



# Patient Characteristics, Testing and Treatment Patterns, and Outcomes in *EGFR*-Mutated Advanced Non-Small Cell Lung Cancer: A Multinational, Real-World Study

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## ABSTRACT

**Introduction:** Treatment landscape for advanced/metastatic NSCLC (aNSCLC) has evolved considerably over the past few decades with the advent of targeted therapies for epidermal growth factor receptor-mutated (*EGFR*<sup>m+</sup>) aNSCLC treatment. This study described real-world patient and disease characteristics, treatment and practice patterns, and clinical, economic, and patient-reported outcomes (PROs) in patients with *EGFR*<sup>m+</sup> aNSCLC.

**Methods:** Data were derived from the Adelphi NSCLC Disease Specific Programme™ (DSP™), a point-in-time survey conducted between July and December 2020. The survey included

oncologists and pulmonologists, and their consulting patients (with physician-confirmed *EGFR*<sup>m+</sup> aNSCLC) from nine countries: the US, Brazil, the UK, Italy, France, Spain, Germany, Japan, and Taiwan. All analyses were descriptive. **Results:** Overall, 542 physicians reported data for 2857 patients (mean age 65.6 years), and most patients were female (56.0%), white (61.0%), and had stage IV disease at initial diagnosis (76.0%), and adenocarcinoma histology (89.0%). Most patients received *EGFR*-tyrosine kinase inhibitors (TKI) therapy in first- (91.0%), second- (74.0%), and third-line (67.0%). The most common tumor samples and methods for *EGFR* detection were *EGFR*-specific mutation detection tests (44.0%) and core needle biopsy (56.0%). Median time to next treatment was 14.0 (IQR 8.0–22.0) months and disease progression was the main physician-reported reason for early discontinuation. The most common physician-reported disease symptoms were cough (51.0%), fatigue (37.0%), and dyspnea (33.0%). In patients

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Yulia D'yachkova is a former employee of Eli Lilly and Company.

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assessed for PROs, mean EQ-5D-5L index and FACT-L health utility scores were 0.71 and 83.5, respectively. On average, patients lost 10.6 h of work/week for approximately 29.2 weeks due to *EGFRm+* aNSCLC.

**Conclusion:** This real-world multinational data set showed that most patients with *EGFRm+* aNSCLC were treated per the country relevant clinical guidelines, with progression as the main reason for early treatment discontinuation. For the included countries, these findings may offer a useful benchmark for decision makers to determine future allocation of healthcare resources for patients with *EGFRm+* aNSCLC.

**Keywords:** Advanced non-small cell lung cancer; Disease Specific Programme™; *EGFR* mutation; Patient-reported outcomes; Point-in-time; Real-world; Survey; Treatment patterns

### Key Summary Points

As the epidermal growth factor receptor-mutated (*EGFRm+*) advanced non-small cell lung cancer (aNSCLC) treatment landscape continues to evolve, and the number of approved and recommended targeted treatments continues to grow, it is important to understand implications on real-world practice and patients.

This study used the Adelphi Disease Specific Programme™ (DSP™) methodology to describe real-world patient and disease characteristics, testing and treatment patterns, clinical and economic outcomes, physician practice patterns and rationale, and patient-reported health-related quality of life (HRQoL), across nine countries.

Overall, *EGFRm+* aNSCLC treatment patterns were in line with international treatment guideline recommendations for targeted therapy with EGFR-tyrosine kinase inhibitors (*EGFR*-TKIs), although regional variation was observed in practice and resource use patterns, suggesting differing approaches to *EGFRm+* aNSCLC management.

The burden of lung cancer symptoms remains high. On average, patients lost about 10.6 h of work per week for about 29 weeks in the 1 year prior to data capture.

According to physicians, inadequate tissue was the main barrier to *EGFR* testing and disease progression was the main reason for early treatment discontinuation.

For included countries, these findings may offer a useful benchmark for decision makers to determine future allocation of healthcare resources for patients with *EGFRm+* aNSCLC.

## INTRODUCTION

Lung cancer remains the leading cause of cancer deaths worldwide, accounting for approximately 1.8 million deaths in 2020 [1]. Non-small cell lung cancer (NSCLC) accounts for more than 82.0% of all lung cancer cases and is often diagnosed at advanced stages IIIB or IV [2–4]. Among the different genetic drivers of advanced or metastatic NSCLC (aNSCLC) cases, epidermal growth factor (*EGFR*) mutation is the second most frequent genetic driver [5]. The recommended standard of care for *EGFR*-mutated aNSCLC (*EGFRm+* aNSCLC) is first-, second-, or third-generation *EGFR*-tyrosine kinase inhibitors (*EGFR*-TKIs) [6], which have demonstrated favorable efficacy and safety over cytotoxic chemotherapy in this setting. However, acquired resistance to *EGFR*-TKIs is inevitable [7, 8], and the 5-year survival rate for patients with *EGFRm+* aNSCLC ranges from 14.6% to 23.8% [9, 10]. More recently, anti-angiogenic antibodies, ramucirumab or bevacizumab, in combination with erlotinib, have been incorporated in the clinical guidelines [6] based on landmark trials demonstrating clinical benefit with these combinations over erlotinib monotherapy in patients with *EGFRm+* aNSCLC [11, 12].

As the *EGFRm+* aNSCLC treatment landscape continues to evolve, and the number of

approved and recommended targeted treatments continues to grow, it is important to understand implications on real-world practice and patients. Earlier studies have described real-world *EGFRm+* aNSCLC treatment and practice patterns; however, most are out of date and were conducted before regulatory approval and market uptake of osimertinib in the first-line (1L) setting. In addition, most previous studies have focused on US populations [13–17] and therefore may not be applicable to the rest of the world (e.g., Asia, with higher prevalence of *EGFRm+* aNSCLC) [18–20]. Lastly, studies determining physician rationale for *EGFRm+* aNSCLC treatment decisions or patient perspectives on disease burden, management, and treatment are also limited [21, 22].

To address these knowledge gaps, this study used the Adelphi Disease Specific Programme™ (DSP™) methodology to describe real-world *EGFRm+* aNSCLC patient and disease characteristics, testing and treatment patterns, clinical and economic outcomes, physician practice patterns and rationale, and patient-reported health-related quality of life (HRQoL), across nine countries in North and South America (the United States [US] and Brazil), Europe (the United Kingdom [UK], Italy, France, Spain, and Germany), and Asia (Taiwan and Japan).

## METHODS

### Study Design and Survey Sample

Data were derived from the Adelphi NSCLC DSP™ with data collected between July and December 2020 from the US, Brazil, the UK, Italy, France, Spain, Germany, Taiwan, and Japan. The UK, France, Italy, Spain, and Germany are referred to as Europe 5 (EU5). DSP™ are large, multinational, point-in-time surveys conducted with physicians and their patients presenting in real-world clinical practice that describe current disease management, disease-burden impact, and associated treatment effects (clinical and physician-perceived). A complete description of the survey methods used for this DSP™ has been previously published and validated [23–25].

Data sources included: (1) a physician interview or physician survey to capture physicians' attitudes; (2) a patient record form (PRF) completed by physicians to document individual patient characteristics, disease history, symptoms, biomarker status, current/prior treatments received, adverse events (AEs), healthcare resource utilization, and supportive therapies; and (3) a voluntary patient self-reported questionnaire (PSC) for patient-reported characteristics, symptoms, outcomes/HRQoL, treatment costs, and health status. Participating physicians included oncologists and pulmonologists (and respiratory surgeons in Japan) treating patients with aNSCLC. Per the inclusion criteria, physicians were eligible for inclusion if they were personally responsible for the management and systemic treatment decisions for patients with aNSCLC and were required to be consulting at least three patients with aNSCLC each month. Per the patient-level inclusion criteria in the patient record form, adult patients with a physician-confirmed diagnosis of aNSCLC, who were not participating in a clinical trial during the survey, were eligible for inclusion in the survey.

Participating physicians were asked to complete the physician survey, and to then select prospective patients presenting with aNSCLC, completing a PRF for each patient selected at the point of consultation. The physician surveys and individual PRFs were administered online, with data anonymized at entry.

Physicians were asked to collect data for their next 13 consecutively consulting eligible patients according to the following quota: six consulting patients agnostic of biomarker status (i.e., aNSCLC generally), then the next five consulting patients with confirmed *EGFRm+* aNSCLC (*EGFRm+* oversample group), and the next two consulting patients with confirmed rearranged during transfection fusions (*RET fusion+*) aNSCLC (*RET+* oversample group, excluding Japan). The overall sample of patients with *EGFRm+* aNSCLC in this analysis ( $n = 2857$ ) was derived from patients with *EGFRm+* from the general sample and the *EGFRm+* oversample, i.e., all patients included in this DSP™ had *EGFRm+* aNSCLC.

Patients for whom a PRF was completed were then given the voluntary PSC by the physicians immediately after completing their consultation at the physician's office. The PSCs were completed by patients without assistance from the physician and returned in a sealed envelope to ensure anonymity of data.

The data collected were divided as follows: (1) pre-index period: used to capture clinical background including initial diagnosis of NSCLC, treatment (e.g., neo/adjuvant treatment), and management of early-stage NSCLC; (2) index date: date of diagnosis of aNSCLC; and (3) post-index period: data collection on aNSCLC treatment and associated outcomes. In the study, post-index (variable period following the index date) was the time of data collection and the other time points were completed retrospectively, i.e., no follow-up periods were there in this point-in-time study (Supplementary Fig. S1).

Using a check box, patients provided informed consent for use of their anonymized and aggregated data for research and publication in scientific journals. Data were collected in such a way that patients and physicians could not be identified directly; all data were aggregated and de-identified before receipt.

Data collection was undertaken in line with European Pharmaceutical Marketing Research Association guidelines [26] and although did not require ethical committee approval, the study materials and protocol were reviewed and approved by the Western Institutional Review Board (study protocol number AG8759). In addition, the survey was performed in full accordance with relevant legislation at the time of data collection, including the US Health Insurance Portability and Accountability Act 1996 [27], and Health Information Technology for Economic and Clinical Health Act legislation [28].

## Study Measures

The primary objectives and measures were to describe (1) patient demographics (age, sex, ethnicity, and smoking status); (2) socioeconomic status (employment, household income,

insurance) and economic burden (healthcare resource utilization); (3) clinical characteristics (disease duration, staging at advanced diagnosis, time from advanced diagnosis to treatment, symptoms, metastatic sites, comorbidities, and Eastern Cooperative Oncology Group [ECOG] performance status); (4) treatment patterns (line of therapy, treatment sequence, treatment discontinuation reasons, treatment duration for each line, and supporting medication); and (5) molecular testing patterns (testing at advanced diagnosis, testing method, sample type, and barriers to molecular testing reported by the physicians testing molecular alterations). The corresponding data were collected using the PRF, except for socioeconomic status and testing patterns. Socioeconomic data were collected using the PSC. Data for molecular biomarker testing patterns and physicians' perceptions on testing patterns data were collected using the PRF and physician survey, respectively. Early treatment discontinuation was defined as failure to complete the full treatment course as intended by the physician, based on a physician response of "no" to the question "Was the full course completed as intended?" on the PRF.

Secondary objectives and corresponding measures of interest included (1) clinical outcomes (in terms of time to next treatment [TTNT], time to treatment failure (TTF), full response [FR], partial response [PR], and no response [NR]), type and severity of aNSCLC symptoms, and AEs of treatment; (2) economic outcomes (frequency and reason for hospitalization, duration of hospitalization, healthcare resource utilization, and loss of productivity for employed patients); and (3) patients' perception of disease burden and management (loss of productivity, attitude toward diagnosis, perceptions toward treatment decision, out-of-pocket expenses, health status, and HRQoL). Tumor response was defined as the physician's assessment and documentation of change in disease burden, and the type of change was classified using predefined categories of FR (full resolution of disease), PR (some reduction in overall disease burden), and NR (increase or no change in overall disease burden). TTNT was defined as the time from start of treatment to start of the next line of treatment. TTF was

defined as the time from start of treatment to date of progression or start of the next line of treatment, whichever occurred first.

HRQoL was determined using standardized patient-reported outcomes (PROs) questionnaires: European Quality of Life 5 Dimension 5 Level (EQ-5D-5L) and EQ-visual analog scale (EQ-VAS) for general health status [29] and Functional Assessment of Cancer Therapy–Lung (FACT-L) and Functional Assessment of Cancer Therapy–General (FACT-G) questionnaires for HRQoL [30, 31]. The EQ-5D-5L descriptive system comprises five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), and each dimension has five response levels: no problems, slight problems, moderate problems, severe problems, unable to/extreme problems. The FACT-G questionnaire includes the Physical Well-Being (PWB), Social/family Well-Being (SWB), Emotional Well-Being (EWB), and Functional Well-Being (FWB) HRQoL domains, and the FACT-L consists of nine items involving common lung cancer symptoms, such as shortness of breath, weight loss, tightness in chest. Each item on the FACT questionnaires is rated on a five-point Likert scale, from 0 (not at all) to 4 (very much). For the EQ-5D-5L and FACT questionnaires, higher scores (e.g., higher total score in EQ-5D-5L) indicate higher HRQoL.

### Statistical Analysis

This paper presented data for patients with *EGFR*<sup>m+</sup> aNSCLC. Descriptive analyses were used for primary and secondary outcome measures: continuous variables were summarized by mean (standard deviation [SD]) and median (interquartile range [IQR], minimum, and maximum), whereas categorical variables were summarized as the number and percentage of subjects in each category. Patients were excluded from specific analyses if their values were missing for any particular variable, but they were considered eligible for other analyses. No imputation of missing values was attempted. Numbers of non-missing values were reported. TTNT, TTF, and time from aNSCLC diagnosis to initiation of treatment were reported as median

and interquartile range (IQR). Patients with ongoing treatment at the time of data collection were censored at the data collection date.

Results were presented for the overall *EGFR*<sup>m+</sup> aNSCLC sample and by country. Data from the UK, Italy, France, Spain, and Germany were combined to present the data for the EU5. All analysis were conducted using the software package IBM SPSS Data Collection Survey Reporter Version 7.5 and STATA® Version 16 (StataCorp LP, College Station, US).

