

# Real-world Treatment Patterns in Patients with EGFR Mutation-positive NSCLC Receiving a First-Line, First- or Second-generation EGFR Tyrosine Kinase Inhibitor in South Korea and Taiwan

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## Abstract

**Introduction:** The preferred first-line (1L) treatment for epidermal growth factor receptor (EGFR) mutation-positive (EGFRm) advanced/metastatic non-small lung cancer (NSCLC) are EGFR-tyrosine kinase inhibitors (TKIs). However, most patients treated with 1L first- or second-generation (1G/2G) EGFR-TKIs acquire resistance; the EGFR T790M mutation is observed in ~30–50% of patients. We report real-world NSCLC treatment and T790M testing patterns in South Korea and Taiwan. **Methods:** Retrospective medical record review of EGFRm advanced/metastatic NSCLC patients from routine practice. 1G/2G EGFR-TKI initiation 1 January 2015–31 December 2017 (follow-up end date: last available medical record or August 2019). Study measures: demographic/disease characteristics, 1L/2L treatment, T790M testing. **Results:** In South Korea, 70% (164/235) and in Taiwan 89% (89/100) experienced 1L disease progression (median [range] follow-up: 22 [2.3–50.7] months). Of those with disease progression, 68% (111/164) and 62% (55/89) had T790M testing in South Korea and Taiwan, respectively. In South Korea, 43% (48/111) were T790M-positive with 88% (n=42/48) receiving osimertinib (mostly 2L). In Taiwan, 18% (10/55) were T790M-positive; 100% received osimertinib. Overall, 73% (120/164) and 63% (63/100) in South Korea and Taiwan, respectively, received 2L therapy, predominantly pemetrexed-containing regimens. Among patients with disease progression, 9% (14/164) and 24% (21/89) died before receiving 2L therapy in South Korea and Taiwan, respectively. **Conclusion:** In both countries, <70% with 1L disease progression were tested for T790M at any point from NSCLC diagnosis, suggesting resistance mutation testing could be improved. Treatment/testing patterns may have changed in both countries since study initiation due to osimertinib reimbursement changes beginning December 2017.

**Keywords:** EGFR mutation- EGFR-TKI- NSCLC- osimertinib- T790M

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## Introduction

Epidermal growth factor receptor (EGFR) mutations (EGFRm) are observed in a greater proportion of patients with non-small cell lung cancer (NSCLC) from Asian populations (32–60%) compared with non-Asian populations (10–30%) [1–3]. In addition, the prevalence of EGFRm in patients with NSCLC from South Korea and Taiwan has been reported to range from 27–51% [4–6] and 34–53% [7–9], respectively.

At the time of this study (2015–2017), guidelines recommended first-line (1L) treatment of EGFRm advanced NSCLC with first- or second-generation (1G/2G) EGFR-tyrosine kinase inhibitors (TKIs) erlotinib, gefitinib or afatinib [10–11]. Despite initial efficacy, most patients with EGFRm advanced or metastatic NSCLC treated with a 1L 1G/2G EGFR-TKI develop resistance, with disease progression occurring after a median of 8 to 16 months [12–14]. The EGFR T790M acquired resistance mutation has been observed in approximately 50% of patients from a meta-analysis of clinical trials [15] while rates of approximately 30% have been reported in real-world studies [16–18].

Osimertinib is a third-generation, irreversible EGFR-TKI that potently and selectively inhibits both EGFR-TKI sensitizing and EGFR T790M resistance mutations, and has demonstrated efficacy in NSCLC central nervous system (CNS) metastases [19–22]. Following the Phase III AURA3 study, in November 2015 osimertinib received accelerated approval from the US Food and Drug Administration (FDA) and the European Medicines Agency for use as a second-line (2L) treatment in patients with EGFRm T790M-positive locally advanced or metastatic NSCLC who had previously received 1G/2G EGFR TKIs. Approval was received in Taiwan and South Korea in March and May 2017, respectively [23–24]. Following approval, the Ministry of Health and Welfare in South Korea granted reimbursement for osimertinib in the 2L setting in December 2017 [23]. In Taiwan, reimbursement for osimertinib in the 2L setting was granted in April 2020 [25]. Testing of tumors for T790M in patients with resistance to 1G/2G EGFR-TKIs in the 1L setting is now mandatory, with osimertinib considered the standard of care for patients with T790M-positive tumors [26].

