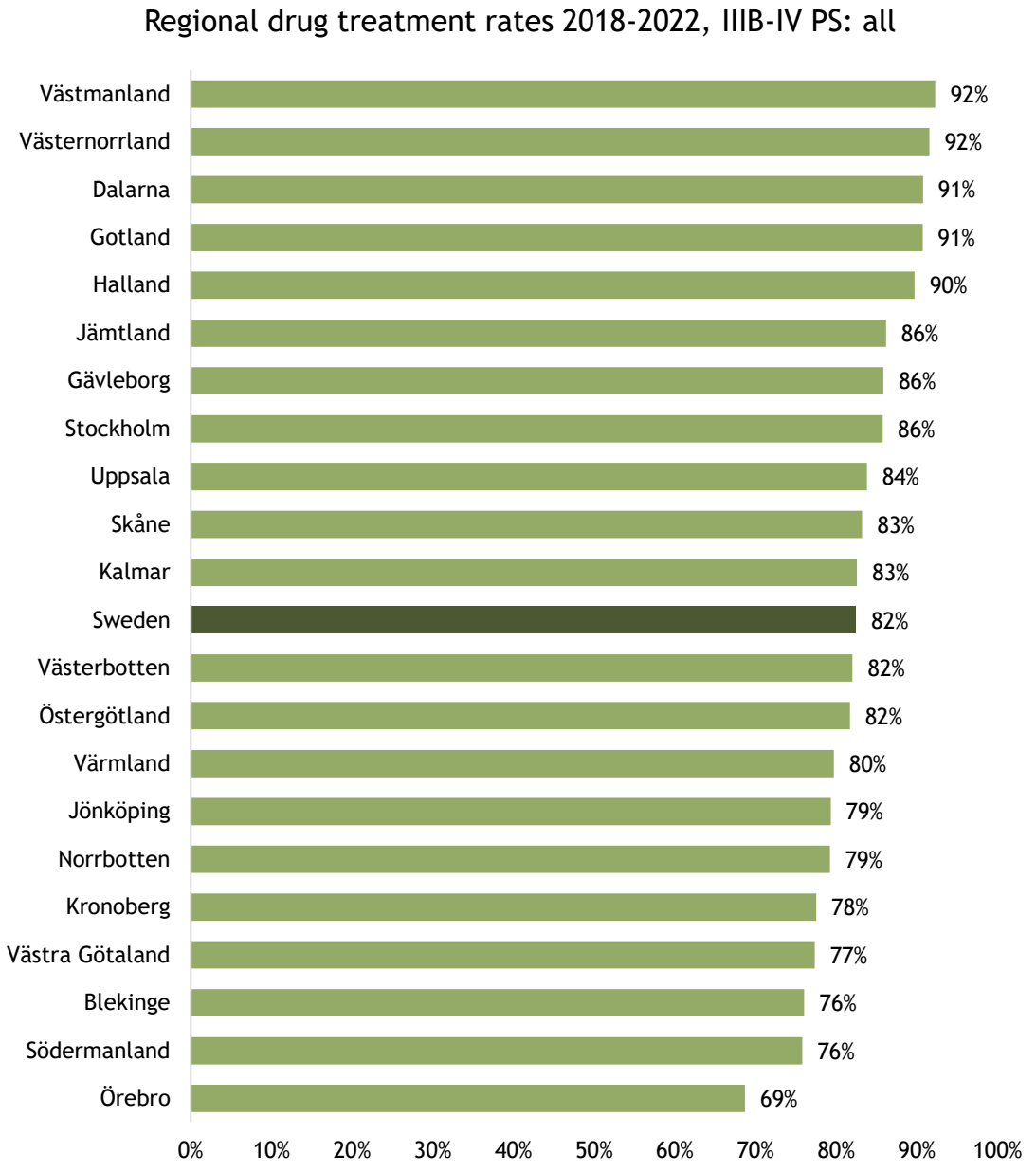
Sweden provides annual drug treatment data through their national lung cancer registry (40). Drug treatment rates in patients with advanced (stage IIIB-IV) disease has increased from 68% in 2012 to 84% in 2022. In patients with good performance status (PS 0-2), 87% received drug treatment (SACT) (40). The figure below illustrates the drug treatment rates in patients with advanced NSCLC, performance status 0-2 and all (i.e., 0-4).



In 2022, 93% of patients with metastatic (stage IV) disease and good performance status (PS: 0-2) received drug treatment. Drug treatment rates have increased from 67% to 90% (PS: all) and 83% to 93% (PS:0-2) (40). Treatment rates by performance status are shown in the figure below.

