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Real-life efficacy of osimertinib in pretreated patients with advanced non-small cell lung cancer harboring EGFR T790M mutation

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ABSTRACT

Objectives The efficacy of osimertinib in pretreated patients with advanced non-small cell lung cancer (NSCLC) harboring EGFR T790 M resistance mutation was demonstrated in clinical trials. However, data on efficacy of osimertinib in real world remain rare.

Materials and methods This retrospective multicentric study analyzed T790M-positive advanced NSCLC patients enrolled in French early access program for osimertinib. Patients were pretreated with first- or second-generation EGFR tyrosine-kinase inhibitor and for a majority with chemotherapy. Primary endpoints were progression-free survival (PFS) and overall survival (OS) from osimertinib initiation.

Results 205 patients (mean age, 69.5 years; female, 68.8%; adenocarcinoma, 97.5%, never-smokers, 71.5%) were analyzed. Osimertinib was used in second and third line in 18.0% and 82.0% of patients, respectively. Median PFS was 12.4 (95% CI, 10.1–15.1) months. In patients with and without cerebral metastasis, PFS was 9.7 (7.7–13.5) and 15.1 (12.0–17.1) months (p = 0.21), respectively. PFS in second and third line or more was 12.6 (6.7–17.5) and 12.4 (9.7–15.3) months, respectively. Median PFS in patients with EGFR exon 19 deletion and exon 21 mutation was 13.5 (10.1–16.0) and 9.7 (7.4–13.2) months, respectively (p = 0.049). Median OS since osimertinib initiation was 20.5 (16.9–24.3) months: 23.1 (18.6–27.8) and 18.0 (12.2–22.2) months in patients without and with cerebral metastasis (p = 0.11); 17.5 (11.6–27.8) and 21.7 (17.3–24.3) months as second or third line of treatment or more (p = 0.46), respectively. Median OS in patients with EGFR exon 19 deletion and exon 21 mutation was 23.1 (18.6–25.7) and 15.3 (11.6–21.7) months, respectively (p = 0.03).

Osimertinib dosage was modified in 8.0% of patients and definitively discontinued for adverse events in 5.9%. Fifty patients benefited from rebiopsy (persistence of T790 M mutation, 44.7%; C797S mutation, 21.1%; cMET amplification, 8.0%).

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Conclusion In pretreated patients with T790M-mutated advanced NSCLC, the efficacy of osimertinib appears similar in real-world setting to that of clinical trials.

1. Introduction

Lung cancer is the most common cancer worldwide and is the leading cause of cancer death in Western countries [1]. Non-small cell lung cancer (NSCLC) is the most common form (80–85%) of lung cancers. At the time of diagnosis, most patients with NSCLC present with metastatic or advanced disease [2]. Activating mutations of the gene encoding the tyrosine kinase of the epidermal growth factor receptor (EGFR) are present in about 10% of NSCLC patients in France [3] and more than 90% of these mutations are reported in exons 19 − 21 [2].

Targeted treatments with specific first- or second-generation tyrosine-kinase inhibitors (TKIs) in advanced NSCLC patients with EGFR mutations have shown a significant clinical benefit with a response rate more than 70%, progression-free survival (PFS) ranging from 9 to 13 months and median overall survival (OS) from 20 to 30 months [4–6]. However, despite these very encouraging results, all patients develop resistance to first/second generation EGFR-TKIs.

Resistance to first or second generation EGFR-TKIs is due to various mechanisms, the most frequent being the T790 M mutation in exon 20 (50–60%) that leads to substitution of methionine for threonine at position 790 in the kinase domain [7,8]. Threonine 790 is a “gatekeeper” residue that regulates the inhibitor affinity in the ATP binding pocket. With the T790 M mutation, the affinity of the ATP binding pocket for ATP is enhanced and confers resistance due to competition with TKIs [7,8].