Based on the results of the Phase III FLAURA study, in 2018 osimertinib received approval as a 1L treatment for patients with metastatic NSCLC whose tumors harbored EGFR-TKI sensitizing mutations (exon 19 deletion [Ex19del] or L858R) [27–28]. In line with this, the current Pan Asian guidelines from 2019 now recommend 1L treatment with EGFR-TKIs, including osimertinib, for patients with metastatic NSCLC with tumors harboring an EGFR-TKI sensitizing mutation [26].

While the use of 1L 1G/2G EGFR-TKIs in patients with EGFRm locally advanced or metastatic NSCLC was well defined at the time of this study, published real-world data for treatment of these patients following NSCLC disease progression are limited in South Korea and Taiwan. This study was designed to review the real-world

treatment patterns and T790M testing practices of patients in these settings.

## Materials and Methods

### *Study Design and Data Source*

This was a retrospective, non-interventional medical record review in selected patients with EGFRm NSCLC from routine clinical practice settings in France, Germany, South Korea, Taiwan, UK and US; here, we describe results from South Korea and Taiwan and data from France, Germany, UK and US are described elsewhere.

Following appropriate ethics submissions and approvals, data were obtained through the use of an electronic data collection form (eDCF), which was completed by physicians or delegated clinical research staff, from medical record reviews of eligible patients. The forms were accessed via a secure web-based link specific to each site and records for each patient in the analytic dataset were then linked by an encrypted identifier. The study was performed in accordance with ethical principles that are consistent with the Declaration of Helsinki, International Conference on Harmonization Good Clinical Practices and local standards in South Korea and Taiwan. Patient consent was not required because of the retrospective nature of the study.

### *Study population*

#### *Physicians*

Physicians participating in the study were required to have treated  $\geq 4$  patients with EGFRm NSCLC in the year preceding the study,  $\geq 2$  years' experience in medical practice managing oncology treatment including responsibility for making treatment decision for patients with NSCLC, and to have spent  $\geq 60\%$  of their time in patient care (as judged by the participating physician).

#### *Patients*

Records for adults  $\geq 20$  years of age at first diagnosis of confirmed EGFRm locally advanced unresectable or metastatic NSCLC, who had received 1L 1G/2G EGFR-TKI treatment were included; at the time of medical record abstraction, patients could have been alive or deceased. 1L EGFR-TKI treatment (afatinib, gefitinib, erlotinib) must have been initiated between January 1 2015 and December 31 2017. Patient data were not included if they had previously been enrolled in an interventional clinical trial for an EGFRm NSCLC-related treatment or received any systemic therapy for locally advanced or metastatic NSCLC prior to 1L EGFR-TKI treatment. Patient data were also excluded if there were missing or unknown dates for: initial NSCLC diagnosis, first diagnosis of progression to advanced or metastatic NSCLC, 1L EGFR-TKI initiation for advanced or metastatic disease, death, or last available follow-up.

#### *Objectives*

The objectives of the study included describing patients' demographic and baseline disease characteristics;

the proportion of patients that had, or went on to develop CNS metastases (diagnosis: tissue biopsy, imaging, spinal tap, neurologic exam) or leptomeningeal disease (LM; diagnosis: cerebrospinal fluid cytology, tissue, imaging); 1L EGFR-TKI type used; and the proportion of patients that experienced disease progression on 1L 1G/2G EGFR-TKIs. In patients with disease progression on 1L EGFR-TKI treatment the objectives were to describe the proportion of patients that received 2L and type of therapy started; the proportion of patients tested for T790M and were positive; of the patients who were T790M tested and who were not tested, what proportion received 2L and type of therapy initiated.