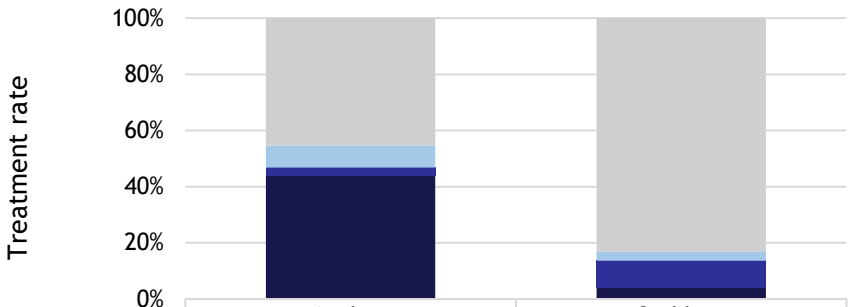


There is a large variation in drug treatment rates across regions in Sweden 2018-2022. The proportion of patients with advanced (stage IIIB-IV) NSCLC receiving drug treatment ranged from 69% in Örebro to 92% in Västmanland and Västernorrland (40). Regional drug treatment rates are shown in the figure below.



In a retrospective cohort investigation conducted in Sweden, the study encompassed the entire adult patient population diagnosed with advanced (stage IIIB-IV) NSCLC between 2012 and 2015. The treatment regimens administered to these patients were tracked in Uppsala and Stockholm University until the conclusion of 2016. The study sample comprised 1,625 individuals diagnosed with advanced NSCLC, reflecting a mean age of 69 years, with males constituting 49% of the cohort. The study found that out of 888 patients, 54% received their initial (first-line) treatment, and among them, 31% went on to receive a second-line treatment. Systemic anti-cancer therapy (SACT) regimens are presented in the figure below.

Drug treatment rates of advanced NSCLC patients by treatment line



	1st line	2nd line
Untreated	45%	83%
Targeted therapy	8%	3%
Non-platinum single agent	3%	10%
Platinum-based chemo therapy	44%	4%

Notes: The analysis includes 1,625 advanced NSCLC patients diagnosed from 2012-2015 and followed in Uppsala and Stockholm University hospitals until 2016. NSCLC = non-small-cell lung cancer, untreated = no SACT regimen. Source: (88)

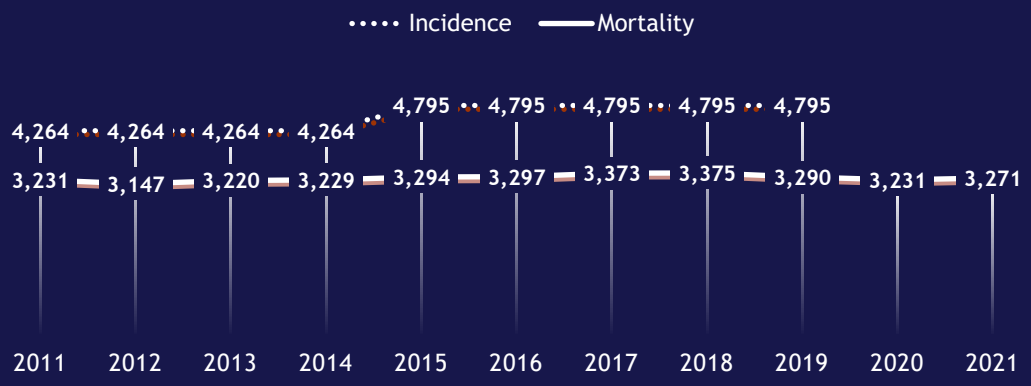
Switzerland

Epidemiology of NSCLC / lung cancer

Population (2022)	8.8 million
Health expenditure (2022)	
in % of GDP	11.3%
per capita in €	€ 10 141

Source: OECD (41, 42)

LUNG CANCER INCIDENCE AND MORTALITY IN TOTAL NUMBERS
2011-2021



DEATH CERTIFICATE ONLY (DCO) CASES: No information available

Notes: Incidence is given in 5-year intervals (2009-2014 and 2015-2021). Source: Incidence (89) Mortality (52)

SHARE OF SCLC VS. NSCLC

Source: Galli et al. (2019) (90)