## RESULTS

Between July and December 2020, 542 physicians participated in the survey (46.0% ( $n = 251$ ) in the EU5, 21.0% ( $n = 116$ ) in Japan, 13.0% ( $n = 71$ ) in the US, 10.0% ( $n = 53$ ) in Brazil, 9.0% ( $n = 51$ ) in Taiwan) and comprised 349 (64.0%) oncologists, 170 (31.0%) pulmonologists, and 23 (4.0%) respiratory surgeons (Supplementary Table S1). The physicians reported data for 2857 patients (i.e., completed PRFs), of whom 942 (33.0%) were eligible for PRO analysis. Table 1 summarizes demographic and clinical characteristics of the overall study cohort and by each of the nine countries.

### Patient Characteristics

Patient characteristics were largely similar across countries (Table 1). Overall, mean age was 65.6 years (standard deviation [SD] 10.6 years) and the majority were female (56.0%, except in Germany with approx. 40.0% being female) and white (61.0%, except in Japan and Taiwan with > 95.0% Asian patients) with the mean (SD) Charlson comorbidity index score of 7.5 (2.2) ( $n = 2728$ ). Most patients had stage IV disease at initial diagnosis (76.0%) and had adenocarcinoma histology (89.0%). At advanced diagnosis 80.0% of the patients had stage IV disease (Table 1, Fig. 1, and Supplementary Table S2). In the overall patient population ( $n = 2857$ ), the most common *EGFR* mutations were exon 19 deletions (38.0%) or exon 21 mutations (16.0%). Co-mutations with *ALK*, *RET*, and *ROS1* aberrations were reported in 4.0%, 3.0%, and 2.0%,

**Table 1** Patient characteristics: overall and by country

Patient characteristics	Overall (n = 2857)	US (n = 422)	BR (n = 313)	UK (n = 279)	IT (n = 287)	FR (n = 285)	ES (n = 302)	DE (n = 284)	EU5 <sup>a</sup> (n = 1437)	TW (n = 390)	JP (n = 295)
Age in years, mean (SD)	65.6 (10.6)	64.9 (10.5)	65.5 (11.3)	65.6 (10.0)	65.2 (10.6)	65.9 (10.8)	64.4 (10.9)	65 (8.2)	65.2 (10.2)	65.6 (11.1)	68.8 (10.3)
Sex, n (%)											
Male	1246 (44.0)	172 (41.0)	150 (48.0)	113 (41.0)	136 (47.0)	118 (41.0)	129 (43.0)	172 (61.0)	668 (47.0)	152 (39.0)	104 (35.0)
Female	1611 (56.0)	250 (59.0)	163 (52.0)	166 (60.0)	151 (53.0)	167 (59.0)	173 (57.0)	112 (39.0)	769 (54.0)	238 (61.0)	191 (65.0)
Ethnicity, n (%)											
Caucasian/White	1755 (61.0)	262 (62.0)	222 (71.0)	211 (76.0)	271 (94.0)	238 (84.0)	287 (95.0)	264 (93.0)	1271 (88.0)	0	0
Asian <sup>b</sup>	730 (26.0)	21 (5.0)	0	23 (8.0)	1 (< 1.0)	14 (5.0)	0	0	38 (3.0)	378 (97.0)	293 (99.0)
Hispanic-Latino	59 (2.0)	16 (4.0)	0	7 (3.0)	8 (3.0)	12 (4.0)	12 (4.0)	4 (1.0)	43 (3.0)	0	0
African American	83 (3.0)	53 (13.0)	30 (10.0)	0	0	0	0	0	0	0	0
Others <sup>c</sup>	260 (9.0)	70 (17.0)	91 (29.0)	38 (14.0)	7 (2.0)	21 (7.0)	3 (1.0)	16 (6.0)	85 (6.0)	12 (3.0)	2 (1.0)
Tumor stage at initial diagnosis, n (%)											
I	53 (2.0)	1 (< 1.0)	10 (3.0)	2 (1.0)	2 (1.0)	1 (< 1.0)	4 (1.0)	2 (1.0)	11 (1.0)	4 (1.0)	27 (9.0)
II	98 (3.0)	6 (1.0)	29 (9.0)	3 (1.0)	4 (1.0)	2 (1.0)	3 (1.0)	25 (9.0)	37 (3.0)	8 (2.0)	18 (6.0)
IIIA	88 (3.0)	10 (2.0)	29 (9.0)	1 (< 1.0)	5 (2.0)	1 (< 1.0)	2 (1.0)	11 (4.0)	20 (1.0)	12 (3.0)	17 (6.0)
IIIB	250 (9.0)	58 (14.0)	34 (11.0)	5 (2.0)	22 (8.0)	13 (5.0)	3 (1.0)	63 (22.0)	106 (7.0)	33 (8.0)	19 (6.0)
IIIC	170 (6.0)	36 (9.0)	26 (8.0)	3 (1.0)	19 (7.0)	22 (8.0)	5 (2.0)	34 (12.0)	83 (6.0)	13 (3.0)	12 (4.0)
IVA	807 (28.0)	130 (31.0)	93 (30.0)	62 (22.0)	68 (24.0)	81 (28.0)	64 (21.0)	80 (28.0)	355 (25.0)	148 (38.0)	81 (27.0)
IVB	1368 (48.0)	181 (43.0)	88 (28.0)	202 (72.0)	149 (52.0)	165 (58.0)	221 (73.0)	69 (24.0)	806 (56.0)	172 (44.0)	121 (41.0)

Table 1 continued

Patient characteristics	Overall ( <i>n</i> = 2857)	US ( <i>n</i> = 422)	BR ( <i>n</i> = 313)	UK ( <i>n</i> = 279)	IT ( <i>n</i> = 287)	FR ( <i>n</i> = 285)	ES ( <i>n</i> = 302)	DE ( <i>n</i> = 284)	EU5 <sup>a</sup> ( <i>n</i> = 1437)	TW ( <i>n</i> = 390)	JP ( <i>n</i> = 295)
Histology, <i>n</i> (%)											
Adenocarcinoma	2553 (89.0)	392 (93.0)	232 (74.0)	271 (97.0)	262 (91.0)	258 (91.0)	287 (95.0)	182 (64.0)	1260 (88.0)	384 (98.0)	285 (97.0)
SCC	189 (7.0)	19 (5.0)	37 (12.0)	6 (2.0)	16 (6.0)	15 (5.0)	7 (2.0)	79 (28.0)	123 (9.0)	3 (1.0)	7 (2.0)
Large cell carcinoma	93 (9.0)	7 (2.0)	43 (14.0)	1 (1.0)	4 (1.0)	10 (4.0)	8 (3.0)	20 (7.0)	43 (3.0)	0	0
Other	13 (1.0)	2 (0)	0	1 (1.0)	1 (<1.0)	1 (0)	0	2 (1.0)	5 (0.3)	3 (1.0)	3 (1.0)
Don't know	9 (0)	2 (0)	1 (0)	0	4 (1.0)	1 (0)	0	1 (<1.0)	6 (<1.0)	0	0
<i>n</i> = 2728		<i>n</i> = 377	<i>n</i> = 303	<i>n</i> = 279	<i>n</i> = 287	<i>n</i> = 285	<i>n</i> = 302	<i>n</i> = 284	<i>n</i> = 1437	<i>n</i> = 390	<i>n</i> = 221
Average CCI score, mean (SD) <sup>c</sup>	7.5 (2.2)	7.1 (2.6)	7.4 (2.8)	8.1 (1.0)	7.6 (2.2)	7.7 (1.8)	8.1 (1.1)	6.2 (3.0)	7.5 (2.1)	7.7 (2.0)	7.4 (2.0)
Smoking history, <i>n</i> (%)											
Yes	1293 (45.0)	202 (48.0)	176 (56.0)	137 (49.0)	119 (41.0)	126 (44.0)	115 (38.0)	201 (71.0)	698 (49.0)	114 (29.0)	103 (35.0)
No	1513 (53.0)	212 (50.0)	137 (44.0)	138 (50.0)	156 (54.0)	157 (55.0)	179 (59.0)	81 (29.0)	711 (50.0)	275 (71.0)	178 (60.3)
Don't know	51 (2.0)	8 (2.0)	0	4 (1.0)	12 (4.0)	2 (1.0)	8 (3.0)	2 (1.0)	28 (2.0)	1 (<1.0)	14 (4.7)
Line of therapy, <i>n</i> (%)											
1st	2364 (83.0)	381 (90.0)	278 (89.0)	226 (81.0)	234 (82.0)	235 (83.0)	266 (88.0)	217 (76.0)	1178 (82.0)	310 (80.0)	217 (73.6)
2nd	409 (14.0)	34 (8.0)	30 (10.0)	52 (19.0)	51 (18.0)	47 (17.0)	35 (12.0)	62 (22.0)	247 (17.0)	54 (14.0)	44 (14.9)
3rd	84 (3.0)	7 (2.0)	5 (2.0)	1 (<1.0)	2 (1.0)	3 (1.0)	1 (<1.0)	5 (2.0)	12 (1.0)	26 (7.0)	34 (11.5)
Exon mutation, <i>n</i> (%)											
Exon 19 deletion	1070 (38.0)	160 (38.0)	74 (24.0)	123 (44.0)	91 (32.0)	100 (35.0)	95 (32.0)	97 (34.0)	506 (35.0)	176 (45.0)	154 (52.2)

Table 1 continued

Patient characteristics	Overall ( <i>n</i> = 2857)	US ( <i>n</i> = 422)	BR ( <i>n</i> = 313)	UK ( <i>n</i> = 279)	IT ( <i>n</i> = 287)	FR ( <i>n</i> = 285)	ES ( <i>n</i> = 302)	DE ( <i>n</i> = 284)	EU5 <sup>a</sup> ( <i>n</i> = 1437)	TW ( <i>n</i> = 390)	JP ( <i>n</i> = 295)
Exon 21 point mutation	468 (16.0)	37 (9.0)	52 (17.0)	51 (18.0)	60 (21.0)	27 (10.0)	36 (12.0)	8 (3.0)	182 (13.0)	130 (33.0)	67 (22.7)
RET results, <i>n</i> (%)											
RET+	83 (3.0)	8 (2.0)	40 (13.0)	5 (2.0)	1 (<1.0)	2 (1.0)	7 (2.0)	13 (5.0)	28 (2.0)	5 (1.0)	2 (0.7)
RET−	824 (29.0)	285 (68.0)	62 (20.0)	50 (18.0)	76 (27.0)	157 (55.0)	67 (22.0)	78 (28.0)	428 (30.0)	17 (4.0)	32 (11.0)
Unknown	1950 (68.0)	129 (31.0)	211 (67.0)	224 (80.0)	210 (73.0)	126 (44.0)	228 (75.0)	193 (68.0)	981 (68.0)	368 (94.0)	261 (88.0)
ALK results, <i>n</i> (%)											
ALK+	124 (4.0)	23 (6.0)	38 (12.0)	2 (1.0)	21 (7.0)	2 (1.0)	10 (3.0)	21 (7.0)	56 (4.0)	4 (1.0)	3 (1.0)
ALK−	2220 (78.0)	349 (83.0)	169 (54.0)	269 (96.0)	250 (87.0)	269 (94.0)	262 (87.0)	179 (63.0)	1229 (86.0)	287 (74.0)	186 (63.0)
Unknown, <i>n</i> (%)	513 (18.0)	50 (12.0)	106 (34.0)	8 (3.0)	16 (6.0)	14 (5.0)	30 (10.0)	84 (30.0)	152 (11.0)	99 (25.0)	106 (36.0)
ROS1 results, <i>n</i> (%)											
ROS1+	60 (2.0)	5 (1.0)	19 (6.0)	3 (1.0)	13 (5.0)	3 (1.0)	1 (<1.0)	12 (4.0)	32 (2.0)	3 (1.0)	1 (0.3)
ROS1−	1827 (64.0)	328 (78.0)	112 (36.0)	206 (74.0)	212 (74.0)	232 (81.0)	251 (83.0)	141 (50.0)	1042 (73.0)	210 (54.0)	135 (46.0)
Unknown	970 (34.0)	89 (21.0)	182 (58.0)	70 (25.0)	62 (22.0)	50 (18.0)	50 (17.0)	131 (46.0)	363 (25.0)	177 (45.0)	159 (54.0)
PD-L1 results, <i>n</i> (%)											
PD-L1+	602 (21.0)	106 (25.0)	73 (23.0)	76 (27.0)	50 (17.0)	74 (26.0)	63 (21.0)	62 (22.0)	325 (23.0)	40 (10.0)	58 (19.7)
PD-L1−	1608 (56.0)	245 (58.0)	123 (39.0)	176 (63.0)	199 (69.0)	186 (65.0)	203 (67.0)	143 (50.0)	907 (63.0)	195 (50.0)	138 (47.0)



Table 1 continued

Patient characteristics	Overall (n = 2857)	US (n = 422)	BR (n = 313)	UK (n = 279)	IT (n = 287)	FR (n = 285)	ES (n = 302)	DE (n = 284)	EU5 <sup>a</sup> (n = 1437)	TW (n = 390)	JP (n = 295)
Unknown	647 (23.0)	71 (17.0)	117 (37.0)	27 (10.0)	38 (13.0)	25 (9.0)	36 (12.0)	79 (28.0)	205 (14.0)	155 (40.0)	99 (34.0)

ALK anaplastic lymphoma kinase, BR Brazil, CCI Charlson Comorbidity Index, DE Germany, ES Spain, EU5 5 countries from the European Union, FR France, IT Italy, JP Japan, PD-L1 programmed death ligand, RET rearranged during transfection, ROS, c-ros oncogene 1, TW Taiwan, UK United Kingdom, US United States

<sup>a</sup>Includes the UK, IT, FR, ES, and DE

<sup>b</sup>Includes Han/Chinese, Japanese, and Southeast Asian

<sup>c</sup>Includes Asian-Indian subcontinent, Asian-Other, Black, Mulatto, Asian, Chinese, Mixed Race, Middle Eastern, Afro-Caribbean, Indigenous Taiwanese, Not answered, and Other

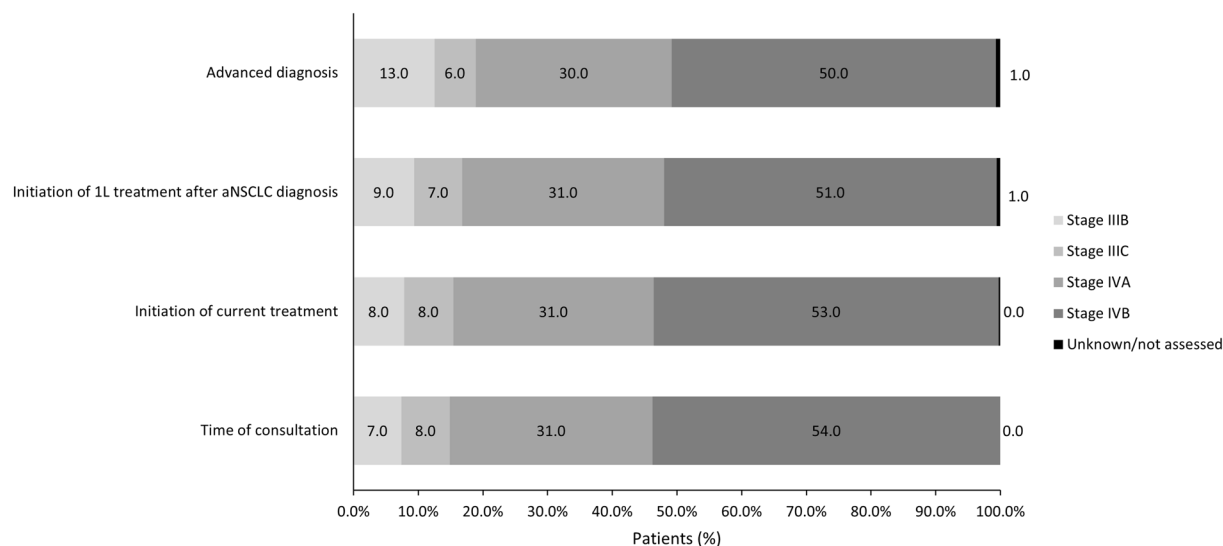
<sup>d</sup>The sample sizes present in the columns for average CCI score are not applicable to any other parameter

respectively, and PD-L1 expression was reported in 21.0% (Table 1). Most patients had no history of prior surgery, radiotherapy, or neo/adjuvant therapy (Table 3). In the overall patient population, 53.0% (n = 1513) had no smoking history ranging from 71.0% in Taiwan to 29.0% in Germany (Table 1).