The EGFR T790 M mutation is specifically targeted by osimertinib, a third-generation EGFR-TKI [9]. Osimertinib demonstrated its efficacy in advanced NSCLC patients with acquired resistance related to T790 M after first- or second-generation TKI treatment [4,10,11]. In AURA3 study, median PFS was significantly longer in patients receiving osimertinib vs. chemotherapy (10.1 vs. 4.4 months; $p < 0.001$) [4]. Objective response rate was significantly higher with osimertinib in comparison with chemotherapy (71% vs. 31%; $p < 0.001$). In FLAURA study, osimertinib was used as first-line treatment achieved a significantly longer median PFS than first-line EGFR-TKIs in EGFR-mutated NSCLC patients (18.9 and 10.2 months, respectively; $p < 0.0001$) [12]. Data on the efficacy of osimertinib in real-life setting remain rare. The present study reports clinical results of an early access program of osimertinib for advanced NSCLC patients with T790 M mutation progressing after first- or second-generation TKI and, for a majority of them, after chemotherapy.

2. Patients and methods

2.1. Study design and patients

The EXPLORE T790 M study (GFPC 01–2016) was a retrospective observational multicenter study performed by physicians in centers of the French Group of Lung Cancers (GFPC) and by prescribers out of GFPC centers. The objective was to describe in real-world setting the clinical characteristics and the outcome of patients with advanced NSCLC harboring T790 M EGFR mutation treated with osimertinib.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the French Advisory Committee on Information Processing in Health Research (CCTIRSS). Written informed consent was obtained from each patient. For dead patients, an exemption of family consent was obtained from CCTIRSS.

The primary objective of the study was to evaluate PFS and OS from osimertinib initiation. The secondary objectives were to describe patient characteristics, methods for diagnosis of T790 M EGFR mutation, osimertinib treatment duration, cancer progression under osimertinib treatment and post osimertinib treatment.

The study population included patients treated with osimertinib within French early access program (from 7 April 2015 to 28 April 2016). Adult patients benefiting from this temporary use authorization were included if they had advanced NSCLC harboring T790 M EGFR mutation regardless of treatment line but after having received first- or second-generation EGFR-TKI therapy and a platinum-based chemotherapy. Participation was nevertheless allowed if a second-line treatment with chemotherapy was not possible.

2.2. Data collection

Patient demographics and clinical characteristics were obtained retrospectively from patient files including age, gender, ethnicity, smoking status, performance status, tumor histology, cancer stage, number and sites of metastases, presence of EGFR-activating mutations, methods of mutation detection, lines of treatment (chemotherapy or TKI) received before osimertinib and characteristics of osimertinib treatment. Clinical outcomes included clinical evolution (regressed, stable or worsened/progressed), date of death (if applicable) and any clinician-defined progression based on increased lesion size, appearance of new lesions or symptomatic findings.

2.3. Statistical analysis

The primary endpoints were physician-assessed PFS and OS from osimertinib initiation. PFS and OS were assessed in the entire cohort and in predefined subgroups: second vs. ≥ third line of treatment or more; presence vs. absence of cerebral metastasis at initiation of osimertinib; T790 M mutation discovery with liquid biopsy vs. tissue rebiopsy.

The secondary endpoints were the followings: description of the clinical and socio-demographic characteristics of patients; type of EGFR-TKIs (first or second generation) used before osimertinib; characteristics of osimertinib treatment (duration, doses, dose modifications, discontinuations); type of progression (site, clinical characteristics); description of concomitant and post osimertinib anticancer treatments; types of EGFR mutations and detection methods for initial testing and at progression on osimertinib treatment.

It was calculated that a sample size of 200 patients was necessary to obtain sufficient precision of PFS at 9–11 months and OS at 18–24 months.

The Kaplan-Meier method was used to estimate PFS and OS for the entire cohort and the log-rank test was used for comparison of survival curves in defined subgroups.