### Data Collection

The index date was defined as the first date on which a patient newly initiated a 1G/2G EGFR-TKI as 1L treatment for EGFRm locally advanced or metastatic NSCLC, and had to occur within a 3-year period from January 1 2015 through December 31 2017 (study entry window); patient data was abstracted through to last available medical record (data cut-off: 01 August 2019). Any data available from before or after the study index date through to the date of the medical record abstraction was subject to review. The study entry window for 1L EGFR TKI initiation was selected to balance the opportunity for maximal follow-up with the capture of recently prevailing patterns of care.

### Statistical Analyses

The study aimed to include 235 patients from South Korea and 100 patients from Taiwan. Each participating physician was anticipated to contribute 15 to 20 patient records. All analyses were descriptive in nature and no statistical comparisons were made between patient data from the two countries. Study variables were summarized using univariate statistics, including mean, standard deviation, median and range for continuous variables and frequency distributions for categorical variables.

## Results

### Physicians

A total of 27 physicians participated in the South Korean study and 13 physicians in the Taiwan study. Their medical specialty was primarily medical/clinical oncologist (South Korea: 74%; Taiwan: 54%), followed by hematologist (South Korea: 26%; Taiwan: 46%). The median (range) number of years in practice was 20 (10–28) and 10 (5–20) years in South Korea and Taiwan, respectively.

### Baseline Patient Demographics and Disease Characteristics

#### South Korea

From South Korea, 235 patients with EGFRm locally advanced or metastatic NSCLC were identified for inclusion in the study (Table 1). The majority of patients had a histologic diagnosis of adenocarcinoma (231; 98%),

median (range) age at index was 70 (40–93) years, with 142 patients (60%)  $\geq 65$  years of age; 149 patients (63%) were female and, overall, 151 (64%) never smokers. At initial NSCLC diagnosis, most patients had metastatic disease (stage IV) [29] (89%), followed by early stage disease (stage IA, IB, IIA and IIB) [29] (8%), limited regional (stage IIIA) [29] (2%), locally advanced (stage IIIB) [29] (2%), and unknown (<1%). At the time of diagnosis with advanced or metastatic NSCLC, 148 patients (63%) had an Eastern Cooperative Oncology Group Performance Status (ECOG PS) score of 0 or 1. The majority of patients tested positive for Ex19del (n=135 [57%]), 89 (38%) tested positive for L858R mutation and 21 (9%) tested positive for other mutations (both single and co-occurring mutations; Table 1). Patients were followed up from index date until last available medical record for a median duration of 23.7 (0.1–56.7) months.

#### Taiwan

One hundred patients from Taiwan with EGFRm NSCLC receiving 1L 1G/2G EGFR TKI treatment were identified for inclusion (Table 1). All patients had a histologic diagnosis of adenocarcinoma. Median (range) age at index was 65 (36–94) years, with 48 patients (48%)  $\geq 65$  years of age, 66 patients (66%) were female and 86 (86%) never smokers. At initial NSCLC diagnosis, most patients had metastatic disease (stage IV) [29] (89%), followed by limited regional (stage IIIA) (5%) [29] early stage disease (stage IA, IB, IIA and IIB) (3%), [29] and locally advanced (stage IIIB) [29] (3%). At the time of diagnosis with advanced or metastatic NSCLC, 65 patients (65%) had an ECOG PS score of 0 or 1. Overall, 44 patients (44%) tested positive for the L858R mutation, followed by Ex19del in 43 patients (43%); eleven patients (11%) tested positive for PD-L1 expression and 20 patients (20%) were positive for uncommon EGFR mutations, in isolation or in combinations. Patients were followed up for a median duration of 22.1 (2.3–50.7) months.

### Incidence of CNS Metastases and LM Disease

In the South Korean cohort, 69 patients (29%) had CNS metastases at diagnosis of locally advanced or metastatic NSCLC, while 162 patients (69%) had no CNS metastases on scans at this first diagnosis, and in 4 patients (2%) presence or absence of CNS metastases were unknown. From the Taiwan cohort, at diagnosis of locally advanced or metastatic NSCLC, 25 patients (25%) had CNS metastases, 72 patients (72%) had no CNS metastases on scans at this first diagnosis, and in 3 patients (3%) presence or absence of CNS metastases were unknown.