At the start of 1L systemic therapy, the mean (SD) time to aNSCLC diagnosis from data collection was 14.5 (16.3) months (Table 2), and most (77.0%) patients had an ECOG performance status of 0 or 1 at advanced diagnosis (Supplementary Table S3). Among the patients with stage IV disease at data capture, the median number of primary metastatic (n = 2396) sites was 2 (IQR 1–2) (Supplementary Fig. S2), with contralateral lung, bone, and distant lymph nodes as the most common sites. About 14.0% had brain/central nervous system metastases at diagnosis of advanced disease (Supplementary Table S4). Most patients were retired (44.0% physician-reported and 48.0% patient-reported) and had health insurance (95.0%) (Supplementary Fig. S3). Supplementary Table S5 summarizes annual household income for eligible patients by country.

### Treatments

Among the overall patient population (n = 2857), 2819 (99.0%) received 1L systemic therapy for EGFRm+ aNSCLC and 38 (1.0%) received best supportive care only (Fig. 2a); 487 (99.0%, n = 493) and 81 (99.0%, n = 84) patients were treated systemically in second line (2L) and third line (3L) respectively (Fig. 2b). In 1L, most patients (91.0%) received targeted agents, 11.0% received chemotherapy, 3.0% received immunotherapy, and 2.0% received other systemic treatments (Fig. 2a). Similar trends were observed in subsequent lines (2L and 3L) and across most countries (Fig. 2b), although chemotherapy and immunotherapy were used relatively more often in some countries (including Brazil, Germany, Taiwan, and Italy) and in subsequent lines than the 1L setting (Figs. 2a, b). Of note, observed variations in patterns of subsequent therapy (especially 3L treatments) across countries were limited by



**Fig. 1** Tumor staging at different time points: overall population. All data are presented as %. 1L first line, aNSCLC advanced non-small cell lung cancer

small numbers of eligible patients in some individual countries. Figure 3 and Supplementary Table S6 present the treatment combinations by overall population and for each country. Table 3 presents the targeted treatment breakdown by generation for overall population and each country.

### EGFR Testing

Tumor samples used to detect *EGFR* gene mutations were mainly tissue biopsy specimens (mostly core needle biopsy [56.0%] and bronchial brush biopsy [19.0%]) followed by liquid biopsy specimens (7.0% globally and highest [16.0%] in Germany) (Table 4). Overall, the most common methods used for *EGFR* detection were *EGFR*-specific mutation detection test (specifics not captured in the survey) (44.0%; especially in Taiwan, Japan, and Brazil), followed by next-generation sequencing (NGS, 27.0%). However, there was variation in the methods used across countries, with higher usage rates of NGS in the US (54.0% for *EGFR* mutations and 80.0% for any molecular marker) and France (47.0% and 56.0%, respectively) and relatively lower rates in Taiwan (3.0% and 14.0%).

*EGFR* tests were mostly requested by the treating physician, except in the UK where 59.0% of tests were requested by a pathologist. For almost all (96.0%) patients, *EGFR* mutation results were known before initiation of 1L therapy for aNSCLC. Overall, physicians reported a median turnaround time of 10.0 (IQR 7.0–14.0) days for *EGFR* test results (Table 4). The most common physician-reported barriers to *EGFR* testing were inadequate tissue (68.0%, especially in Taiwan [86.0%]) and time delay in getting results (28.0%), although one in three physicians in Brazil also reported test availability, cost, and reimbursement issues as key barriers (Table 4). For the 172 patients with available testing data in the post-progression setting, T790M was tested in 79 patients (46.0%), of whom 56 (71.0%) were T790M positive.

### Outcomes

#### Effectiveness

In the 1L setting, the median (IQR) TTNT and TTF were 14.0 (IQR 8.0–22.0) and 13.3 (IQR 7.9–20.9) months, respectively. Of the 2857 patients, a response assessment was given for 311 patients. Of the 2857 with documented response in 1L ( $n = 311$ ), FR and PR to 1L

**Table 2** Disease timeline: overall and by country

	Overall ( <i>n</i> = 2857)	US ( <i>n</i> = 422)	BR ( <i>n</i> = 313)	UK ( <i>n</i> = 279)	IT ( <i>n</i> = 287)	FR ( <i>n</i> = 285)	ES ( <i>n</i> = 302)	DE ( <i>n</i> = 284)	EU5 <sup>a</sup> ( <i>n</i> = 1437)	TW ( <i>n</i> = 390)	JP ( <i>n</i> = 295)
Time between early-stage and advanced-stage diagnosis	<i>n</i> = 208	<i>n</i> = 12	<i>n</i> = 53	<i>n</i> = 7	<i>n</i> = 7	<i>n</i> = 2	<i>n</i> = 9	<i>n</i> = 37	<i>n</i> = 62	<i>n</i> = 23	<i>n</i> = 58
Months, mean (SD)	26.8 (17.9)	28.1 (13.2)	26.3 (16.4)	45.1 (46.8)	18 (7.5)	42.5 (12.8)	20.1 (12.5)	31.7 (14.8)	30.4 (20.9)	19.9 (16)	25.9 (16.6)
Time to advanced diagnosis from data collection	<i>n</i> = 2630	<i>n</i> = 374	<i>n</i> = 276	<i>n</i> = 244	<i>n</i> = 239	<i>n</i> = 274	<i>n</i> = 285	<i>n</i> = 271	<i>n</i> = 1313	<i>n</i> = 390	<i>n</i> = 277
Months, mean (SD)	14.5 (16.3)	13.9 (14.5)	14.4 (15.6)	14.2 (13.7)	14.0 (14.5)	11.3 (12.1)	9.7 (10.4)	9.7 (10.2)	11.7 (12.3)	20.0 (18.6)	20.6 (25.9)
Time between advanced diagnosis and initiation of the 1st line of advanced treatment	<i>n</i> = 2547	<i>n</i> = 355	<i>n</i> = 254	<i>n</i> = 237	<i>n</i> = 238	<i>n</i> = 271	<i>n</i> = 266	<i>n</i> = 265	<i>n</i> = 1277	<i>n</i> = 389	<i>n</i> = 272
Months, mean (SD)	1.6 (4.3)	2.4 (5.0)	2.2 (3.3)	1.4 (2.7)	1.5 (2.7)	0.9 (1.1)	0.8 (1.6)	1.4 (4.7)	1.2 (2.9)	1.3 (4.1)	2.2 (8.2)
Time since 1st line of advanced treatment	<i>n</i> = 2603	<i>n</i> = 363	<i>n</i> = 269	<i>n</i> = 240	<i>n</i> = 249	<i>n</i> = 278	<i>n</i> = 266	<i>n</i> = 274	<i>n</i> = 1307	<i>n</i> = 389	<i>n</i> = 275
Months, mean (SD)	12.8 (15.5)	10.8 (12.4)	11.9 (15.4)	12.8 (13.3)	12.3 (14.1)	10.1 (11.6)	9.2 (10.7)	8.3 (9.3)	10.4 (12.0)	18.8 (18.1)	18.6 (24)
Time since metastatic diagnosis	<i>n</i> = 490	<i>n</i> = 42	<i>n</i> = 33	<i>n</i> = 48	<i>n</i> = 42	<i>n</i> = 46	<i>n</i> = 36	<i>n</i> = 80	<i>n</i> = 252	<i>n</i> = 84	<i>n</i> = 79
Months, mean (SD)	13.4 (17.5)	14.2 (14.8)	15.9 (14.0)	8.0 (7.9)	8.5 (7.4)	7.7 (7.2)	6.5 (3.9)	7.2 (7.3)	7.6 (7.0)	16.4 (16.2)	27.1 (31.4)

Table 2 Continued

	Overall ( <i>n</i> = 2857)	US ( <i>n</i> = 422)	BR ( <i>n</i> = 313)	UK ( <i>n</i> = 279)	IT ( <i>n</i> = 287)	FR ( <i>n</i> = 285)	ES ( <i>n</i> = 302)	DE ( <i>n</i> = 284)	EU5 <sup>a</sup> ( <i>n</i> = 1437)	TW ( <i>n</i> = 390)	JP ( <i>n</i> = 295)
Time between advanced and metastatic diagnosis	<i>n</i> = 99	<i>n</i> = 8	<i>n</i> = 41	<i>n</i> = 2	<i>n</i> = 6	<i>n</i> = 7	<i>n</i> = 3	<i>n</i> = 12	<i>n</i> = 30	<i>n</i> = 8	<i>n</i> = 12
Months, mean (SD)	10.8 (12.3)	13.5 (21.3)	8.1 (13.8)	13.6 (12.1)	13.1 (9.3)	16.8 (11.8)	10.5 (6.7)	10 (7.7)	12.5 (9.1)	14.3 (9.8)	11.6 (6.4)

BR Brazil, DE Germany, ES Spain, EU5 5 countries from the European Union, FR France, IT Italy, JP Japan, SD standard deviation, TW Taiwan, UK United Kingdom, US United States

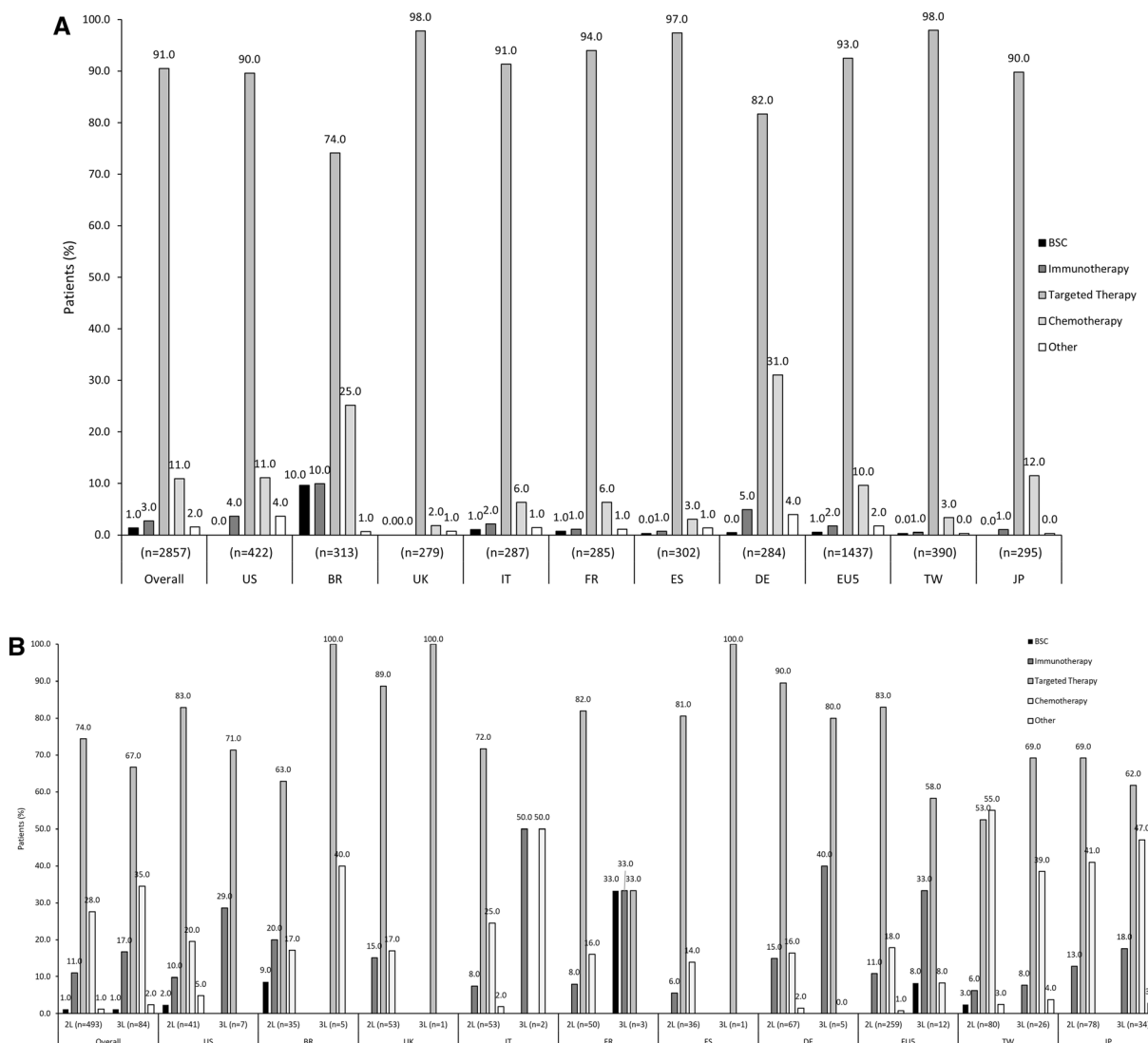
<sup>a</sup>Includes the UK, IT, FR, ES, and DE

therapy were reported in 12.0% and 83.0%, respectively, with 5.0% showing no response. Generally similar results were observed across countries, although Brazil had a relatively higher rate of no response (18.0%) (Supplementary Table S7). Response rates for overall population by each line of therapy are presented in Fig. 4. In the overall patient population (*n* = 2857), the mean (SD) duration of 1L treatment was 14.3 (11.2) months and the median number of treatment lines received was 1 (IQR 1–1). Mean (SD) duration of 2L therapy was 12.3 (10.7) months. The main physician-reported reason for early discontinuation of 1L (*n* = 223) or 2L therapy (*n* = 29), in all countries, was disease progression (77.0% for 1L and 83.0% for 2L), followed by side effects (20.0% for 1L and 17.0% for 2L) and lack of response (12.0% for 1L and 7.0% for 2L) (Supplementary Table S7).

