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Non-small-cell lung cancer patients with EGFR mutation: therapeutic sequences in a real-life setting

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**SEQUENCE THERAPEUTIQUE EN VRAIE VIE DES PATIENTS
PRESENTANT UN CARCINOME BRONCHIQUE NON A PETITES
CELLULES AVEC MUTATION ACTIVATRICE DE L'EGFR**

THÈSE
POUR LE DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

SPÉCIALITÉ : PNEUMOLOGIE
FST ONCOLOGIE

Par Mme Giulia BERARDI

[Données à caractère personnel]

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Abréviations

NSCLC: non small cell lung cancer

EGFR: epidermal growth factor receptor

TKI : tyrosine kynase inhibitor

1G/2G : first or second generation

3G : third generation

TTF : Time To Treatment Failure

OS : Overall Survival

WHO: World Health Organization

CNS: central nervous system

SCC: squamous cell carcinoma

ICI : immune check point inhibitor

**Non-small-cell lung cancer patients with *EGFR* mutation:
therapeutic sequences in a real-life setting**

**Giulia Berardi, Nicolas Girard, Florence de Fraipont, Chantal Decroisette, Sylvie Gazzeri,
Lidia Petit, Nicolas Albin, Denis Moro-Sibilot, Anne-Claire Toffart**

ABSTRACT

Background. – The treatment of *EGFR*-mutated metastatic non-small-cell lung cancer (NSCLC) has been modified over the last years with the advent of osimertinib. Identifying the optimal sequence of treatment is a real challenge. We aimed to analyze the proportion of patients treated with osimertinib in second-line, time to treatment failure (TTF), and overall survival (OS) according to the tyrosine kinase inhibitor (TKI) sequence.

Methods. –This retrospective, multicenter study enrolled patients with metastatic NSCLC displaying *EGFR* exon 19 deletion or exon 21 mutation in the *EGFR* gene, with molecular analysis conducted between 2015 and 2019.

Results. – Overall, 254 patients were studied (median age, 70 years; female, 74%; adenocarcinoma, 96%; never-smokers, 64%). At progression after the first-line of first- or second-generation TKIs, another biopsy was carried out in 62/150 patients (41%), with T790M mutations identified in 29 (46%) patients. Among patients who started second-line treatment after first- or second-generation TKI (n=112), 62 (55%) received osimertinib with a median first-line OS of 41.3 months (IQR 25%–75%, 25.5–NR). Using first-line osimertinib, median TTF was 20.6 months (IQR 25%–75%, 13–NR), with median OS not reached. After first-line treatment discontinuation (n=150), 46 patients did not receive any second-line therapy. Seventy-five patients benefited from three treatment lines. After second-line osimertinib failure, 25 (93%) patients received chemotherapy in third-line.

Conclusions. – In a real-life setting, half of pretreated patients with *EGFR* mutations benefited from second-line osimertinib, with a median OS of 3.5 years. TKI sequencing in the setting of *EGFR*-mutant NSCLC is thus highly feasible in a real-world setting. With new therapeutic options still emerging, TKI sequencing remains clinically relevant.

Keywords: non-small-cell lung cancer; tyrosine kinase inhibitor; EGFR mutation; osimertinib;
treatment sequence

1. Introduction

Over the last two decades, the survival of lung cancer patients has markedly improved for those with oncogenic addictions, particularly patients with *epidermal growth factor receptor (EGFR)* mutations treated with targeted therapies. *EGFR* mutations are present in 10% of patients with non-small-cell lung cancer (NSCLC) in France, more commonly in women and non-smokers [1]. Tyrosine kinase inhibitors (TKIs) are used in first-line in patients with metastatic disease [2] and in the adjuvant setting, as well [3].

In metastatic disease patients, first-generation (erlotinib and gefitinib) [4,5] and second-generation (afatinib) [6] TKIs have been available since the early 2000's, with median overall survival (OS) of 25.8 months (95% confidence interval [CI], 23.8–27.5) [7]. However, acquired resistance to TKIs is very common. The most common resistance mutation is the EGFR exon 20 T790M missense mutation, which is detected in over 50% of patients displaying disease progression [8]. Osimertinib is an irreversible third-generation EGFR-TKI that selectively inhibits both EGFR-TKI-sensitizing and EGFR T790M-resistance mutations. Initially, this compound was approved in second-line in refractory patients exhibiting EGFR T790M mutation [9].