Two patients in each cohort (representing <1% and 2% of the study populations from South Korea and Taiwan, respectively) had LM disease at advanced/metastatic NSCLC diagnosis; at index 3 patients (1%) in the South Korean cohort and 1 patient (1%) in the Taiwan cohort had LM disease. Four patients (2%) in the South Korean cohort and 5 patients (5%) from the Taiwan cohort, who did not have LM disease at advanced/metastatic NSCLC diagnosis, subsequently developed LM disease.

Table 1. Patient Demographics and Disease Characteristics

Characteristic, n (%)	South Korean population	Taiwan population
	N=235	N=100
Age at index date <sup>a</sup> , Median (Min, Max)	70 (40–93)	65 (36–94)
Distribution, years		
31–50	15 (6)	11 (11)
51–65	78 (33)	41 (41)
66–75	73 (31)	25 (25)
75+	69 (29)	23 (23)
Sex, n (%)		
Male	86 (37)	34 (34)
Female	149 (63)	66 (66)
Smoking status at initial NSCLC diagnosis		
Current smoker	19 (8)	5 (5)
Former smoker	58 (25)	9 (9)
Never smoker	151 (64)	86 (86)
Unknown	7 (3)	0 (0)
Stage <sup>b</sup> at initial NSCLC diagnosis		
Early (Stage IA, IB, IIA, IIB)	18 (8)	3 (3)
Limited Regional (Stage IIIA)	4 (2)	5 (3)
Locally Advanced (Stage IIIB)	4 (2)	3 (3)
Metastatic (Stage IV)	208 (89)	89 (89)
Unknown	1 (<1)	0 (0)
EGFR mutation type (tested positive) <sup>c,d</sup>		
Exon 19 deletion	135 (57)	43 (43)
L858R mutation	89 (38)	44 (44)
Uncommon	18 (8)	19 (19)
Exon20/T790M	3 (1)	1 (1)
Other mutations (tested positive) <sup>c</sup>		
PD-L1 expression	14 (6)	11 (11)
ALK rearrangement	15 (6)	0
KRAS	0	0
ROS-1 translocation	0	0
BRAF mutation	0	0
RET rearrangement	0	0
HER2 exon 20 insertion	0	0
TP53 (any variant)	0	0
None of the mutations listed above	176 (75)	3 (3)
Unknown	30 (13)	86 (86)
ECOG PS at first diagnosis of locally advanced/metastatic NSCLC		
0	78 (33)	19 (19)
1	70 (30)	46 (46)
2	10 (4)	8 (8)
3	5 (2)	3 (3)
4	0	0 (0)
ECOG not recorded at initial NSCLC diagnosis	72 (31)	24 (24)

ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; <sup>a</sup>Index date defined as first date on which a patient newly initiated a 1G/2G EGFR TKI as 1L treatment for EGFR-mutated locally advanced or metastatic NSCLC; <sup>b</sup>AJCC TMN Classification of Lung Cancer (7<sup>th</sup> edition); <sup>c</sup>Categories not mutually exclusive; column percentages may sum to greater than 100%; <sup>d</sup>Mutations other than del-19 or L858R, for example, L861Q, T790M, G719X, V769M, M631, exon 21, p.L861Q

Table 2. Treatment Patterns among Patients Positive for EGFR Mutations During 1L, 2L and 3L Therapy