#### Disease Symptoms and Side Effects

In the overall population, the top five physician-reported disease symptoms in the overall cohort (*n* = 2857) were cough (51.0%), fatigue (37.0%), dyspnea (33.0%), persistent cough (24.0%), and weight loss (22.0%) (Table 5). Analysis of patient-reported disease symptoms in the subset of patients with eligible PSC data (*n* = 962, 34.0% of overall cohort) showed a similar trend. However, patient-reported rates trended higher than physician-reported rates, especially for weight loss (33.0% and 22.0%), low mood (24.0% and 14.0%, respectively), and anxiety (27.0% and 14.0%) (Table 5). Table 5 also includes the patient- and physician-reported symptoms across all counties.

Among the 733 patients (26.0% of the overall cohort) with available safety data (reported AEs), the majority were grade 1 or grade 2 in severity. The most common any grade AEs were rash (46.0%, 334/733) and diarrhea (45.0%, 333/733), followed by dry skin (32.0%, 235/733), fatigue (28.0%, 204/733), loss of appetite (26.0%, 191/733), and nausea (24.0%, 178/733) (Supplementary Fig. S4). Patterns of disease symptoms and therapy AEs were generally similar across countries as summarized in Supplementary Table S8.



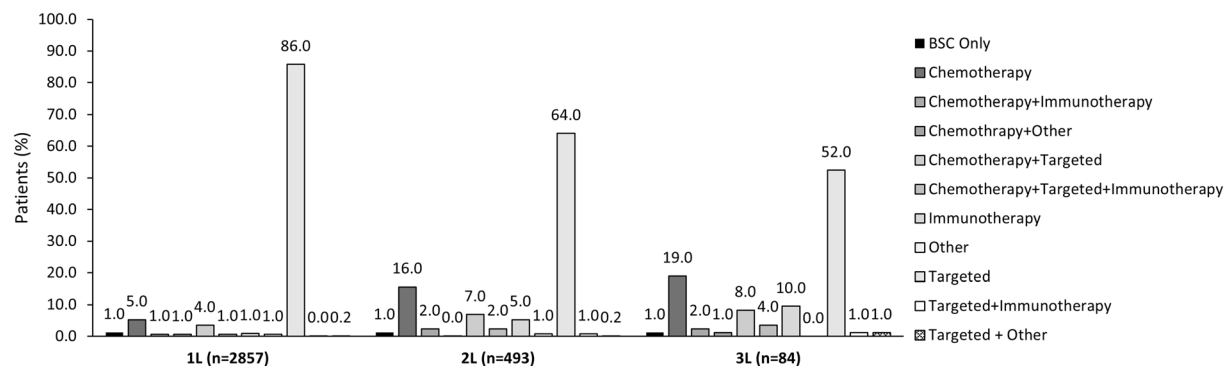
**Fig. 2** Treatment patterns: overall population and by country. **a** 1L. **b** 2L and 3L. All data are presented as %. 1L first line, 2L second line, 3L third line, BR Brazil, BSC best supportive care, DE Deutschland, ES Spain, EU5 5 countries from the European Union, FR France, IT Italy, JP Japan, TW Taiwan, UK United Kingdom, US United States

**Patient-Reported Outcomes**

The mean (SD) EQ-5D-5L index score for the 934 patients with available PSC data was 0.7 (0.2) and mean (SD) EQ-5D VAS for 947 patients was 69.7 (17.6) (Table 6). Some or extreme problems were reported by at least 40.0% of patients across most domains (self-care, 35.0%; mobility, 42.0%; usual activities, 55.0%; anxiety/depression, 64.0%; pain/discomfort, 66.0%) (Supplementary Table S9).

The mean (SD) FACT-L score was 83.5 (21.0) (Table 6), with subscale mean scores ranging

from 13.8 for the emotional well-being subscale to 19.7 for the physical well-being subscale (Supplementary Table S10). Almost all the patients (942/956 patients, 99.0%) felt completely informed by their physicians about their disease and treatment options (reported in patient self-reported questionnaire), and involved in their treatment decisions (88.0%, 831/945), with key treatment goals of maintaining or improving NSCLC symptoms (59.0%, 556/950) and prolonging life (47.0%, 442/950).



**Fig. 3** Treatment combinations: overall population. All data are presented as %. 1L first line, 2L second line, 3L third line, BSC best supportive care

### Healthcare Resource Utilization

Over the 12 months prior to data capture, almost all patients (98.0%) consulted with the physician involved in data capture with mean (SD) 1.0 (0) consultations for the overall population. Among hospitalized patients ( $n = 827$ ), the mean (SD) number of hospital visits in the last 12 months was 1.5 (1.5). Other healthcare providers involved in the ongoing management of patients are summarized in Table 7. Patients lost about mean (SD) 10.6 (6.6) h of work per week for approximately mean (SD) 29.2 (25.7) weeks. Approximately one in three patients (31.0%, 288/916) incurred out-of-pocket expenses for NSCLC treatment. Table 7 summarizes the proportion of patients incurring out-of-pocket costs and median (IQR) out-of-pocket costs by country. Out of the 2857 patients, 827 (29.0%) were admitted to the hospital at some point in time for a mean of 1.5 visits. Mean hospital length of stay ranged from 7 to 9 nights. About one of three hospitalizations involved emergency care (e.g., 35.0% for the first hospitalization) and 7.0% of hospitalizations involved intensive care (Table 7). Most of the hospitalizations were to treat a complication, except for biopsy which was the main reason (38.0%) for the first hospitalization (Supplementary Table S11).

At data capture, most (58.0%) patients had received supportive therapy, and patterns of supportive therapy use were generally consistent across countries as summarized in Table 8. Procedures or tests performed in diagnosis and monitoring of *EGFRm+* mutated aNSCLC are

summarized in Fig. 5 and Supplementary Table S12. Overall, the most used tests for diagnosis included biopsy (76.0%), chest computerized tomography (CT) scans (74.0%), and X-ray (50.0%). These tests were also commonly used for disease monitoring, albeit at lower rates especially for biopsy testing (18.0% for monitoring and 76.0% for diagnosis). Testing patterns were largely consistent across countries but the use of specific imaging techniques varied between countries: ultrasound use ranged from 2.0% in the UK to 50.0% in Germany, X-ray usage ranged from 27.0% in the US to 81.0% in Japan, magnetic resonance imaging [MRI] use ranged from 16.0% in Japan to 72.0% in Taiwan). In addition, most patients in Japan did not receive biopsy testing for either diagnosis (51.0%) or monitoring (94.0%) of *EGFRm+* aNSCLC.

## DISCUSSION

Findings from this large multiregion data set reflect real-world treatment practice and outcomes for *EGFRm+* aNSCLC across nine countries, during a period when the treatment landscape was rapidly changing with implementation of third-generation *EGFR*-TKI and dual *EGFR*-VEGF pathway inhibition as guideline-recommended treatment strategies [6, 32, 33]. Our results set an important baseline for care as evaluation for increased adoption of new regimens and ongoing shifting treatment algorithms are affecting patient outcomes.

**Table 3** Treatments received in each line: overall and by country

Targeted Treatment for EGFR+ aNSCLC	Overall	US	BR	UK	IT	FR	ES	DE	EU5 <sup>a</sup>	TW	JP
Non-drug treatment	<i>n</i> = 2857 (3.0)	<i>n</i> = 422 (4.0)	<i>n</i> = 313 (2.0)	<i>n</i> = 279 (2.0)	<i>n</i> = 287 (4.0)	<i>n</i> = 285 (1.0)	<i>n</i> = 302 (1.0)	<i>n</i> = 284 (3.0)	<i>n</i> = 1437 (2.0)	<i>n</i> = 390 (4.0)	<i>n</i> = 295 (3.0)
Surgery	74	15	7	5	11	2	3	9	30	14	9
Radiotherapy	573 (20.0)	103 (24.0)	73 (23.0)	49 (18.0)	60 (21.0)	49 (17.0)	37 (12.0)	44 (15.0)	239 (17.0)	101 (26.0)	57 (19.0)
Surgery and radiotherapy	118 (4.0)	9 (2.0)	8 (3.0)	6 (2.0)	7 (2.0)	9 (3.0)	2 (1.0)	64 (23.0)	88 (6.0)	10 (3.0)	2 (1.0)
None	2092 (73.0)	295 (70.0)	225 (72.0)	219 (78.0)	209 (73.0)	225 (79.0)	260 (86.0)	167 (59.0)	1080 (75.0)	265 (68.0)	227 (77.0)
Neoadjuvant therapy received	<i>n</i> = 192 (21.0)	<i>n</i> = 24 (25.0)	<i>n</i> = 15 (13.0)	<i>n</i> = 11 (0)	<i>n</i> = 18 (39.0)	<i>n</i> = 11 (0)	<i>n</i> = 5 (20.0)	<i>n</i> = 73 (19)	<i>n</i> = 118 (27)	<i>n</i> = 24 (5)	<i>n</i> = 11 (0)
Adjuvant therapy received	<i>n</i> = 192 (55.0)	<i>n</i> = 24 (71.0)	<i>n</i> = 15 (60.0)	<i>n</i> = 11 (2)	<i>n</i> = 18 (13)	<i>n</i> = 11 (2)	<i>n</i> = 5 (40.0)	<i>n</i> = 73 (43)	<i>n</i> = 118 (62)	<i>n</i> = 24 (14)	<i>n</i> = 11 (4)
1L advance treatment	<i>n</i> = 2857 (11.0)	<i>n</i> = 422 (11.0)	<i>n</i> = 313 (25.0)	<i>n</i> = 279 (2.0)	<i>n</i> = 287 (6.0)	<i>n</i> = 285 (6.0)	<i>n</i> = 302 (3.0)	<i>n</i> = 284 (88)	<i>n</i> = 1437 (138)	<i>n</i> = 390 (13)	<i>n</i> = 295 (34)
Chemotherapy	311	47	79	5	18	18	9	88	138	13	34
Targeted	2586 (91.0)	378 (90.0)	232 (74.0)	273 (98.0)	262 (91.0)	268 (94.0)	294 (97.0)	232 (82.0)	1329 (92.0)	382 (98.0)	265 (90.0)
1st/2nd generation EGFR-TKI	1413 (49.0)	122 (29.0)	122 (39.0)	232 (83.0)	124 (43.0)	157 (55.0)	156 (52.0)	89 (31.0)	758 (53.0)	310 (79.0)	101 (34.0)
3rd generation EGFR-TKI	957 (33.0)	220 (52.0)	61 (19.0)	39 (14.0)	128 (45.0)	104 (36.0)	126 (42.0)	89 (31.0)	486 (34.0)	37 (9.0)	153 (52.0)
EGFR-TKI and anti-VEGF	41 (1.0)	5 (1.0)	1 (< 1.0)	0	3 (1.0)	0	1 (< 1.0)	2 (1.0)	6 (< 1.0)	24 (6.0)	5 (2.0)
Other targeted therapy	175 (6.0)	31 (7.0)	48 (15.0)	2 (1.0)	7 (2.0)	7 (2.0)	11 (4.0)	52 (18.0)	79 (5.0)	11 (3.0)	6 (2.0)

Table 3 continued

Targeted Treatment for EGFR+ aNSCLC	Overall	US	BR	UK	IT	FR	ES	DE	EU5 <sup>a</sup>	TW	JP
Immunotherapy	76 (3.0)	15 (4.0)	31 (10.0)	0	6 (2.0)	3 (1.0)	2 (<1.0)	14 (5.0)	25 (2.0)	2 (1.0)	3 (1.0)
Other	43 (2.0)	15 (4.0)	2 (1.0)	2 (1.0)	4 (1.0)	3 (1.0)	4 (1.0)	11 (4.0)	24 (2.0)	1 (<1.0)	1 (<1.0)
Best supportive care	349 (12.0)	47 (11.0)	109 (35.0)	5 (2.0)	21 (7.0)	20 (7.0)	10 (3.0)	89 (31.0)	145 (11.0)	14 (4.0)	34 (12.0)
2L advance treatment	<i>n</i> = 493	<i>n</i> = 41	<i>n</i> = 35	<i>n</i> = 53	<i>n</i> = 53	<i>n</i> = 50	<i>n</i> = 36	<i>n</i> = 67	<i>n</i> = 259	<i>n</i> = 80	<i>n</i> = 78
Chemotherapy	136 (28.0)	8 (20.0)	6 (17.0)	9 (17.0)	13 (25.0)	8 (16.0)	5 (14.0)	11 (16.0)	46 (18.0)	44 (55.0)	32 (41.0)
Targeted	367 (74.0)	34 (83.0)	22 (63.0)	47 (89.0)	38 (72.0)	41 (82.0)	29 (81.0)	60 (90.0)	215 (83.0)	42 (53.0)	54 (69.0)
1st/2nd generation EGFR-TKI	67 (14.0)	5 (12.0)	8 (23.0)	4 (8.0)	5 (9.0)	6 (12.0)	9 (25.0)	13 (19.0)	37 (14.0)	5 (6.0)	12 (15.0)
3rd generation EGFR-TKI	236 (48.0)	24 (59.0)	13 (37.0)	37 (70.0)	29 (55.0)	33 (66.0)	20 (56.0)	28 (42.0)	147 (57.0)	24 (30.0)	28 (36.0)
EGFR-TKI and anti-VEGF	3 (1.0)	0	0	0	0	0	0	0	0	2 (3.0)	1 (1.0)
Other targeted therapy	61 (12.0)	5 (12.0)	1 (3.0)	6 (11.0)	4 (8.0)	2 (4.0)	0	19 (28.0)	31 (12.0)	11 (14.0)	13 (17.0)
Immunotherapy	54 (11.0)	4 (10.0)	7 (20.0)	8 (15.0)	4 (8.0)	4 (8.0)	2 (6.0)	10 (15.0)	28 (11.0)	5 (6.0)	10 (13.0)
Other	6 (1.0)	2 (5.0)	0	0	1 (2.0)	0	0	1 (1.0)	2 (1.0)	2 (3.0)	0
Best supportive care	142 (29.0)	9 (22.0)	9 (26.0)	9 (17.0)	13 (25.0)	8 (16.0)	5 (14.0)	11 (16.0)	46 (18.0)	46 (58.0)	32 (41.0)
3L advance treatment	<i>n</i> = 84	<i>n</i> = 7	<i>n</i> = 5	<i>n</i> = 1	<i>n</i> = 2	<i>n</i> = 3	<i>n</i> = 1	<i>n</i> = 5	<i>n</i> = 12	<i>n</i> = 26	<i>n</i> = 34
Chemotherapy	29 (35.0)	0	2 (40.0)	0	1 (50.0)	0	0	0	1 (8.0)	10 (38.0)	16 (47.0)
Targeted	56 (67.0)	5 (71.0)	5 (100.0)	1 (100.0)	0	1 (33.0)	1 (100.0)	4 (80.0)	7 (58.0)	18 (69.0)	21 (62.0)
1st/2nd generation EGFR-TKI	18 (21.0)	0	0	0	0	0	0	0	0	7 (27.0)	11 (32.0)