Starting in 2019, osimertinib has been made available as frontline therapy, with a median OS of 38.6 months (95% CI, 34.5–41.8) [10]. For patients treated with first-/second-generation EGFR-TKIs, osimertinib is still an alternative with consistent data, yet applicable only to patients developing T790M mutation [11]. These resistance mutations can be researched for on tumor tissues, using a tissue or liquid biopsy (circulating tumor DNA [ctDNA] on a blood sample) [12]. This work aimed to evaluate treatment strategies in a real-life setting for NSCLC patients harboring *EGFR* mutations.

2. Materials and methods

2.1. Design and setting

This retrospective study was conducted at Grenoble Alpes University Hospital, Grenoble Daniel Hollard Institute, Annecy Genevois Hospital, Alpes Leman Hospital, and Curie Institute in Paris, France.

Study ethics approval was obtained on 08 September (CECIC Rhône-Alpes-Auvergne, Clermont-Ferrand, IRB 5891). An information letter was sent to each living patient, providing the opportunity to refuse study participation.

The primary objective was to determine the proportion of patients having access to osimertinib in second-line following first- or second-line TKI generation. The secondary objectives were to describe the therapeutic sequences, resistance mutations identified by routine analyses, and survival according to the therapeutic sequence order.

2.2. Study population

Patients with metastatic NSCLC and *EGFR* mutations (exon 19 deletion, exon 21 L858R and L861Q, or exon 20 T790M missense mutation), treated in one of the five centers, having undergone a molecular biology analysis (at diagnosis or during the follow-up) between 2015 and 2019 were included.

Exclusion criteria were patients under 18 years of age at diagnosis, patient's opposition to using their data, exclusive presence of an *EGFR* TKI resistance mutation (exon 18, insertion / deletion / duplication of exon 20), and patients who exclusively benefited from palliative care.

2.3. Data collection

Patients were identified using the molecular biology platforms of Grenoble (that performs analyses for Grenoble, Annecy Genevois and Alpes Leman hospital) and Curie Institute. Clinical data were retrieved based on the patients' computerized medical charts from the different centers. Thereafter, data were anonymized, centralized, and analyzed at Grenoble Alpes University Hospital.

Demographic and clinical patient characteristics at diagnosis were collected, including gender, age, Charlson comorbidity score, smoking status, ECOG performance status (PS), as well as central nervous system (CNS) or hepatic metastases.

At diagnosis and each new biopsy, we recorded the following items: biopsy type, histological diagnosis, molecular analysis results (*EGFR* mutation and mutation identified as resistance mutation: *T790M*, *C797S*, *HER2* or *Met* amplification, or *PIK3CA*), date of molecular analysis, ctDNA realization, as well as their impact on treatments (start, continuation, TKI stop or switch, another treatment start, as well as all treatment discontinuation). The first three treatment lines were recorded, along with beginning and end of the treatment dates, response, and reasons for treatment withdrawing. The vital status was recorded, as well.

2.4. Statistical analysis

Continuous variables have been expressed as median (25–75% interquartile range [IQR]), and categorical variables as numbers (percentages). OS data were calculated from first-line or second-line treatment initiation to death. Time to treatment failure (TTF) was defined as the time separating treatment initiation to treatment stop. Survival curves were obtained using Kaplan-Meier methodology and compared using the log-rank testing. Patients lost to follow-up on March 2021 were considered censored. All statistical analyses were performed using SAS 4.0.

3. Results

3.1. Patient characteristics

Of the 433 patients that were screened between 2015 and 2019, 254 patients were included in the analysis (Fig. 1). Most patients were non-smokers (n=155, 64%), women (74%), and ECOG-PS 0–1 (n=185, 80%), with a median age of 70 years (IQR 25%–75%, 63–77) (Table 1). The most common comorbidity was prior cancer in 44 patients (17%). All patients displayed adenocarcinoma excepting four (1.5%) who exhibited squamous cell carcinoma, yet with exon 19 deletion. Overall, 10 patients displayed a co-mutation in the *EGFR* gene. Two patients exhibited *cMet* amplification at diagnosis, as well.