3. Results

3.1. Clinical characteristic of patients at diagnosis

Two hundred five patients managed in 52 centers were included. The mean (SD) age of patients was 69.6 (11.2) years, 68.8% were female and 71.5% were never-smokers (Table 1). At NSCLC diagnosis performance status was 0–1 for 84.0% of patients. NSCLC was adenocarcinoma and stage IV in 97.5% and 87.9% respectively. (Table 1).

EGFR-activating mutations were detected at diagnosis in 97.5% of patients and during follow-up in 2.5% of cases (Table 1). Diagnosis of EFGR mutation was performed in 72.1% of cases on primary tumor,

Table 1
Characteristics of study patients at diagnosis of NSCLC.

	N = 205
Age (years), mean (SD)	69.6 (11.2)
Female gender, n (%)	141 (68.8)
Ethnicity, n (%)	
Caucasian	163 (83.6)
Asian	14 (7.2)
Other	18 (9.2)
Missing	10
Smoking, n (%)	
Current smoker	12 (6.0)
Former smoker	45 (22.5)
Never-smoker	143 (71.5)
Missing	5
ECOG performance status, n (%)	
0	52 (31.9)
1	85 (52.1)
≥ 2	26 (16.0)
Missing	42
Histology, n (%)	
Adenocarcinoma	198 (97.5)
Large-cell carcinoma	4 (2.0)
Squamous cell carcinoma	1 (0.5)
Missing	2
Stage IV, n (%)	174 (87.9)
Missing	7
Detection of EGFR mutation in initial sample, n (%)	
At diagnosis	193 (97.5)
During follow-up	5 (2.5)
Missing	7
Type of EGFR mutation, n (%)	
T790 M *de novo* (exon 20)	20 (10.5)
L858R (exon 21)	58 (30.4)
Exon 19 deletion	127 (66.5)
G719X (exon 18)	6 (3.1)
S768I (exon 20)	1 (0.5)
V774 M (exon 20)	1 (0.5)
Missing	14
Other mutations at diagnosis, n (%)	5 (2.6)
ALK	1
BRAF	1
Missing	3

23.5% on metastasis and 0.6% on liquid biopsy (circulating tumor DNA). The most frequent methods for detection of EGFR mutation were pyrosequencing (44.8%) and Sanger sequencing (24.0%).

3.2. EGFR status at diagnosis

EGFR mutations were mainly exon 19 deletion (66.5%) and L858R on exon 21 (30.4%); *de novo* T790 M mutation on exon 20 was reported in 10.5% of patients (Table 1).

3.3. Treatments before osimertinib initiation

First-line treatment was first- or second-generation EGFR-TKI for 61.5% of patients and platinum-based doublet chemotherapy for 38.5% (Table 2). The mean (SD) durations of EGFR-TKI treatment and chemotherapy first-line treatments were 18.3 (13.8) months and 5.4 (7.4) months, respectively.

Overall, 82.0% (168/205) of patients received at least two lines of treatment before osimertinib initiation (median, 2.0 lines of treatment) (Table 2). Second-line treatments were chemotherapy for 47.6% (80/168), first- or second-generation EGFR-TKI for 51.2% (86/168) and immunotherapy for 1.2% (2/168). The French early access program allowed the use of osimertinib in second-line treatment in case of chemotherapy contraindication (18.0%, 37/205).

3.4. Clinical characteristic at osimertinib initiation

At osimertinib initiation, T790 M mutation was discovered on liquid biopsy in 34.4% of cases and tissue rebiopsy in 65.6% (8 patients had detectable T790 M mutation both in liquid biopsy and tissue rebiopsy) (Table 2); 54.0% of patients had a performance status of 0–1, 18.4% had a body weight loss > 5 kg and 67.3% had cancer-related symptoms. The most frequent metastatic sites were bone (55.3%), brain and central nervous system (CNS) (43.7%), contralateral lung (41.2%), pleura (32.2%) and liver (30.7%).

The dose of osimertinib was 80 mg once a day for 99.5% of patients and mean (SD) treatment duration was 13.9 (8.7) months. Osimertinib dosage was modified in 8.0% of patients, temporary discontinued in 8.8% and definitely stopped for adverse events in 5.9%, progression in 69.6%, death in 20.7% and others in 3.7%.