**Table 3** continued

Targeted Treatment for EGFR+ aNSCLC	Overall	US	BR	UK	IT	FR	ES	DE	EU5 <sup>a</sup>	TW	JP
3rd generation EGFR-TKI	24 (29.0)	5 (71.0)	3 (60.0)	1 (100.0)	0	1 (33.0)	1 (100.0)	3 (60.0)	6 (50.0)	6 (23.0)	4 (12.0)
EGFR-TKI and anti-VEGF	1 (1.0)	0	0	0	0	0	0	0	0	1 (4.0)	0
Other targeted therapy	13 (15.0)	0	2 (40.0)	0	0	0	0	1 (20.0)	1 (8.0)	4 (15.0)	6 (18.0)
Immunotherapy	14 (17.0)	2 (29.0)	0	0	1 (50.0)	1 (33.0)	0	2 (40.0)	4 (33.0)	2 (8.0)	6 (18.0)
Other	2 (2.0)	0	0	0	0	0	0	0	0	1 (4.0)	1 (3.0)
Best supportive care	30 (36.0)	0	2 (40.0)	0	1 (50.0)	1 (33.0)	0	0	2 (17.0)	10 (38.0)	16 (47.0)

All data are presented as *n* (%), unless specified. *n* = 2857, unless specified

BR Brazil, DE Germany, ER emergency room, ES Spain, EU5 5 countries from the European Union, FR France, ICU intensive-care unit, IT Italy, JP Japan, SD standard deviation, TW Taiwan, UK United Kingdom, US United States

Chemotherapy: carboplatin, cisplatin, paclitaxel, Nab-paclitaxel, docetaxel, gemcitabine, vinorelbine, pemetrexed, irinotecan, S-1

Targeted therapy: afatinib, erlotinib, gefitinib, osimertinib, dacomitinib, ceruximab, necitumumab, crizotinib, alectinib, ceritinib, brigatinib, lorlatinib, dabrafenib + trametinib, bevacizumab, nintedanib, ramucirumab, entrectinib

Immunotherapy: pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab

Other: any additional treatments not mentioned

1st generation EGFR-TKI included TKI, erlotinib, gefitinib; 2nd generation EGFR-TKI included afatinib, dacomitinib; 3rd generation EGFR-TKI included osimertinib

<sup>a</sup>Includes the UK, IT, FR, ES, and DE

<sup>b</sup>Reported in > 3.0% of the patients

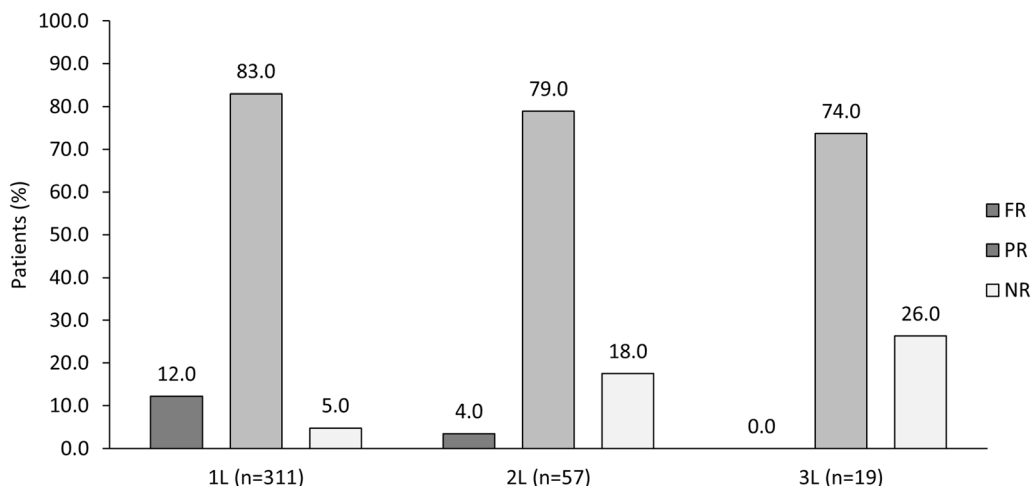
**Table 4** *EGFR* testing: type of test, sample used, and physician-reported measures

	Overall	US	BR	UK	IT	FR	ES	DE	EU5 <sup>a</sup>	TW	JP
Test used for <i>EGFR</i>	<i>n</i> = 2857	<i>n</i> = 422	<i>n</i> = 313	<i>n</i> = 279	<i>n</i> = 287	<i>n</i> = 285	<i>n</i> = 302	<i>n</i> = 284	<i>n</i> = 1437	<i>n</i> = 390	<i>n</i> = 295
NGS	775 (27.0)	226 (54.0)	50 (16.0)	63 (23.0)	79 (28.0)	133 (47.0)	76 (25.0)	87 (31.0)	438 (31.0)	13 (3.0)	48 (16.0)
<i>EGFR</i> mutation detection	1246 (44.0)	116 (28.0)	165 (53.0)	121 (43.0)	72 (25.0)	87 (31.0)	110 (36.0)	120 (42.0)	510 (36.0)	257 (66.0)	198 (67.0)
FISH	201 (7.0)	32 (8.0)	50 (16.0)	12 (4.0)	33 (12.0)	21 (7.0)	20 (7.0)	25 (9.0)	111 (8.0)	6 (2.0)	2 (1.0)
IHC	299 (11.0)	44 (10.0)	88 (28.0)	11 (4.0)	49 (17.0)	19 (7.0)	32 (11.0)	11 (4.0)	122 (9.0)	39 (10.0)	6 (2.0)
DNA sequencing (Sanger)	77 (3.0)	6 (1.0)	15 (5.0)	7 (3.0)	15 (5.0)	1 (< 1.0)	1 (< 1.0)	15 (5.0)	39 (3.0)	17 (4.0)	0
RT-PCR	416 (15.0)	6 (1.0)	36 (12.0)	32 (12.0)	67 (23.0)	2 (1.0)	70 (23.0)	9 (3.0)	180 (13.0)	154 (40.0)	40 (14.0)
Digital PCR	20 (1.0)	1 (< 1.0)	1 (< 1.0)	4 (1.0)	2 (1.0)	0	0	3 (1.0)	9 (1.0)	7 (2.0)	2 (1.0)
Other	2 (< 1.0)	1 (< 1.0)	1 (< 1.0)	0	0	0	0	0	0	0	0
Don't know	270 (10.0)	50 (12.0)	11 (4.0)	42 (15.0)	32 (11.0)	50 (18.0)	23 (8.0)	54 (19.0)	201 (14.0)	0	8 (3.0)
Samples used of <i>EGFR</i> test	<i>n</i> = 2857	<i>n</i> = 422	<i>n</i> = 313	<i>n</i> = 279	<i>n</i> = 287	<i>n</i> = 285	<i>n</i> = 302	<i>n</i> = 284	<i>n</i> = 1437	<i>n</i> = 390	<i>n</i> = 295
Core needle biopsy	1592 (56.0)	263 (62.0)	136 (44.0)	217 (78.0)	165 (58.0)	188 (66.0)	233 (77.0)	93 (33.0)	896 (62.0)	225 (58.0)	72 (24.0)
Bronchial brush biopsy	529 (19.0)	39 (9.0)	105 (34.0)	20 (7.0)	19 (7.0)	65 (23.0)	24 (8.0)	40 (14.0)	168 (12.0)	63 (16.0)	154 (52.0)
Mediastinoscopy	69 (2.0)	7 (2.0)	26 (8.0)	6 (2.0)	11 (4.0)	1 (< 1.0)	7 (2.0)	1 (< 1.0)	26 (2.0)	7 (2.0)	3 (1.0)
Fine needle aspiration	334 (12.0)	81 (19.0)	38 (12.0)	19 (7.0)	48 (17.0)	12 (4.0)	30 (10.0)	73 (26.0)	182 (13.0)	25 (6.0)	8 (3.0)
Thoracentesis	142 (5.0)	20 (5.0)	4 (1.0)	5 (2.0)	15 (5.0)	1 (< 1.0)	6 (2.0)	2 (1.0)	29 (2.0)	69 (18.0)	20 (7.0)
Liquid biopsy	185 (7.0)	24 (6.0)	28 (9.0)	5 (2.0)	15 (5.0)	13 (5.0)	16 (5.0)	46 (16.0)	95 (7.0)	32 (8.0)	6 (2.0)
Other	144 (5.0)	7 (2.0)	3 (1.0)	7 (3.0)	14 (5.0)	13 (5.0)	8 (3.0)	6 (2.0)	48 (3.0)	39 (10.0)	47 (16.0)
Don't know	139 (5.0)	34 (8.0)	8 (3.0)	11 (4.0)	24 (8.0)	10 (4.0)	9 (3.0)	38 (13.0)	92 (6.0)	0	5 (2.0)
Requesting <i>EGFR</i> tests (physician-reported)	<i>n</i> = 513	<i>n</i> = 60	<i>n</i> = 50	<i>n</i> = 49	<i>n</i> = 47	<i>n</i> = 48	<i>n</i> = 50	<i>n</i> = 47	<i>n</i> = 241	<i>n</i> = 51	<i>n</i> = 111
Self (treating physician)	431 (84.0)	46 (77.0)	48 (96.0)	25 (51.0)	43 (92.0)	35 (73.0)	33 (66.0)	45 (96.0)	181 (75.0)	50 (98.0)	106 (96.0)
Pulmonologist	62 (12.0)	7 (12.0)	4 (8.0)	8 (16.0)	8 (17.0)	10 (21.0)	3 (6.0)	3 (6.0)	32 (13.0)	5 (10.0)	14 (13.0)
Medical oncologist	43 (8.0)	13 (22.0)	8 (16.0)	4 (8.0)	7 (15.0)	2 (4.0)	1 (2.0)	5 (11.0)	19 (8.0)	2 (4.0)	1 (1.0)
Pathologist	104 (20.0)	14 (23.0)	3 (6.0)	29 (59.0)	7 (15.0)	15 (31.0)	21 (42.0)	1 (2.0)	73 (30.0)	5 (10.0)	9 (8.0)
Interventional radiologist	6 (1.0)	2 (3.0)	0	1 (2.0)	1 (2.0)	0	0	2 (4.0)	4 (2.0)	0	0
Surgeon	16 (3.0)	1 (2.0)	4 (8.0)	2 (4.0)	4 (9.0)	1 (2.0)	0	2 (4.0)	9 (4.0)	1 (2.0)	1 (1.0)
Radiation oncologist	12 (2.0)	1 (2.0)	1 (2.0)	3 (6.0)	4 (9.0)	0	0	2 (4.0)	9 (4.0)	1 (2.0)	0
Primary physician/general practitioner	2 (< 1.0)	1 (2.0)	1 (2.0)	0	0	0	0	0	0	0	0
Nurse	4 (1.0)	1 (2.0)	2 (4.0)	1 (2.0)	0	0	0	0	1 (< 1.0)	0	0