	South Korean population N=235	Taiwan population N=100
Regimen distribution in 1L, n (%)		
Median (range) duration of 1L treatment, months	10.3 (0.1–37.2)	9.9 (1.9–42.4)
EGFR-TKI treatment		
Erlotinib	30 (13)	37 (37)
Gefitinib	100 (43)	36 (36)
Afatinib	105 (45)	27 (27)
Second-line treatment regimen, n (%)	(n=120)	(n=63)
Median (range) duration of 2L treatment, months	3.2 (0.1–26.9)	3.3 (0.03–19.8)
Chemotherapy only		
Cisplatin + pemetrexed	17 (14)	28 (44)
Carboplatin + pemetrexed	0	5 (8)
Cisplatin + gemcitabine	2 (2)	3 (5)
Pemetrexed	49 (41)	3 (3)
Carboplatin + gemcitabine	4 (3)	1 (2)
Bevacizumab + carboplatin + gemcitabine	0	1 (2)
Gemcitabine + vincristine	1 (1)	0
Gemcitabine	1 (1)	0
Cisplatin + docetaxel + pemetrexed	0	1 (2)
Docetaxel	1 (1)	0
EGFR-TKI treatment		
Osimertinib	38 (32)	16 (25)
Afatinib	2 (2)	0
Erlotinib	1 (1)	1 (2)
EGFR-TKI + chemotherapy		
Carboplatin + osimertinib + paclitaxel	0	1 (2)
Carboplatin + osimertinib + pemetrexed	0	1 (2)
Osimertinib + pemetrexed	0	1 (2)
Immunotherapy		
Cisplatin + pembrolizumab	0	2 (3)
Pembrolizumab	1 (1)	0
Nivolumab	1 (1)	0
ROS1/ALK inhibitors		
Crizotinib	2 (2)	0

1L, first line; 2L, second line; 3L, third line; 4L, fourth line; EGFR epidermal growth factor receptor; TKI, tyrosine kinase inhibitor

### 1L EGFR-TKI Treatment Patterns

At diagnosis of locally advanced or metastatic NSCLC, all patients received a 1L 1G/2G EGFR-TKI as monotherapy (Table 2). In the South Korea cohort, 45% of patients received afatinib, 43% received gefitinib and 13% received erlotinib; the median duration of 1L treatment was 10.3 (0.1–37.2) months. In the Taiwan cohort, a similar proportion of patients received afatinib (27%), erlotinib (37%) or gefitinib (36%) as their 1L EGFR TKI treatment; the median duration of 1L treatment was 9.9 (1.9–42.4) months.

### 2L Therapy after 1L Treatment Progression

In the South Korea cohort, 120/164 patients (73%) who experienced disease progression on 1L treatment received

2L therapy (Table 2). Fourteen patients (9%) of the 164 with a progression event died before they received 2L. Pemetrexed was the most common 2L treatment received (49/120; 41%), followed by osimertinib (38/120; 32%), and cisplatin plus pemetrexed (17/120; 14%; Table 2). The median (range) duration of 2L treatment was 3.2 (0.1, 26.9) months.

Eighty-nine patients experienced disease progression on 1L treatment in the Taiwan cohort, of whom 63 (71%) received a 2L therapy (Table 2). Of the 89 patients who had disease progression 21 (24%) died before receiving 2L therapy. The most frequently received 2L therapy was cisplatin plus pemetrexed in 28/63 patients (44%), followed by osimertinib monotherapy in 16/63 patients (25%). The median (range) duration of 2L therapy was