3.5. Efficacy of osimertinib in entire population and in subgroups of interest

Progression under osimertinib treatment was reported in 72.5% of patients, related to pre-existing cancer lesions for 71.4%. The main sites with progression were bone 28.6%, brain and meninges (27.5%), lung (27.5%) and liver (26.4%). A new metastatic site was reported in 51.6% of patients. The main new metastatic sites were brain and meninges (28.8%), bone (24.2%) and liver (21.2%).

Median PFS of the entire cohort, from osimertinib initiation was 12.4 (95% CI, 10.1–15.1) months (Fig. 1). The rates of PFS were 75.6% at 6 months, 51.9% at 12 months and 14.2% at 24 months.

Median PFS was 12.6 (95% CI, 6.7–17.5) months for osimertinib as second line and 12.4 (95% CI, 9.7–15.3) months as third line or more (p = 0.95) (Fig. 2 and Table 3); 9.7 (95% CI, 7.7–13.5) months in patients with cerebral metastasis and 15.1 (95% CI, 12.0–17.1) months in patients without cerebral metastasis (p = 0.21); 15.2 (95% CI, 10.9–17.6) months in patients with tissue rebiopsy as discovery test of T790 M compared with 8.8 (7.5–12.4) months with liquid biopsy (p = 0.0005) (Table 3).

Median OS since osimertinib initiation was 20.5 (95% CI,

Table 2
Characteristics of non-small cell lung cancer at initiation of osimertinib.

	N = 205
Median duration from NSCLC diagnosis to osimertinib initiation, years	4.7
Number of metastatic sites, n (%)	
1	50 (24.6)
2	62 (30.4)
≥ 3	92 (45.1)
Missing	1
Brain and CNS metastases, n (%)	87 (43.7)
Method for detection of T790 M mutation at osimertinib initiation, n (%)[a]	
Tissue rebiopsy	126 (65.6)
Liquid biopsy	66 (34.4)
Missing	13
Lines of treatments prior initiation of osimertinib	
Median	2.0
Only one line, n (%)	37 (18.0)
≥ 2 lines, n (%)	168 (82.0)
First-line treatment, n (%)	
Chemotherapy	79 (38.5)
With bevacizumab	18/79 (22.8)
With maintenance	20/79 (27.8)
EGFR-TKI	126 (61.5)
Gefitinib	66/126 (52.4)
Erlotinib	56/126 (44.4)
Afatinib	4/126 (3.2)

EGFR-TKI, epidermal growth factor receptor-tyrosine kinase inhibitor.
[a] For some patients with *de novo* T790 M mutation at NSCLC diagnosis, T790 M mutation test was not repeated before initiation of osimertinib treatment.