**Table 4** continued

	Overall	US	BR	UK	IT	FR	ES	DE	EU5 <sup>a</sup>	TW	JP
Other	6 (1.0)	2 (3.0)	0	2 (4.0)	0	1 (2.0)	1 (2.0)	0	4 (2.0)	0	0
Don't know	0	0	0	0	0	0	0	0	0	0	0
Barriers to EGFR testing (physician-reported)	<i>n</i> = 513	<i>n</i> = 60	<i>n</i> = 50	<i>n</i> = 49	<i>n</i> = 47	<i>n</i> = 48	<i>n</i> = 50	<i>n</i> = 47	<i>n</i> = 241	<i>n</i> = 51	<i>n</i> = 111
Inadequate tissue	348 (68.0)	37 (62.0)	34 (68.0)	36 (74.0)	34 (72.0)	28 (58.0)	37 (74.0)	28 (60.0)	163 (68.0)	44 (86.0)	70 (63.0)
Time delay in getting results	144 (28.0)	16 (27.0)	19 (38.0)	14 (29.0)	15 (32.0)	8 (17.0)	11 (22.0)	11 (23.0)	59 (25.0)	7 (14.0)	43 (39.0)
Cost per test	73 (14.0)	10 (17.0)	20 (40.0)	2 (4.0)	6 (13.0)	3 (6.0)	2 (4.0)	6 (13.0)	19 (8.0)	9 (18.0)	15 (14.0)
Reimbursement issue	73 (14.0)	11 (18.0)	18 (36.0)	4 (8.0)	1 (2.0)	2 (4.0)	2 (4.0)	7 (15.0)	16 (7.0)	8 (16.0)	20 (18.0)
Test availability	44 (9.0)	3 (5.0)	16 (32.0)	3 (6.0)	2 (4.0)	3 (6.0)	3 (6.0)	4 (9.0)	15 (6.0)	9 (18.0)	1 (1.0)
Patient refusal	40 (8.0)	10 (17.0)	3 (6.0)	6 (12.0)	2 (4.0)	3 (6.0)	0	5 (11.0)	16 (7.0)	9 (18.0)	2 (2.0)
Other	8 (2.0)	2 (3.0)	0	3 (6.0)	0	1 (2.0)	0	1 (2.0)	5 (2.0)	0	1 (1.0)
None	94 (18.0)	16 (27.0)	3 (6.0)	9 (18.0)	10 (21.0)	13 (27.0)	5 (10.0)	12 (26.0)	49 (20.0)	3 (6.0)	23 (21.0)
Physicians testing proportion of their patients at advanced diagnosis (physician-reported)	<i>n</i> = 542	<i>n</i> = 71	<i>n</i> = 53	<i>n</i> = 51	<i>n</i> = 49	<i>n</i> = 51	<i>n</i> = 50	<i>n</i> = 50	<i>n</i> = 251	<i>n</i> = 51	<i>n</i> = 116
Tested for any molecular biomarkers via NGS (physician-reported)	499 (92.0)	66 (94.0)	44 (84.0)	49 (96.0)	43 (88.0)	47 (91.0)	48 (95.0)	45 (89.0)	231 (92.0)	49 (96.0)	108 (93.0)
Tested for EGFR at advanced stage (physician-reported)	207 (38.0)	56 (80.0)	25 (47.0)	13 (25.0)	16 (33.0)	28 (56.0)	14 (29.0)	15 (30.0)	86 (34.0)	7 (14.0)	34 (29.0)
Turnaround time for EGFR test results, median (IQR) days	389 (72.0)	44 (63.0)	34 (65.0)	38 (75.0)	40 (82.0)	42 (83.0)	41 (82.0)	34 (68.0)	195 (78.0)	48 (94.0)	68 (58.0)
	<i>n</i> = 540	<i>n</i> = 71	<i>n</i> = 53	<i>n</i> = 51	<i>n</i> = 49	<i>n</i> = 51	<i>n</i> = 50	<i>n</i> = 48	<i>n</i> = 249	<i>n</i> = 51	<i>n</i> = 116
	10.0	7.0 (5/	15.0	10.0	14.0	14.0	8.0	7.0	10.0	7.0	7.0
	(7.0–14.0)	0–14.0)	(10.0–25.0)	(7.0–14.0)	(8.0–14.0)	(10.0–18.5)	(7.0–10.0)	(6.5–12.0)	(7.0–14.0)	(7.0–12.0)	(7.0–10.0)

All data are presented as *n* (%); % rounded off to nearest 0, unless otherwise indicated  
 EGFR mutation detection test: specifics not captured in the survey  
 BR Brazil, DE Germany, DNA deoxyribonucleic acid, EGFR endothelial growth factor receptor, ES Spain, EU5 US countries from the European Union, FISH fluorescence in situ hybridization, FR France, IHC immunohistochemistry, IT Italy, JP Japan, NGS next-generation sequencing, PCR polymerase chain reaction, RT-PCR reverse-transcription polymerase chain reaction, TW Taiwan, UK United Kingdom, US United States  
<sup>a</sup>Includes the UK, IT, FR, ES, and DE



**Fig. 4** Response rates after end of treatment: overall population. All data are presented as %. 1L first line, 2L second line, 3L third line, FR full response, NR no response, PR partial response

Overall, *EGFRm+* aNSCLC treatment patterns across all regions were in line with international treatment guideline recommendations for systemic therapy with targeted regimens and consistent with the available treatment options covered for reimbursement [6, 32, 33]. However, regional variation was observed in treatment and resource use patterns, suggesting differing approaches to *EGFRm+* aNSCLC management. As guidelines and treatment patterns will change with the development of new treatment options, future studies should assess the place in therapy for these newer agents.

Consistent with most *EGFR* aNSCLC populations, adenocarcinoma was the most common histology in this study, most patients were older, had cardiovascular comorbidities, and contralateral lungs as the main site of metastasis [14, 34–36]. While most (74.0–98.0%) patients received *EGFR*-TKIs in the 1L setting, reflecting current European Society for Medical Oncology (ESMO) [33], American Society of Clinical Oncology (ASCO) [32], and National Comprehensive Cancer Network (NCCN) guideline [6] recommendations, the relative use of first/second-generation *EGFR*-TKIs and third-generation TKIs (i.e., osimertinib) varied across countries. First/second-generation *EGFR*-TKIs were the most common 1L treatment in most of the countries, except in the US and Japan where osimertinib (3rd generation *EGFR*-TKI) was the

most common treatment and in Germany and Italy with similar usage of these regimens. As osimertinib is the preferred 1L treatment option in clinical guidelines [37] our finding suggests differential adoption of innovative therapies, possibly owing to differences in access, reimbursement, or physician behavior across countries. Hence, these and other data in this study should be considered in the context of the country in which the data were collected and may not be globally applicable.

Although clinical guidelines also recommend anti-angiogenic antibodies, ramucirumab or bevacizumab, in combination with erlotinib as alternative 1L treatments [6, 32, 33], there was little use of these regimens (1%) in our data set. This was likely due to the recent approval of ramucirumab plus erlotinib by the EMA (December 2019) and FDA (May 2020) [38, 39] and its incorporation into guidelines [38, 40, 41], which limits the time period for evaluation for these therapies. In spite of specific recommendations, some patients (about 14.0% overall) in our study received chemotherapy and/or immunotherapy instead of *EGFR*-TKIs, suggesting incomplete adherence to the guideline's recommendations and further dissemination and clarification may be needed.

In this study, a partial or full response to therapy was reported for 83.0% and 12.0%, respectively, of the overall patient population.

**Table 5** Disease symptoms and side effects: overall and by country

	<b>Overall</b> ( <i>n</i> = 2857)	<b>US</b> ( <i>n</i> = 422)	<b>BR</b> ( <i>n</i> = 313)	<b>UK</b> ( <i>n</i> = 279)	<b>IT</b> ( <i>n</i> = 287)	<b>FR</b> ( <i>n</i> = 285)	<b>ES</b> ( <i>n</i> = 302)	<b>DE</b> ( <i>n</i> = 284)	<b>EUS<sup>a</sup></b> ( <i>n</i> = 1437)	<b>TW</b> ( <i>n</i> = 390)	<b>JP</b> ( <i>n</i> = 295)
<b>Comorbidities at advanced diagnosis<sup>b</sup></b>											
Hypertension	913 (32.0)	180 (43.0)	116 (37.0)	86 (31.0)	102 (36.0)	80 (28.0)	77 (26.0)	112 (39.0)	457 (32.0)	104 (27.0)	56 (19.0)
Dyslipidemia	391 (14.0)	97 (23.0)	34 (11.0)	32 (12.0)	54 (19.0)	32 (11.0)	45 (15.0)	48 (17.0)	211 (15.0)	26 (7.0)	23 (8.0)
COPD	295 (10.0)	64 (15.0)	50 (16.0)	25 (9.0)	31 (11.0)	12 (4.0)	6 (2.0)	52 (18.0)	126 (9.0)	39 (10.0)	16 (5.0)
Diabetes without chronic complications	256 (9.0)	32 (8.0)	25 (8.0)	31 (11.0)	40 (14.0)	15 (5.0)	43 (14.0)	36 (13.0)	165 (12.0)	25 (6.0)	9 (3.0)
Renal disease	133 (5.0)	23 (6.0)	23 (7.0)	10 (4.0)	13 (5.0)	14 (5.0)	6 (2.0)	18 (6.0)	61 (4.0)	19 (5.0)	7 (2.0)
Peripheral vascular disease	109 (4.0)	16 (4.0)	19 (6.0)	12 (4.0)	12 (4.0)	14 (5.0)	16 (5.0)	11 (4.0)	65 (5.0)	7 (2.0)	2 (1.0)
Mild liver disease	91 (3.0)	11 (3.0)	9 (3.0)	4 (1.0)	11 (4.0)	4 (1.0)	8 (3.0)	24 (9.0)	51 (4.0)	11 (3.0)	9 (3.0)
<b>Current comorbidities<sup>b</sup></b>											
Hypertension	925 (32.0)	187 (44.0)	125 (40.0)	85 (31.0)	100 (35.0)	79 (28.0)	76 (25.0)	104 (37.0)	444 (31.0)	110 (28.0)	59 (20.0)
Dyslipidemia	402 (14.0)	104 (25.0)	44 (14.0)	31 (11.0)	48 (17.0)	32 (11.0)	47 (16.0)	46 (16.0)	204 (14.0)	27 (7.0)	23 (8.0)
COPD	310 (11.0)	68 (16.0)	63 (20.0)	25 (9.0)	31 (11.0)	12 (4.0)	5 (2.0)	52 (18.0)	125 (9.0)	40 (10.0)	14 (5.0)
Diabetes without chronic complications	257 (9.0)	35 (8.0)	25 (8.0)	32 (12.0)	40 (14.0)	15 (5.0)	44 (15.0)	35 (12.0)	166 (12.0)	23 (6.0)	8 (3.0)
Renal disease	151 (5.0)	25 (6.0)	34 (11.0)	10 (4.0)	17 (6.0)	14 (5.0)	6 (2.0)	16 (6.0)	63 (4.0)	20 (5.0)	9 (3.0)
Peripheral vascular disease	115 (4.0)	15 (4.0)	30 (10.0)	11 (4.0)	12 (4.0)	14 (5.0)	14 (5.0)	11 (4.0)	62 (4.0)	8 (2.0)	0
Mild liver disease	109 (4.0)	11 (3.0)	17 (5.0)	4 (1.0)	14 (5.0)	4 (1.0)	10 (3.0)	21 (7.0)	53 (4.0)	18 (5.0)	10 (3.0)

Table 5 continued

	Overall (n = 2857)	US (n = 422)	BR (n = 313)	UK (n = 279)	IT (n = 287)	FR (n = 285)	ES (n = 302)	DE (n = 284)	EU5 <sup>a</sup> (n = 1437)	TW (n = 390)	JP (n = 295)
Physician-reported symptoms at current consultation <sup>c</sup>	n = 2857	n = 422	n = 313	n = 279	n = 287	n = 285	n = 302	n = 284	n = 1437	n = 390	n = 295
Cough	1461 (51.0)	232 (55.0)	170 (54.0)	123 (44.0)	159 (55.0)	152 (53.0)	143 (47.0)	146 (51.0)	723 (50.0)	242 (62.0)	94 (32.0)
Fatigue	1055 (37.0)	163 (39.0)	115 (37.0)	118 (42.0)	119 (42.0)	135 (47.0)	101 (33.0)	152 (54.0)	625 (44.0)	111 (29.0)	41 (14.0)
Dyspnea/breathing complications	935 (33.0)	154 (37.0)	105 (34.0)	95 (34.0)	117 (41.0)	116 (41.0)	111 (37.0)	119 (42.0)	558 (39.0)	104 (27.0)	14 (5.0)
Persistent cough	675 (24.0)	145 (34.0)	107 (34.0)	33 (12.0)	66 (23.0)	41 (14.0)	75 (25.0)	101 (36.0)	316 (22.0)	91 (23.0)	16 (5.0)
Weight loss	627 (22.0)	90 (21.0)	115 (37.0)	41 (15.0)	64 (22.0)	69 (24.0)	55 (18.0)	88 (31.0)	317 (22.0)	93 (24.0)	12 (4.0)
Loss of appetite	597 (21.0)	71 (17.0)	91 (29.0)	51 (18.0)	55 (19.0)	63 (22.0)	52 (17.0)	97 (34.0)	318 (22.0)	97 (25.0)	20 (7.0)
Chest pain	559 (20.0)	48 (11.0)	75 (24.0)	31 (11.0)	62 (22.0)	58 (20.0)	66 (22.0)	102 (36.0)	319 (22.0)	90 (23.0)	27 (9.0)
Bone pain	522 (18.0)	46 (11.0)	86 (28.0)	39 (14.0)	69 (24.0)	54 (19.0)	58 (19.0)	75 (26.0)	295 (21.0)	73 (19.0)	22 (8.0)
Hoarseness	375 (13.0)	47 (11.0)	71 (23.0)	17 (6.0)	49 (17.0)	25 (9.0)	45 (15.0)	77 (27.0)	213 (15.0)	38 (10.0)	6 (2.0)
Low mood	390 (14.0)	18 (4.0)	79 (25.0)	18 (7.0)	30 (11.0)	31 (11.0)	29 (10.0)	80 (28.0)	188 (13.0)	84 (22.0)	21 (7.0)
Anxiety	405 (14.0)	42 (10.0)	74 (24.0)	22 (8.0)	44 (15.0)	47 (17.0)	38 (13.0)	31 (11.0)	182 (13.0)	99 (25.0)	8 (3.0)
Weak limbs	363 (13.0)	31 (7.0)	66 (21.0)	7 (3.0)	68 (24.0)	27 (10.0)	26 (9.0)	60 (21.0)	188 (13.0)	62 (16.0)	16 (5.0)
Headache/dizziness	285 (10.0)	41 (10.0)	57 (18.0)	11 (4.0)	36 (13.0)	27 (10.0)	25 (8.0)	44 (16.0)	143 (10.0)	32 (8.0)	12 (4.0)
None of the above	378 (13.0)	29 (7.0)	26 (8.0)	41 (15.0)	29 (10.0)	31 (11.0)	26 (9.0)	6 (2.0)	133 (9.0)	59 (15.0)	131 (44.0)