ECOG PERFOMANCE STATUS AT DIAGNOSIS OF NSCLC / LUNG CANCER

PS 0	PS 1	PS 2	PS 3	PS 4	Other/unknown

No information available

STAGE DISTRIBUTION OF LUNG CANCER

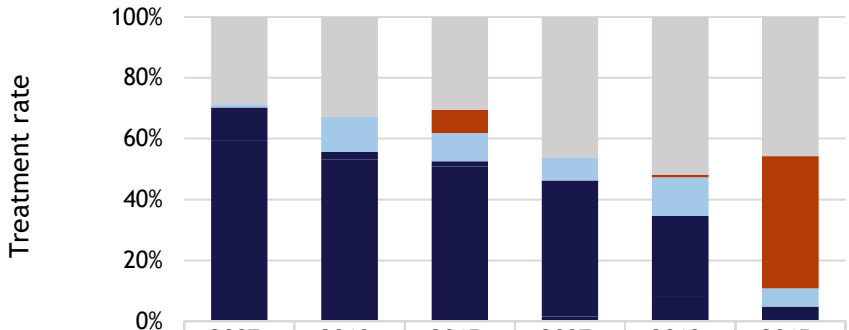
Stage I	Stage II	Stage III	Stage IV	Unknown
19%	8%	16%	34%	23%

Source: Galli et al. (2019) (90)

Drug treatment rates

A comprehensive study conducted an analysis of data encompassing all sequential patients diagnosed with metastatic stage (IV) non-small cell lung cancer (NSCLC) within a community hospital located in Basel, Switzerland. The data collection period spanned from 2007 to 2018. The patient population was stratified into three distinct groups for comparative evaluation: i) Patients diagnosed before 2009, ii) Patients diagnosed between 2009 and 2015, marking the introduction of targeted therapies, and iii) Patients diagnosed after 2015, signifying the introduction of immunotherapy (35). Changes in treatment pattern over time by line of therapy are presented in the figure below.

Drug treatment rates for metastatic NSCLC patients by treatment line



	2007-2009 (n=94)	2010-2015 (n=196)	2015-2018 (n=118)	2007-2009 (n=67)	2010-2015 (n=133)	2015-2018 (n=82)
	1st line			2nd line		
Best supportive care	29%	33%	31%	46%	52%	46%
Immunotherapy	0%	0%	8%	0%	1%	44%
Targeted therapy	1%	12%	9%	7%	13%	6%
Non-platinum single agent	11%	3%	2%	45%	26%	5%
Platinum-based chemo therapy	60%	53%	51%	1%	8%	0%

Source: (35)