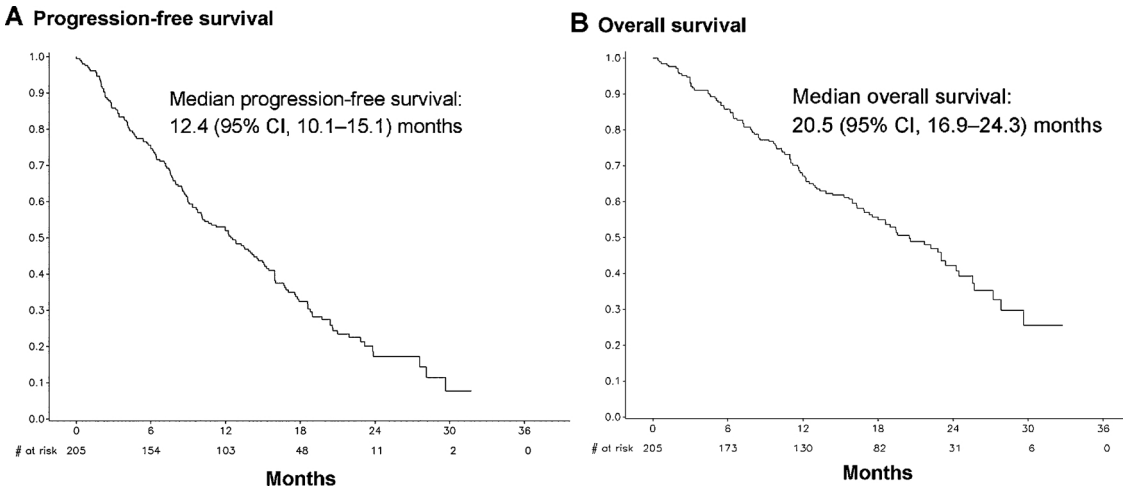

Fig. 1. Progression-free survival (A) and overall survival (B) of the entire cohort from osimertinib initiation.

16.9–24.3) months (Fig. 1). OS rates were 85.7% at 6 months, 67.1% at 12 months and 42.2% at 24 months.

Median OS were 17.5 (95% CI, 11.6–27.8) and 21.7 (95% CI, 17.3–24.3) months according to the use of osimertinib as second or third line of treatment or more, respectively (p = 0.46) (Fig. 2); 23.1 (95% CI, 18.6–27.8) months and 18.0 (95% CI, 12.2–22.2) months in patients without and with cerebral metastasis, respectively (p = 0.11) (Table 3).

Median OS for patients with *de novo* EGFR T790 M (n = 20) since osimertinib initiation and diagnosis were 22.8 (95% CI, 7.33–not reached) months and 6.8 (95% CI, 2.1–9.7) years, respectively.

3.6. Efficacy of osimertinib according to EGFR status at diagnosis

Median PFS since osimertinib initiation in patients with EGFR exon 19 deletion and exon 21 mutation was 13.5 (95% CI, 10.1–16.0) and 9.7 (95% CI, 7.4–13.2) months, respectively (p = 0.049) (Fig. 3 and Table 3).

Median OS since osimertinib initiation in patients with EGFR exon 19 deletion and exon 21 mutation was 23.1 (95% CI, 18.6–25.7) and 15.3 (95% CI, 11.6–21.7) months, respectively (p = 0.03) (Fig. 3 and Table 3).

Median OS since diagnosis in patients with EGFR exon 19 deletion and exon 21 mutation was 6.1 (95% CI, 4.6–6.8) and 3.9 (95% CI, 3.5–6.1) years, respectively (p < 0.001)

3.7. Rebiopsy at osimertinib progression

Fifty patients had tissue biopsy or/and liquid biopsy at progression with osimertinib: primary lung tumor site for 18.4% (9/49), metastatic site for 40.8% (20/49) and liquid biopsy for 26.5% (13/49); 5 patients had biopsy of primary lung tumor plus liquid biopsy, 1 patient had biopsy of primary lung tumor plus metastatic site and 1 patient had biopsy of metastatic site plus liquid biopsy (missing data for one patient) (Table 4). The EGFR mutations detected were deletion of exon 19 (65.8%; 25/38), T790 M (44.7%; 17/38), L858R (21.1%; 8/38), C797S (21.1%; 8/38) and others (18.4%; 7/38): cMET amplification (n = 3), PTEN mutation (n = 1), KRAS G12 mutation (n = 1) and TP53 mutation (n = 2) (missing data, n = 12). Histological change was reported in 6 patients (13.6%; 6/44) (missing data, n = 6) (Table 4).

After disease progression, osimertinib was continued for 41.5% (54/130) of patients and a local treatment was performed in addition to osimertinib beyond progression for 26 patients: radiotherapy (69.2%; 18/26), surgery (11.5%; 3/26), radiofrequency (7.7%; 2/26) and others (11.5%; 3/26).

A total of 80 patients benefited from a post osimertinib treatment: mainly chemotherapy alone (55.0%; 44/80), immunotherapy alone (8.0%; 10/80), EGFR-TKI alone (5.0%; 4/80) and chemotherapy plus EGFR-TKI (6.3%; 5/80).