Table 5 continued

	Overall (n = 2857)	US (n = 422)	BR (n = 313)	UK (n = 279)	IT (n = 287)	FR (n = 285)	ES (n = 302)	DE (n = 284)	EU5 <sup>a</sup> (n = 1437)	TW (n = 390)	JP (n = 295)
Patient-reported symptoms at current consultation	n = 962	n = 160	n = 128	n = 55	n = 79	n = 79	n = 127	n = 151	n = 491	n = 49	n = 134
Cough	543 (56.0)	105 (66.0)	79 (62.0)	15 (27.0)	42 (53.0)	47 (60.0)	75 (59.0)	97 (64.0)	276 (56.0)	31 (63.0)	52 (39.0)
Fatigue	361 (38.0)	49 (31.0)	42 (33.0)	9 (16.0)	36 (46.0)	46 (58.0)	62 (49.0)	72 (48.0)	225 (46.0)	14 (29.0)	31 (23.0)
Weight loss	313 (33.0)	32 (20.0)	68 (53.0)	16 (29.0)	26 (33.0)	27 (34.0)	41 (32.0)	52 (34.0)	162 (33.0)	19 (39.0)	32 (24.0)
Loss of appetite	291 (30.0)	24 (15.0)	62 (48.0)	16 (29.0)	18 (23.0)	27 (34.0)	43 (34.0)	60 (40.0)	164 (33.0)	19 (39.0)	22 (16.0)
Anxiety	258 (27.0)	42 (26.0)	68 (53.0)	11 (20.0)	13 (17.0)	22 (28.0)	28 (22.0)	24 (16.0)	98 (20.0)	13 (27.0)	37 (28.0)
Chest pain	242 (25.0)	22 (14.0)	46 (36.0)	1 (2.0)	18 (23.0)	15 (19.0)	44 (35.0)	52 (34.0)	130 (27.0)	13 (27.0)	31 (23.0)
Dyspnea/breathing complications	238 (25.0)	48 (30.0)	34 (27.0)	18 (33.0)	7 (9.0)	16 (20.0)	26 (21.0)	78 (52.0)	145 (30.0)	10 (20.0)	1 (1.0)
Low mood	228 (24.0)	12 (8.0)	67 (52.0)	5 (9.0)	16 (20.0)	16 (20.0)	34 (27.0)	38 (25.0)	109 (22.0)	13 (27.0)	27 (20.0)
Persistent cough	223 (23.0)	30 (19.0)	43 (34.0)	7 (13.0)	21 (27.0)	14 (18.0)	37 (29.0)	45 (30.0)	124 (25.0)	17 (35.0)	9 (7.0)
Bone pain	195 (20.0)	20 (13.0)	56 (44.0)	5 (9.0)	15 (19.0)	12 (15.0)	26 (21.0)	33 (22.0)	91 (19.0)	17 (35.0)	11 (8.0)
Weak limbs	182 (19.0)	22 (14.0)	44 (34.0)	2 (4.0)	18 (23.0)	7 (9.0)	23 (18.0)	23 (15.0)	73 (15.0)	12 (25.0)	31 (23.0)
Hoarseness	166 (17.0)	7 (4.0)	44 (34.0)	4 (7.0)	11 (14.0)	6 (8.0)	20 (16.0)	49 (33.0)	90 (18.0)	9 (18.0)	16 (12.0)
Headache/dizziness	143 (15.0)	14 (9.0)	50 (39.0)	4 (7.0)	7 (9.0)	13 (17.0)	17 (13.0)	17 (11.0)	58 (12.0)	13 (27.0)	8 (6.0)
Coughing blood	112 (12.0)	7 (4.0)	26 (20.0)	4 (7.0)	10 (13.0)	16 (20.0)	9 (7.0)	28 (19.0)	67 (14.0)	6 (12.0)	6 (5.0)
Stomach problem	101 (11.0)	5 (3.0)	19 (15.0)	2 (4.0)	3 (4.0)	8 (10.0)	12 (9.0)	31 (21.0)	56 (11.0)	6 (12.0)	15 (11.0)
Difficulty in swallowing	64 (7.0)	0	30 (23.0)	0	5 (6.0)	2 (3.0)	8 (6.0)	10 (7.0)	25 (5.0)	5 (10.0)	4 (3.0)
Swelling of extremities	56 (6.0)	0	26 (20.0)	3 (6.0)	1 (1.0)	2 (3.0)	2 (2.0)	5 (3.0)	13 (3.0)	1 (2.0)	16 (12.0)

Table 5 continued

	Overall ( <i>n</i> = 2857)	US ( <i>n</i> = 422)	BR ( <i>n</i> = 313)	UK ( <i>n</i> = 279)	IT ( <i>n</i> = 287)	FR ( <i>n</i> = 285)	ES ( <i>n</i> = 302)	DE ( <i>n</i> = 284)	EU5 <sup>a</sup> ( <i>n</i> = 1437)	TW ( <i>n</i> = 390)	JP ( <i>n</i> = 295)
Lump in neck/lymph node	47 (5.0)	0	17 (13.0)	2 (4.0)	3 (4.0)	3 (4.0)	4 (3.0)	3 (2.0)	15 (3.0)	6 (12.0)	9 (7.0)
None of the above	65 (7.0)	11 (7.0)	2 (2.0)	5 (9.0)	7 (9.0)	5 (6.0)	6 (5.0)	3 (2.0)	26 (5.0)	3 (6.0)	23 (17.0)

All data are presented as *n* (%), unless specified. *n* = 2857, unless specified

BR Brazil, COPD chronic obstructive pulmonary disease, DE Germany, ER emergency room, ES Spain, EU5 5 countries from the European Union, FR France, ICU intensive care unit, IT Italy, JP Japan, SD standard deviation, TW Taiwan, UK United Kingdom, US United States

<sup>a</sup>Includes the UK, IT, FR, ES, and DE

<sup>b</sup>Reported in > 3.0% of the patients

<sup>c</sup>Reported in > 10.0% of the patients

As these rates are based on the physician's own clinical judgment in routine practice, and not based on protocol-driven Response Evaluation Criteria in Solid Tumors (RECIST) criteria, direct comparison with previous studies [42–44] is difficult. In addition, the median TTNT of 14.0 months was within the range (10.6–14.2 months) reported in previous observational studies of patients with *EGFRm+* aNSCLC [17, 42]. The most common reason for stopping 1L treatment in this data set was disease progression (77.0%). As most patients received first/second-generation *EGFR*-TKI monotherapy in this study, the time to progression may change with the use of newer treatment options [45].

The burden of lung cancer symptoms remains high, and HRQoL continues to be impaired for patients with *EGFRm+* aNSCLC, highlighting the need for more effective and targeted treatment strategies and symptom control in this setting [46–48]. Consistent with previous studies, coughing, fatigue, breathing complications, and appetite or weight loss were the most common symptoms observed in this data set [49, 50]. However, in our study there seemed to be some discordance between patients and physicians in the assessment of symptoms, especially low mood, anxiety, and weight loss [51]. Future research should investigate associated factors for the discordance as the disagreement could lead to suboptimal management and outcomes for *EGFRm+* aNSCLC. A more comprehensive clinical picture of symptom burden captured from both patient perspective (subjective) and physician perspective (objective) could help optimize patient management and outcomes.

The overall mean EQ-5D derived health utility score in this study was 0.7, which is similar to that previously reported for *EGFR*-TKI trial populations [52, 53]. This suggests that patients with *EGFRm+* aNSCLC are generally in good health, as the score is only marginally lower than the average utility score (0.81) of the general UK population of similar age [54]. In addition, the score is similar to that reported in a small observational *EGFRm+* aNSCLC cohort (*n* = 183) with disease progression in Canada (0.70) but lower than the score of 0.81 observed



**Table 6** EQ-5D-5L, EQ-VAS, and FACT scores: overall population

PRO	PRO score (min–max)			
	Overall	1L	2L	3L
EQ-5D-5L	<i>n</i> = 934 0.7 (0.2)	<i>n</i> = 764 0.7 (0.3)	<i>n</i> = 138 0.7 (0.3)	<i>n</i> = 32 0.8 (0.3)
EQ-VAS	<i>n</i> = 947 69.7 (17.6)	<i>n</i> = 776 70.7 (17.4)	<i>n</i> = 138 63.7 (17.7)	<i>n</i> = 33 71.8 (16.9)
FACT-L <sup>a</sup>	<i>n</i> = 930 83.5 (21.0)	<i>n</i> = 764 83.9 (21.4)	<i>n</i> = 135 79.6 (18.9)	<i>n</i> = 31 90.5 (16.4)
FACT-G <sup>b</sup>	<i>n</i> = 931 66.1 (17.4)	<i>n</i> = 765 66.4 (17.8)	<i>n</i> = 135 63.2 (15.6)	<i>n</i> = 31 71.5 (13.5)
Trial index outcomes <sup>c</sup>	<i>n</i> = 935 51.1 (14.9)	<i>n</i> = 768 51.6 (15.0)	<i>n</i> = 136 47.5 (14.0)	<i>n</i> = 31 56.1 (14.2)

All values are presented as mean (SD)

1L first line, 2L second line, 3L third line, EQ-5D-5L European Quality of Life 5 Dimension 5 Level, EQ-VAS EuroQoL visual analog scale, FACT-L Functional Assessment of Cancer Therapy–Lung, FACT-G Functional Assessment of Cancer Therapy–General

<sup>a</sup>Includes all 5 individual parameters

<sup>b</sup>Includes social/family well-being subscale, emotional well-being subscale, functional well-being subscale, and physical well-being subscale

<sup>c</sup>Includes functional well-being subscale, physical well-being subscale, and lung cancer subscale

in the subgroup of patients with stable disease in that study [55]. FACT-L scores in our study were also within the range reported in a previous data set of patients with aNSCLC in France and Germany [22], although the absolute values were higher in this study (71.4 vs 83.5, respectively), possibly because our study focused only on patients with EGFRm+ aNSCLC and did not include as many patients receiving later lines of therapy as the previous study had. With limited real-world health utility information available for EGFRm+ aNSCLC, utility and functional scores in this study could be considered in future economic evaluations of EGFR targeted treatments.

In line with previous studies of patients with aNSCLC, resource use was high in this study, including diagnostic testing, treatments, multiple office visits, hospitalizations, and supportive care [56–58]. However, there was regional variation in resource use measures,

with more frequent hospitalizations in Japan (48.0%), Germany (43.0%), and Taiwan (42.0%), relative to the other countries (29.0% overall). In addition, the mean length of each hospital stay varied across countries (ranging from 3.0 nights in the US to 10.8 in Japan). While the rate of hospital admission via the emergency room also varied, the lowest rates were observed in Germany (5.0%) and Japan (9.0%) versus the US (72.0%) and overall population (35.0%), further suggesting that clinical preference and practices varied across the countries as reported previously [59, 60]. The costs associated with healthcare resource use in this study were not evaluated; however, hospitalizations are known to be a key driver of healthcare costs in many countries [48, 58]. In terms of productivity, on average, patients in this data set lost about 11 h of work per week for about 29 weeks in the 1 year prior to data capture, and about one in three incurred direct out-of-pocket expenses for aNSCLC.

**Table 7** Healthcare resource utilization: by country

	Overall (n = 2857)	US (n = 422)	BR (n = 313)	UK (n = 279)	IT (n = 287)	FR (n = 285)	ES (n = 302)	DE (n = 284)	EU5 <sup>a</sup> (n = 1437)	TW (n = 390)	JP (n = 295)
HCPs involved in management in last 12 months											
Physicians involved in data capture	2814 (98.0)	413 (98.0)	306 (98.0)	272 (97.0)	279 (97.0)	284 (100.0)	294 (97.0)	282 (99.0)	1411 (98.0)	389 (100.0)	295 (100.0)
Pulmonologist	1025 (36.0)	125 (30.0)	111 (35.0)	109 (39.0)	104 (36.0)	130 (46.0)	160 (53.0)	162 (57.0)	665 (46.0)	79 (20.0)	45 (15.0)
Oncologist	842 (29.0)	138 (33.0)	90 (29.0)	74 (27.0)	141 (49.0)	85 (30.0)	84 (28.0)	112 (39.0)	496 (35.0)	93 (24.0)	25 (8.0)
Primary care physician	772 (27.0)	126 (30.0)	31 (10.0)	85 (30.0)	104 (36.0)	129 (45.0)	95 (31.0)	139 (49.0)	552 (38.0)	37 (9.0)	26 (9.0)
Radio oncologist/radiologist	650 (23.0)	94 (22.0)	69 (22.0)	40 (14.0)	98 (34.0)	77 (27.0)	63 (21.0)	94 (33.0)	372 (26.0)	90 (23.0)	25 (8.0)
Specialist nurse	630 (22.0)	25 (6.0)	72 (23.0)	152 (54.0)	56 (20.0)	90 (32.0)	93 (31.0)	64 (23.0)	455 (32.0)	43 (11.0)	35 (12.0)
Specialist cancer surgeon	357 (12.0)	32 (8.0)	64 (20.0)	21 (8.0)	60 (21.0)	31 (11.0)	44 (15.0)	59 (21.0)	215 (15.0)	36 (9.0)	10 (3.0)
Internist	279 (10.0)	12 (3.0)	36 (12.0)	20 (7.0)	32 (11.0)	24 (8.0)	38 (13.0)	59 (21.0)	173 (12.0)	48 (12.0)	10 (3.0)
Other	43 (2.0)	4 (1.0)	6 (2.0)	1 (0)	6 (2.0)	5 (2.0)	3 (1.0)	3 (1.0)	18 (1.0)	10 (3.0)	5 (2.0)
Don't know	47 (2.0)	8 (2.0)	10 (3.0)	6 (2.0)	6 (2.0)	0	5 (2.0)	10 (4.0)	27 (2.0)	1 (0)	1 (0)
Hospitalization in the last 12 months											
Yes	827 (29.0)	74 (18.0)	110 (35.0)	36 (13.0)	62 (22.0)	79 (28.0)	39 (13.0)	122 (43.0)	338 (24.0)	165 (42.0)	140 (48.0)
No/unknown	2030 (71.0)	348 (83.0)	203 (65.0)	243 (87.0)	225 (78.0)	206 (72.0)	263 (87.0)	162 (57.0)	1099 (77.0)	225 (58.0)	155 (53.0)
Admitted through ER											
1st visit	n = 827	n = 74	n = 110	n = 36	n = 62	n = 79	n = 39	n = 122	n = 338	n = 165	n = 140
2nd visit	287 (35.0)	53 (72.0)	77 (70.0)	25 (69.0)	25 (40.0)	22 (28.0)	21 (54.0)	7 (5.0)	100 (30.0)	44 (27.0)	13 (9.0)
3rd visit	88 (11.0)	15 (20.0)	31 (28.0)	5 (14.0)	3 (5.0)	10 (13.0)	3 (8.0)	5 (4.0)	26 (8.0)	13 (8.0)	3 (2.0)
4th visit	22 (3.0)	2 (3.0)	13 (12.0)	1 (3.0)	1 (2.0)	1 (1.0)	0	0	4 (1.0)	4 (2.0)	0
5th visit	10 (1.0)	0	7 (6.0)	1 (3.0)	0	1 (1.0)	0	0	2 (0.6)	0	1 (1.0)
Admitted through ICU	2 (< 1.0)	0	1 (6.0)	0	0	0	0	0	0	1 (1.0)	0
Admitted through ICU											
1st visit	n = 827	n = 74	n = 110	n = 36	n = 62	n = 79	n = 39	n = 122	n = 338	n = 165	n = 140
2nd visit	61 (7.0)	5 (7.0)	27 (25.0)	2 (6.0)	2 (3.0)	3 (4.0)	1 (3.0)	10 (8.0)	18 (5.0)	8 (5.0)	3 (2.0)
3rd visit	14 (2.0)	3 (4.0)	7 (6.0)	1 (3.0)	0	1 (1.0)	3 (8.0)	1 (1.0)	6 (2.0)	0	1 (1.0)
4th visit	12 (2.0)	1 (1.0)	8 (7.0)	1 (3.0)	1 (2.0)	0	0	0	2 (1.0)	1 (1.0)	1 (1.0)
5th visit	2 (< 1.0)	0	2 (2.0)	0	0	0	0	0	0	0	0
Mean nights in hospital, mean (SD)	1 (< 1.0)	0	0	0	0	0	0	0	0	0	1 (1.0)
1st visit	n = 679	n = 47	n = 92	n = 27	n = 42	n = 57	n = 31	n = 98	n = 255	n = 157	n = 128