List of EMA-approved medicines

Table A1: Novel EMA-approved cancer medicines in aNSCLC

Active substance	Trade name	Indication (short description)	Year of EMA approval
Immunotherapy			
(1) PD-L1 positive			
First line			
Pembrolizumab	Keytruda	1L, mono, metastatic, PD-L1 with ≥50% TPS, EGFR- & ALK-	2017
Atezolizumab	Tecentriq	1L, mono, metastatic, PD-L1 with ≥50% TPS, EGFR- & ALK-	2021
Cemiplimab	Libtayo	1L, mono, locally advanced/metastatic, PD-L1 ≥50%, EGFR- & ALK- & ROS1-	2021
Cemiplimab	Libtayo	1L, combo with Pt-chemo, locally advanced/metastatic, PD-L1 ≥1%, EGFR- & ALK- & ROS1-	2023
Second line			
Pembrolizumab	Keytruda	2L, mono, locally advanced/metastatic, PD-L1 with ≥1% TPS	2016
Durvalumab	Imfinzi	2L, mono, stage III unresectable, PD-L1 ≥ 1%	2018
(2) PD-L1 negative / all comers			
First line			
Pembrolizumab	Keytruda	1L, combo with pemetrexed & Pt-chemo, metastatic NSC, EGFR- & ALK-	2018
Pembrolizumab	Keytruda	1L, combo with carboplatin & either paclitaxel or nab-paclitaxel, metastatic SC	2019
Atezolizumab	Tecentriq	1L, combo with bevacizumab, paclitaxel & carboplatin, metastatic NSC	2019
Atezolizumab	Tecentriq	1L, combo with nab-paclitaxel & carboplatin, metastatic NSC, EGFR- & ALK-	2019
Nivolumab & Ipilimumab	Opdivo & Yervoy	1L, combo with ipilimumab & 2 cycles Pt-chemo, metastatic, EGFR/ALK-	2020
Durvalumab & Tremelimumab	Imfinzi & Imjudo	1L, combo with tremelimumab and Pt-chemo, metastatic, EGFR- & ALK-	2023
Second line			
Atezolizumab	Tecentriq	2L, mono, locally advanced/metastatic	2017
Nivolumab	Opdivo	2L, mono, locally advanced/metastatic	2015/2016 [a]
Targeted therapy			
(1) EGFR inhibitors			
Fist line			
Gefitinib	Iressa	1L, mono, locally advanced/metastatic, EGFR	2009
Erlotinib	Tarceva	1L, mono, locally advanced/metastatic, EGFR	2011
Afatinib	Giotrif	1L, mono, locally advanced/metastatic, EGFR	2013
Osimertinib	Tagrisso	1L, mono, locally advanced/metastatic, EGFR	2016/2018 [b]
Dacomitinib	Vizimpro	1L, mono, locally advanced/metastatic, EGFR	2019
Second line			
Erlotinib	Tarceva	2L, mono, switch maintenance, locally advanced/metastatic, EGFR	2016
Osimertinib	Tagrisso	2L, mono, locally advanced/metastatic, EGFR T790M	2016
Amivantamab	Rybrevant	2L, mono, advanced, EGFR Ex20Ins	2021
(2) ALK inhibitors			
First line			
Crizotinib	Xalkori	1L, mono, advanced, ALK	2015
Ceritinib	Zykadia	1L, mono, advanced, ALK	2017
Alectinib	Alecensa	1L, mono, advanced, ALK	2017
Brigatinib	Alunbrig	1L, mono, advanced, ALK	2020
Lorlatinib	Lorviqua	1L, mono, advanced, ALK	2022
Second line			
Crizotinib	Xalkori	2L, mono, advanced, ALK	2012
Ceritinib	Zykadia	2L after crizotinib, mono, advanced, ALK	2015
Alectinib	Alecensa	2L after crizotinib, mono, advanced, ALK	2017
Brigatinib	Alunbrig	2L after crizotinib, mono, advanced, ALK	2018
Lorlatinib	Lorviqua	2L & 3L after ALK-TKIs, mono, advanced, ALK	2019
(3) ROS1 inhibitors			
First line			
Crizotinib	Xalkori	1L, mono, advanced, ROS1	2016
Entrectinib	Rozlytrek	1L, mono, advanced, ROS1	2020
(4) BRAF inhibitors			
First line			
Dabrafenib+Trametinib	Tafinlar+Mekinist	1L, combo with trametinib, advanced, BRAF V600	2017
(5) NTRK inhibitors			
First line			
Larotrectinib	Vitrakvi	1L, mono, locally advanced/metastatic, NTRK	2019
Entrectinib	Rozlytrek	1L, mono, locally advanced/metastatic, NTRK	2020
(6) RET inhibitors			
First line			
Pralsetinib	Gavreto	1L, mono, advanced, RET	2021
Selpercatinib	Retsevmo	1L, mono, advanced, RET	2022
Second line			
Selpercatinib	Retsevmo	2L, mono, advanced, RET	2021 [c]
(7) KRAS inhibitors			
Second line			
Sotorasib	Lumykras	2L, mono, advanced, KRAS G12C	2022
(8) MET inhibitors			
Second line			
Tepotinib	Tepmetko	2L, mono, advanced, METex14	2022
Capmatinib	Tabrecta	2L, mono, advanced, METex14	2022
(9) HER2 inhibitors			
Second line			
Trastuzumab deruxtecan	Enhertu	2L, mono, advanced, HER2	2023

Notes: 1L = first line, 2L = second line, mono = monotherapy, combo = combination.
[a] On Oct 28, 2015, the label included only squamous patients. This restriction was removed on April 4, 2016.
[b] On Feb 2, 2016, the label included only patients with "EGFR-T790M". This restriction was removed on June 7, 2018.
[c] This indication was replaced by the first-line indication on Jun 21, 2022.
Additional EMA approvals include bevacizumab in combination with erlotinib (2016), ramucirumab in combination with erlotinib (2020), and necitumumab in combination with gemcitabine and cisplatin (2016, withdrawn 2021) for EGFR-positive patients in first line, nab-paclitaxel in combination with carboplatin in first line, nintedanib in combination with docetaxel (2014), afatinib as a monotherapy (2016), ramucirumab in combination with docetaxel (2016), erlotinib as a monotherapy (2017) in second line. EMA approvals for older chemotherapies include docetaxel (2000) and pemetrexed (2004). The chemotherapies carboplatin, cisplatin, gemcitabine, paclitaxel, and vinorelbine are also used in practice but were launched before the establishment of the EMA in 1995.
Source: EMA Union Register of medicinal products for human use.

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