From NSCLC diagnosis, the median OS of the entire cohort was 5.9 (95% CI, 4.5–6.8) years: 3.5 (95% CI, 2.8–6.8) years for patients

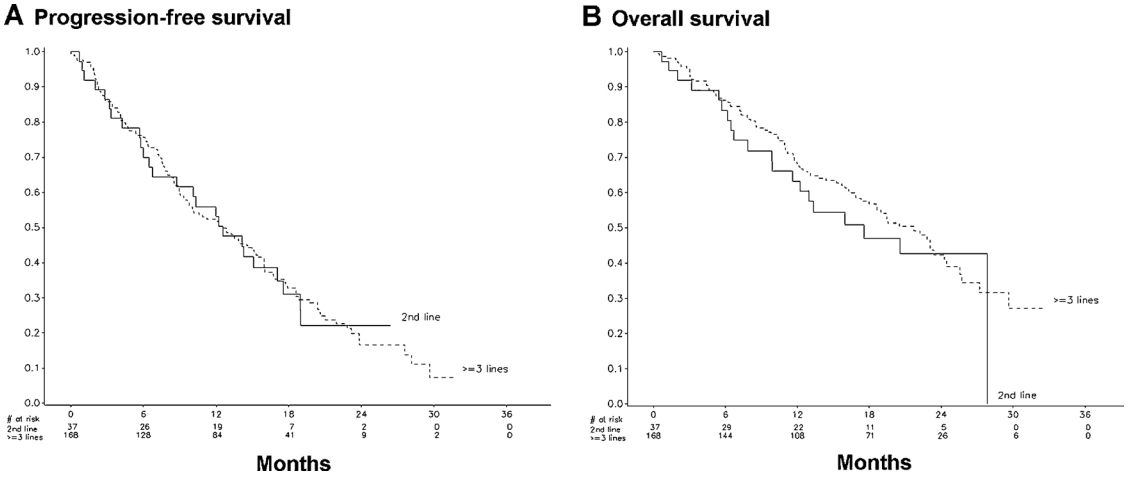

Fig. 2. Progression-free survival (A) and overall survival (B) from osimertinib initiation according to line of treatment with osimertinib (second line vs. third or more).

Table 3
Progression-free survival and overall survival from initiation of osimertinib for all patients and subgroups.

	N	Survival (median)	95% CI	P[a]
Progression-free survival (months)				
All patients	205	12.4	10.1–15.1	
Line of treatment				
2nd line	37	12.6	6.7–17.5	0.95
3rd line or more	168	12.4	9.7–15.3	
Cerebral metastases				
No	114	15.1	12.0–17.1	0.21
Yes	91	9.7	7.7–13.5	
Discovery test of T790 M mutation				
Tissue rebiopsy	126	15.2	10.9–17.6	0.0005
Liquid biopsy	66	8.8	7.5–12.4	
EGFR type				
Exon 19 deletion		13.5	10.1–16.0	0.049
Exon 21 mutation		9.7	7.4–13.2	
Overall survival (months)				
All patients	205	20.5	16.9–24.3	
Line of treatment				
2nd line	37	17.5	11.6–27.8	0.46
3rd line or more	168	21.7	17.3–24.3	
Cerebral metastases				
No	114	23.1	18.6–27.8	0.11
Yes	91	18.0	12.2–22.2	
EGFR type				
Exon 19 deletion		23.1	18.6–25.7	0.03
Exon 21 mutation		15.3	11.6–21.7	

[a] Log-rank test.

Table 4
Rebiopsy at osimertinib progression.