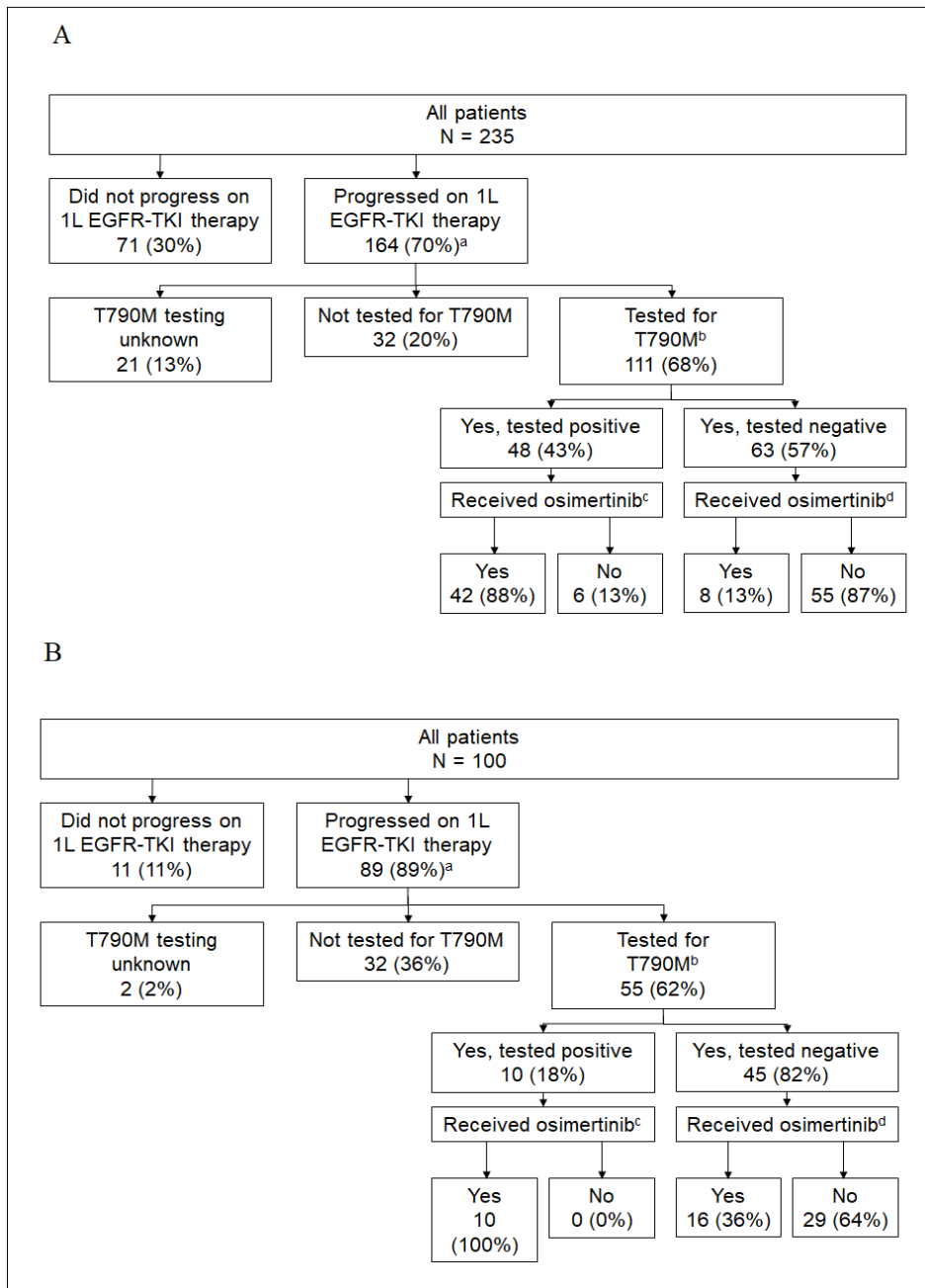


Figure 1. T790M Testing Performed and Outcomes in Patients with NSCLC Treated with a 1L EGFR-TKI A) South Korean cohort; B) Taiwan Cohort. A, <sup>a</sup>14/164 (9%) patients who progressed on 1L EGFR-TKI treatment died, prior to receiving 2L. <sup>b</sup>Calculated as the proportion of patients who progressed on 1L EGFR-TKI treatment. Patients could have been tested at any point from initial NSCLC diagnosis to end of follow-up period. <sup>c</sup>Calculated as the proportion of patients who tested positive for T790M, patients could have received osimertinib at second-line or later. <sup>d</sup>Calculated as the proportion of patients who tested negative for T790M, patients could have received osimertinib at second-line or later. EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor. B, EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor. <sup>a</sup>21/89 (24%) patients who progressed on 1L EGFR-TKI treatment died, prior to receiving 2L. <sup>b</sup>Calculated as the proportion of patients who progressed on 1L EGFR-TKI treatment. Patients could have been tested at any point from initial NSCLC diagnosis to end of follow-up period. <sup>c</sup>Calculated as the proportion of patients who tested positive for T790M, patients could have received osimertinib at second-line or later. <sup>d</sup>Calculated as the proportion of patients who tested negative for T790M, patients could have received osimertinib at second-line or later.