Table 7 continued

	Overall (n = 2857)	US (n = 422)	BR (n = 313)	UK (n = 279)	IT (n = 287)	FR (n = 285)	ES (n = 302)	DE (n = 284)	EU5 <sup>a</sup> (n = 1437)	TW <sup>b</sup> (n = 390)	JP (n = 295)
2nd visit	7.0 (7.3)	3.0 (1.6)	5.6 (4.0)	5.6 (5.1)	5.4 (4.1)	6.2 (6.0)	5.5 (2.8)	6.2 (4.7)	5.9 (4.76)	7.8 (6.6)	10.8 (12.3)
	n = 176	n = 13	n = 38	n = 6	n = 3	n = 18	n = 4	n = 9	n = 40	n = 39	n = 46
3rd visit	7.5 (7.6)	4.4 (2.1)	6.2 (3.6)	8 (11.7)	8.0 (5.6)	5.2 (1.7)	3.5 (2.1)	5.1 (3.8)	5.7 (5.05)	6.9 (5.5)	11.6 (12.0)
	n = 69	n = 3	n = 20	n = 1	n = 1	n = 2	n = 0	n = 2	n = 6	n = 22	n = 18
4th visit	8.1 (7.1)	8.0 (7.8)	9.0 (5.2)	6 (0)	10.0	5.5 (0.7)	0	2.0	5.2 (2.99)	6.3 (7.4)	10.5 (9.1)
	n = 34	n = 1	n = 9	n = 0	n = 0	n = 1	n = 0	n = 0	n = 1	n = 15	n = 8
5th visit	6.9 (7.2)	4.0	8.3 (5.0)	0	0	4.0	0	0	4.0	4.3 (6.4)	10.9 (9.8)
	n = 22	n = 0	n = 3	n = 0	n = 0	n = 0	n = 0	n = 0	n = 0	n = 13	n = 6
Out-of-pocket expense for NSCLC	9.2 (14.2)	0	11.0 (5.0)	0	0	0	0	0	0	7.0 (15.4)	13.2 (15.4)
	n = 916	n = 156	n = 128	n = 51	n = 77	n = 73	n = 121	n = 138	n = 460	n = 49	n = 123
Median (IQR) out-of-pocket expense per month	288 (31.0)	82 (53.0)	46 (36.0)	1 (2.0)	7 (9.0)	3 (4.0)	7 (6.0)	40 (29.0)	58 (13.0%)	12 (24.0)	90 (73.0)
	–	\$50 (40–100)	R\$500 (200–762.5)	–	–	–	–	–	EUR 25 (10–60)	NT\$50,000 (30,000–60,000)	¥20,000 (10,000–44,550)

All data are presented as n (%), unless specified. n = 2857, unless specified

BR Brazil, DE Germany, ER emergency room, ES Spain, EU5 5 countries from the European Union, FR France, ICU intensive-care unit, IT Italy, JP Japan, SD standard deviation, TW Taiwan, UK United Kingdom, US United States

<sup>a</sup>Includes the UK, IT, FR, ES, and DE

<sup>b</sup>Reported in > 10.0% of the patients

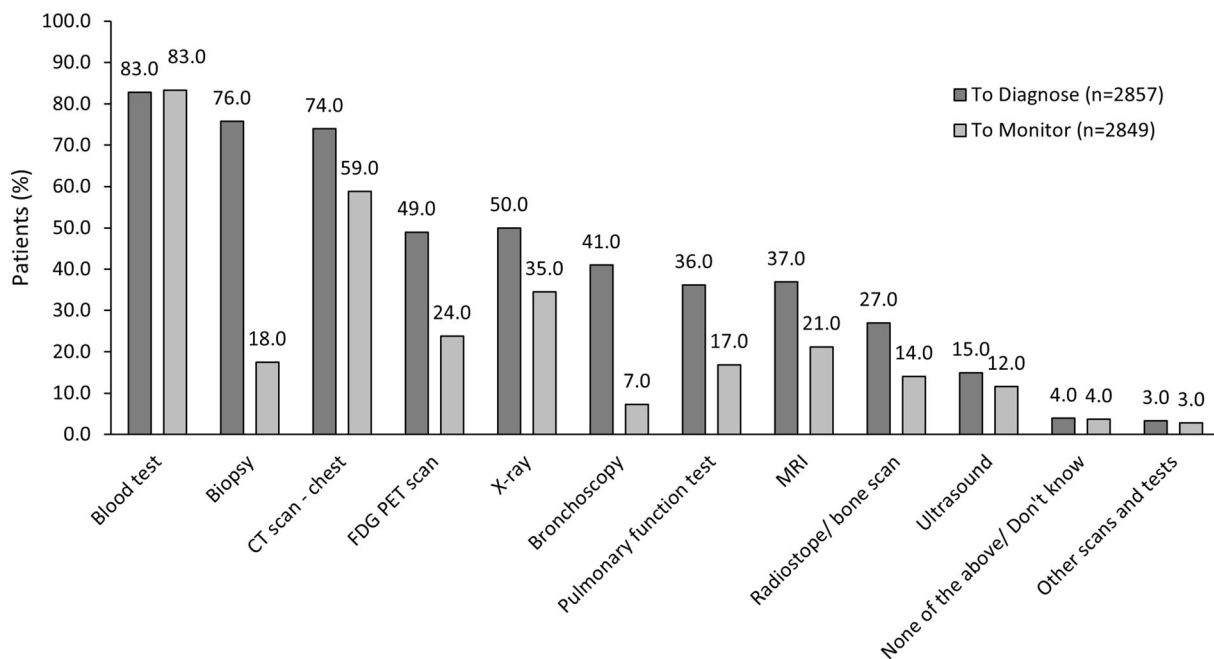
**Table 8** Supportive treatment patterns in advanced non-small cell lung cancer

Treatment	Overall	US	BR	UK	IT	FR	ES	DE	EU5 <sup>a</sup>	TW	JP
Supportive therapy	n = 2857	n = 422	n = 313	n = 279	n = 287	n = 285	n = 302	n = 284	n = 1437	n = 390	n = 295
Bisphosphonates	476 (17.0)	55 (13.0)	100 (32.0)	40 (14.0)	39 (14.0)	42 (15.0)	51 (17.0)	52 (18.0)	224 (16.0)	69 (18.0)	28 (10.0)
Antiemetics	538 (19.0)	108 (26.0)	88 (28.0)	28 (10.0)	44 (15.0)	43 (15.0)	22 (7.0)	106 (37.0)	243 (17.0)	66 (17.0)	33 (11.0)
Antidiarrheals	467 (16.0)	87 (21.0)	52 (17.0)	50 (18.0)	62 (22.0)	27 (10.0)	16 (5.0)	61 (22.0)	216 (15.0)	96 (25.0)	16 (5.0)
Corticosteroids	457 (16.0)	18 (4.0)	78 (25.0)	23 (8.0)	65 (23.0)	47 (17.0)	44 (15.0)	66 (23.0)	245 (17.0)	95 (25.0)	21 (7.0)
Oxygen	233 (8.0)	35 (8.0)	48 (15.0)	2 (1.0)	24 (8.0)	21 (7.0)	10 (3.0)	37 (13.0)	94 (7.0)	54 (14.0)	2 (1.0)
Opioids	367 (13.0)	47 (11.0)	76 (24.0)	14 (5.0)	54 (19.0)	28 (10.0)	36 (12.0)	39 (14.0)	171 (12.0)	60 (15.0)	13 (4.0)
Non-opioid analgesics	513 (18.0)	46 (11.0)	54 (17.0)	33 (12.0)	46 (16.0)	51 (18.0)	70 (23.0)	122 (43.0)	322 (22.0)	72 (19.0)	19 (6.0)
Erythropoietin	35 (1.0)	13 (3.0)	8 (3.0)	0	4 (1.0)	0	7 (2.0)	3 (1.0)	14 (1.0)	0	0
G-CSF	43 (2.0)	7 (2.0)	6 (2.0)	1 (<1.0)	6 (2.0)	5 (2.0)	2 (1.0)	1 (<1.0)	15 (1.0)	9 (2.0)	6 (2.0)
Antihypertensives	199 (7.0)	16 (4.0)	42 (13.0)	5 (2.0)	35 (12.0)	8 (3.0)	5 (2.0)	44 (16.0)	97 (7.0)	31 (8.0)	13 (4.0)
Antimicrobials	75 (3.0)	16 (4.0)	14 (5.0)	3 (1.0)	6 (2.0)	2 (1.0)	1 (<1.0)	8 (3.0)	20 (1.0)	20 (5.0)	5 (2.0)
Blood transfusion	65 (2.0)	9 (2.0)	15 (5.0)	5 (2.0)	2 (1.0)	5 (2.0)	0	2 (1.0)	14 (1.0)	26 (7.0)	1 (<1.0)
Other	43 (2.0)	7 (2.0)	4 (1.0)	10 (4.0)	1 (<1.0)	2 (1.0)	2 (1.0)	0	15 (1.0)	10 (3.0)	7 (2.0)
No therapy received	1201 (42.0)	165 (39.0)	97 (31.0)	147 (53.0)	110 (38.0)	148 (52.0)	151 (50.0)	60 (21.0)	616 (43.0)	133 (34.0)	190 (64.0)

All data are presented as n (%)

BR Brazil, DE Germany, ES Spain, EU5 5 countries from the European Union, FR France, G-CSF granulocyte-colony stimulating factor, IT Italy, JP Japan, TW Taiwan, UK United Kingdom, US United States

<sup>a</sup>Includes the UK, IT, FR, ES, and DE



**Fig. 5** Types of tests performed for diagnosis and monitoring: overall population. All data are presented as %. CT computed tomography, FDG-PET fluorodeoxyglucose-positron emission tomography, MRI magnetic resonance imaging

For most patients, *EGFR* mutation status was known before initiation of 1L treatment, and turnaround time for testing was within international guidelines recommendations [32, 33, 46]. However, only a small proportion of patients ( $n = 172$ , 6.0%) showed disease progression on 1L therapy, of whom 52.0% ( $n = 90$ ) were retested for molecular markers, despite prevalent use of first/second-generation *EGFR*-TKIs and osimertinib in 1L and 2L settings, respectively. While this study did not investigate why fewer patients than expected (65.0%)—instead of all patients as recommended by guidelines [33, 46]—underwent testing at the time of disease progression, potential reasons include previously reported difficulties in conducting re-biopsy as a result of patient intolerance or tumor location, failed re-biopsies, and financial limitations [33, 61, 62]. According to the physicians who participated in this study, inadequate tissue was the main barrier to *EGFR* testing irrespective of timing. These challenges may suggest the need for increased adoption of blood biopsy specimens that are easier to collect and NGS-based approaches with the advantages of sparing tissue samples,

detecting *EGFR*-TKI resistance mutations in plasma ctDNA samples with high sensitivity, avoiding multiple sequential single gene tests for prognostic markers such as co-occurring *TP53* mutations, and minimizing delays for patients. Overall, liquid biopsy specimens and NGS were used to detect *EGFR* mutations for about 6.0% and 27.0% of patients in this study, respectively, although testing rates varied across countries likely owing to differences in access to healthcare systems and economic barriers between countries. Of note, the proportion of T790M positive patients in this study (56 of 79 patients tested, 71.0%) is comparable with that reported earlier [63, 64], although this result should be interpreted cautiously given the small sample size for patients who showed disease progression in this cohort.

Strengths of this descriptive study include the large real-world data set obtained from nine geographically diverse countries with different health systems. The data set reflects relatively recent clinical practices for the diagnosis and management of *EGFRm+* aNSCLC. Several limitations also apply to this study. While minimal inclusion criteria were applied to increase the

generalizability of the data, the study cohort does not represent a true random sample of the broader *EGFRm+* aNSCLC population as physician and patient participation was influenced by their willingness to complete the survey. Therefore, selection and survival bias were possible, and our findings may be considered generalizable to consulting patients with *EGFRm+* aNSCLC in the countries studied. Similar studies should be conducted to evaluate treatment patterns and patient burden in countries not included in this study. Study data were collected during the COVID-19 pandemic (July–December 2020) and thus may not reflect current practice, as previous reports suggest that cancer care was negatively impacted (e.g., delayed testing and treatment) in different countries by pandemic restrictions [65, 66]. However, our findings may serve as a useful point of reference for future studies in the post-COVID-19 pandemic era. The patient survey was cross-sectional and therefore cannot be used to demonstrate cause and effect. Tumor response and progression outcomes were based on physician assessment in routine clinical practice and not according to RECIST criteria, which limits direct comparison with clinical trial end points. All comparisons between countries were descriptive. As no formal statistical testing was applied, use of comparative terms such as “lower” or “more” does not imply statistical significance.

## CONCLUSION

This large real-world multinational data set showed that most patients with *EGFRm+* aNSCLC were treated per the country relevant clinical guidelines for *EGFR* targeted therapy. However, progression continues to be the main reason for early treatment discontinuation, which along with high patient symptom and associated economic burdens, highlights the need for increased adoption of newer, more effective, and safer treatments that delay disease progression. For the included countries, these findings may offer a useful benchmark for decision makers to determine future allocation of healthcare resources for patients with

*EGFRm+* aNSCLC. Future research should further evaluate the country-specific variability in clinical practices to identify unmet needs for patients with *EGFRm+* aNSCLC.

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**Data Availability.** All data that support the findings of this study are the intellectual property of Adelphi Real World. All requests for access should be addressed directly to Hollie Bailey at [hollie.bailey@adelphigroup.com](mailto:hollie.bailey@adelphigroup.com).

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