	N = 50
Liquid biopsy (cDNA)	13 (26.5)
Tissue biopsy	29 (59.2)
Metastasis	20 (40.8)
Lung	9 (18.4)
Missing	1
EGFR mutation	
T790 M (exon 20)	17 (44.7)
L858R (exon 21)	8 (21.1)
Exon 19 deletion	25 (65.8)
C797S	8 (21.1)
Other mutation[a]	7 (18.4)
Missing	12

Results are presented as n (%).
[a] cMET amplification (n = 3), PTEN mutation (n = 1), KRAS G12 mutation (n = 1) and TP53 mutation (n = 2).

receiving osimertinib as second line of treatment and 6.1 (95% CI, 4.7–7.4) years for those treated with osimertinib as third line of treatment or more (p = 0.067). Nevertheless, for patients who received a sequence of EGFR-TKI followed with chemotherapy before osimertinib treatment, median OS was 4.3 (95% CI, 3.5–not reached) years (p = 0.44 in comparison with patients who received the sequence EGFR-TKI and osimertinib).

4. Discussion

The present study included EGFR T790M-positive advanced NSCLC patients in the setting of the French early access program for osimertinib in 2015–2016. The characteristics of patients were as expected at inclusion with high proportions of adenocarcinoma (97.5%), women (68.8%) and never-smokers (71.5%). In comparison with patients included in clinical trials, patients in our cohort were more fragile (46.0% with performance status ≥ 2), more heavily pretreated and with a greater proportion of brain metastases (43.7%).

Despite these poor prognostic factors, the median PFS of the cohort (12.4 months) was comparable to the median PFS (9.9 months) reported in the pooled analysis of two phase 2 studies (AURA extension and AURA2) that included T790M-positive advanced NSCLC pretreated patients who received osimertinib after failure of first- or second-generation EGFR TKIs [13]. The median PFS of our cohort was also similar to the median PFS of osimertinib (10.1 months) reported in the AURA3 study, a phase 3 trial that compared osimertinib to patients with advanced NSCLC progressing harboring T790 M mutation after first-generation TKI [4]. In the study of Janne et al (AURA study), the median PFS was 9.6 months (95% CI, 8.3–not reached) in a subgroup of patients with EGFR T790M-positive NSCLC [10]. Median OS from osimertinib initiation (20.5 months) observed in our heavily treated patients was also consistent with the median OS (26.8 months) of the pooled analysis of AURA extension and AURA2 [13].

Cerebral metastases are frequent in patients with advanced NSCLC and their incidence increases in patients with EGFR mutations thus resulting in poor prognosis and limitation of treatment options [14]. This increased incidence could be due to the relative improvement of survival and the incomplete penetrance of the drugs in the CNS [15].