3.3 (0.03–19.8) months.

### *T790M Mutation Testing*

Of the 164 patients who experienced disease progression on 1L treatment in the South Korea cohort, 111 patients (68%) received testing for T790M, with 48/111 patients (43%) whose tumors tested positive (Figure 1A); in addition, 47/71 patients (66%) who did not experience disease progression on 1L treatment were tested for T790M. In the majority of patients, the test type was categorized as ‘other’ (106/158; 67%), with the PNA Clamp™ EGFR mutation detection kit v2.0 most commonly used (49/106; 46%). The test type was not known in 50/158 patients (32%). Of the 48 patients whose tumors tested positive for T790M, 42 (88%) subsequently received osimertinib (Figure 1A). Of the 63 patients (57%) whose tumors tested negative for T790M, 8 (13%) received osimertinib at 2L or later (Figure 1). Median time to next treatment in patients whose tumors were T790M tested was 16.4 months (13.9, 17.5) and 16.5 months (12.2, 22.5) in patients who were not tested.

In the Taiwan cohort, of the 89 patients who experienced disease progression on 1L treatment, 55 patients (62%) underwent T790M testing, with 10 patients (18%) whose tumors tested T790M positive (Figure 1B); in addition, the tumors of 7 of the 11 patients (64%) who did not experience disease progression on 1L treatment were tested for T790M. Most patients had their T790M mutation status confirmed by test type categorized as ‘other’ (46/62; 74%); the most common test type used in this category was the MassARRAY genotyping kit (37/46; 80%). The test type was categorized as unknown for 5 patients (8%). Of the 10 patients who had tumors that tested positive for T790M, all received osimertinib 2L or later (Figure 1B). From the 45/55 patients (82%) with 1L disease progression whose tumors tested negative for T790M, 16/45 (36%) subsequently received regimens including osimertinib 2L or later. Median time to next treatment in patients who were T790M tested was 12.6 months (9.6, 17.1) and 12.7 months (9.9, 42.3) in patients who were not tested.

### *Osimertinib Treatment and Line of Treatment*

Overall, 54/235 patients (23%) in the South Korea cohort and 27/100 patients (27%) in the Taiwan cohort received osimertinib at 2L or later. The majority (38/54 [70%] patients and 16/27 [59%] for South Korea and Taiwan, respectively) received osimertinib monotherapy in the 2L setting.

## **Discussion**

This retrospective, non-interventional medical record review evaluated real-world treatment patterns and T790M testing practices in patients with EGFRm advanced/metastatic NSCLC receiving 1L 1G/2G EGFR-TKIs in populations in South Korea and Taiwan.

The demographics of the patients eligible for inclusion in this analysis were generally similar to those observed in randomized, clinical trials of EGFRm NSCLC in Asian

cohorts, with the exception of the high proportion of never smokers in the Taiwan cohort (86% vs ~60%) [30-31] and the older population in the South Korea cohort compared with Taiwan; the median age of patients from South Korea was 70 years (>60% aged ≥65 years) whereas in clinical trials, the median age of patients was up to 7 years younger [30, 32-33].