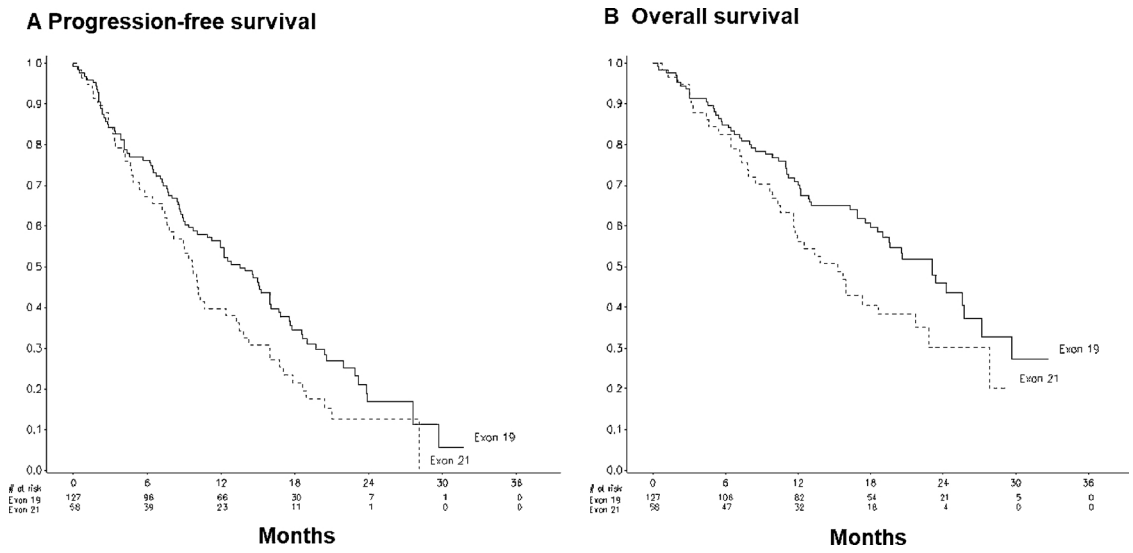

Fig. 3. Progression-free survival (A) and overall survival (B) from osimertinib initiation according to EGFR exon 19 deletion and exon 21 mutation.

Compared to the other TKIs, osimertinib demonstrated greater penetration of the blood-brain barrier [16]. In AURA3 study, median PFS in patients with CNS metastases was 11.7 months vs. 5.6 months in patients treated with chemotherapy [17]. In the FLAURA study, the incidence of CNS progression events was lower with osimertinib vs. chemotherapy (6% vs. 15%) regardless of the presence of CNS metastases at inclusion [12]. In our cohort, 43.7% of patients had brain and/or CNS metastases with no significant difference in terms of OS between patients without and with CNS involvement (23.1 and 18.0 months, respectively) confirming a favorable efficacy of osimertinib on CNS metastases.

No significant difference for survival was observed in patients receiving osimertinib as second treatment line or third line or more.

The meta-analysis of Lee et al showed that the clinical benefit of TKI treatment was higher in patients with exon 19 deletion [18]. We report a similar result in patients treated with osimertinib: both PFS and OS were increased in patients with exon 19 deletion compared to exon 21 mutation. Similar results were also reported in AURA3 study for PFS [4] and in the study of Ke et al for PFS and OS [19].

In our cohort, T790 M mutation was identified on tissue biopsy in two thirds of patients and on liquid biopsy in one third, but liquid biopsy was not systematically performed in 2015–2016 in French study centers. Patients with T790 M mutation identified in tissue had a longer median PFS compared with patients with T790 M identified in liquid biopsy (15.2 vs. 8.8 months; $p = 0.0005$). In the AURA3 study, patients with a T790M-positive liquid biopsy (in addition to a positive tissue biopsy for eligibility) treated with osimertinib had a shorter median PFS compared to patients with only a positive tissue biopsy: 8.2 (95% CI, 6.8–9.7) months vs. 10.1 (8.3–12.3) months, respectively) [20].

The reasons for the significant difference observed in our cohort between PFS according to liquid or tissue biopsy remain unclear. The lower PFS in patients with T790 M identified by liquid biopsy could reflect a poorer general status at initiation of osimertinib. Another possibility is that patients with higher tumor size associated with a poorer prognosis have higher concentrations of circulating DNA and achieve more frequently the detection threshold of liquid biopsy methods. It is possible also that the detection of the T790 M mutation in circulating tumor DNA does not reflect the proportion of the T790 M clone within the tumor. Thus, patients with a low proportion of cells harboring T790 M mutation will have a poorer response to osimertinib treatment [21].

Osimertinib treatment was continued in 54 patients beyond disease progression. This strategy is recommended by ESMO guidelines for first- and second-generation EGFR-TKIs in patients with radiological progression in a single site who continue to be dependent on the driver oncogene and without rapid systemic progression [22]. In this case, continuation of EGFR-TKI treatment with local treatment is considered as a reasonable strategy [23]. Our study has some limitations. Data were obtained retrospectively from patient medical records and unknown selected biases cannot be discarded. Another limitation is disease progression which was defined by the investigators. Study patients had received a median of two lines of treatments at inclusion and were therefore selected on the basis of their survival before osimertinib treatment, thus explaining the favorable results for OS from NSCLC diagnosis.

In conclusion, in pretreated patients with T790M-mutated advanced NSCLC, the efficacy of osimertinib appears similar in real-world setting to that of clinical trials.

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Conflict of interest statement

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