In the Taiwan cohort, 1L afatinib, erlotinib and gefitinib were prescribed at similar frequencies. By contrast, in the South Korean cohort nearly half (45%) of the patients received the second-generation EGFR-TKI afatinib as 1L treatment, with a similar proportion (43%) receiving gefitinib, while erlotinib was only prescribed to 13% of patients. This prescribing pattern, with a preference for gefitinib over erlotinib as the 1L treatment, may reflect the different AE profiles of the two treatment and physician/patient choice of treatment. In particular, higher rates of anorexia and skin rash have been reported with erlotinib compared with gefitinib, which may impact treatment choice, particularly in older patients and female patients who may be concerned about the cosmetic impact of skin reactions [32, 34-35]. These prescribing patterns may reflect the older and predominantly female patient population in the South Korean cohort. However, it would be expected that physicians/patients in Taiwan would have similar considerations, so the different prescribing patterns noted between countries may also be due to the small sample size of Taiwanese patients. In another real-world study which enrolled nearly 6000 patients with stage IIIB and IV NSCLC receiving EGFR-TKIs in Taiwan between 2011 to 2015, 67% of patients received gefitinib, while 20% of patients received erlotinib [36], which is more in line with the relative proportions of gefitinib and erlotinib used in South Korean patients in our study. Also, in this larger Taiwanese study, there were more elderly (≥65 years: 55% versus 50%) and female patients (66% vs 56%) in the gefitinib group compared with the erlotinib group [36].

Our study showed that 70% and 89% of patients in the South Korean and Taiwan cohorts, respectively, had disease progression during the study period and a considerable proportion of the patients who experienced disease progression (20% and 36%, respectively) did not receive a test for the T790M resistance mutation. Of patients with disease progression, the majority (67% in South Korea and 70% in Taiwan) did not receive any line of osimertinib. Osimertinib was prescribed off-label in patients who tested negative for T790M in both South Korea (8/63; 13%) and Taiwan (16/45; 36%). Although the reasons for why patients’ tumors were not tested for T790M or did not receive 2L therapy were not recorded in the eDCF, this finding suggested a potential unmet need in disease management and treatment in these populations.

The number of patients in the Taiwan cohort with T790M-positive tumors was low (18% vs 43% in the South Korean cohort), which is more similar to that observed in other real-world studies with Asian and non-Asian cohorts (approximately 30%) [16-18] than in clinical trials (approximately 50%) [15, 37]. It is worth

noting that the incidence of uncommon/complex EGFR mutations (20%) in the Taiwan cohort was slightly higher than rates seen in other studies (12–16%) of Asian patient cohorts [38-39].

In both countries, approximately a quarter of patients had CNS metastases at diagnosis of locally advanced or metastatic NSCLC and a further 15% and 10% of patients, respectively, went on to develop CNS metastases during the study. CNS metastases frequently occur in patients with EGFRm NSCLC and are associated with poor outcomes [40]. In the 1L setting in the FLAURA study, osimertinib has been shown to reduce the risk of CNS progression by 52% versus comparator EGFR-TKIs (HR, 0.48; P=0.014) [21]. Early intervention with osimertinib could reduce the risk of CNS progression in patients with CNS metastases.

Limitations of the study included the retrospective nature of a chart review, meaning data were more likely to be missing, along with the potential for selection bias in patients included in the study. While all patients who met the inclusion criteria were included, patients who died early on in the study period may have been less likely to be included than those who were alive at data abstraction. Furthermore, it was not possible to determine why testing for T790M was not completed in all patients who had experienced disease progression. During the majority of this study, osimertinib was not approved or reimbursed in South Korea or Taiwan, which may have resulted in lower than expected T790M testing and treatment with 2L osimertinib. Since the study was completed, treatment and testing patterns may have changed due to changes in 2L osimertinib reimbursement status and the approval of osimertinib in the 1L setting. Finally, data were abstracted from medical records of 27 physicians in South Korea and 13 physicians in Taiwan, thus limiting the generalizability of treatment patterns across the countries as a whole.

In conclusion, our real-world study of treatment patterns and T790M testing practices in patients with advanced/metastatic EGFRm NSCLC receiving 1L 1G/2G EGFR TKI treatment indicated that a large proportion of patients in South Korea and Taiwan did not receive 2L therapy after disease progression, highlighting the importance of 1L treatment decisions. In addition, improvements in resistance mutation testing were needed, although 2L therapy utilization was as per the recommendations for the majority of T790M-positive patients. These treatment patterns may have changed since study initiation as osimertinib received reimbursement status for 2L treatment in South Korea and Taiwan from December 2017 onwards, so follow-up studies are required.

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## Author Disclosures

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