3.2. First-line treatment

A large majority of patients (n=228, 90%) received EGFR TKI as frontline treatment (Table 2). A first- (1G) or second-generation (2G) TKI (1G/2G TKI) was used for 177 (70%) patients, including afatinib (n=41, 16%), erlotinib (n=72, 28%), and gefitinib (n=64, 25%), whereas a third-generation (3G) TKI was employed in 51 (20%) patients. Overall, 25 (10%) patients were treated with chemotherapy, as well as one patient with immunotherapy (immune checkpoint inhibitor [ICI]) in the first-line setting. In this patient group, molecular analysis was unavailable prior to treatment initiation in 21 patients (75%), while the treatment was switched to 1G/2G or 3G TKIs after receiving molecular analysis results, with a median duration of first-line treatment of 1.2 months (IQR 25%–75%, 0.3–2.5).

Responses were recorded only for TKI-treated patients. Among these, treatment response could not be assessed in 17 (7.5%) patients, including six who stopped treatment for toxicity reasons without undergoing their CT reassessment and three who started their treatment just prior to the end of data collection, whereas eight patients were lost to follow-up before the first reassessment.

At the follow-up's end, 60 (23.6%) patients were still on first-line treatment and 46 patients did not undergo any second-line treatment, owing to palliative care or death after first-line therapy.

3.3. Outcome after first-/second-generation tyrosine kinase inhibitors in first line

Of the 177 patients treated with 1G/2G TKIs in a first-line setting, the best response rate was 65%, disease control rate being 95%. The main reason of treatment discontinuation was disease progression (n=104; 84%). Following disease progression, a new biopsy was realized in 62 patients, representing 41% of the 150 patients who withdrew first-line treatment. This biopsy revealed the presence of *EGFR* T790M mutations in 29 patients (46%). A ctDNA analysis was performed in 62 (34%) patients, resulting in diagnosing T790M in 22/62 (35%) patients. Other resistance mutations were emergence of *cMet* amplification for two patients and *HER 2* amplification for one. According to these results, 62 (55%) patients were treated in second-line with 3G TKIs, including osimertinib (n=61) and rociletinib (n=1). Twelve patients received osimertinib following 1G/2G TKIs without any T790M mutation identified. Fifteen patients (13%) underwent another 1G/2G TKI regimen in second-line, and these were mainly patients who discontinued first-line therapy for toxicity (n=11). Thirty-five patients (31%) underwent chemotherapy or ICI in second-line.

For patients treated with 3G TKI in second-line following 1G/2G TKI, the disease control rate was about 85%. After progression in second-line, a third biopsy was performed in 22 patients, (52% of the 42 patients who withdrew 3G TKIs in second-line). A resistance mechanism was identified in 8/22 patients, including six patients exhibiting a loss of T790M mutation, one patient with a *cMet* amplification, and another one with a C797S mutation. Twenty-seven patients underwent third-line treatment (40%), with chemotherapy provided to most of them (n=25, 93%).

When a 1G/2G TKI was employed as frontline treatment, after a median follow-up of 21.9 months [IQR 25%–75%, 10–30.5], median TTF was 11.2 months (IQR 25%–75%, 5.5–20.8) with an OS of 31.4 months (IQR 25%–75%, 17.3–69.2).

When osimertinib was used as second-line therapy following 1G/2G TKI, after a median follow-up of 12.8 months (IQR 25%–75%, 6.6–18), median TTF was 8.9 months (IQR 25%–75%, 4.1–15). OS from osimertinib initiation was 19.7 months (IQR 25%–75%, 12.8–NR) and OS was 41.3 months (IQR 25%–75%, 25.5–NR).

3.4. Outcome after third-generation tyrosine kinase inhibitors in first line

Among the 51 patients treated with 3G TKI in first-line, best response rate was 78%, and disease control rate was 100%. At the follow-up's end, 33 patients were still on treatment. The main reason of treatment discontinuation was disease progression (n=10/13; 77%).

After disease progression, a new biopsy was realized in 12 patients, involving 66% of the 18 patients who withdrew first-line treatment. A ctDNA was performed in two patients. The resistance mutations in this group were amplification of *cMet* for two patients, whereas C797S and PIK3CA mutations were present in one patient each. For these patients, second-line therapy mainly consisted of chemotherapy with or without ICI therapy (n=7, 70%).

When osimertinib was used in frontline, after a median follow up of 12.3 months (IQR 25%–75%, 9.2–18.5), TTF was 20.6 months (IQR 25%–75%, 13–NR), whereas the median OS was not reached. For first-line TKI, median TTF was significantly longer in patients with osimertinib than in those with 1G/2G TKI regimens (P-value=2.10⁻³). There was no statistically significant difference between both groups in terms of OS (P-value=0.6) (Fig. 2 and 3).

4. Discussion

In this large multicenter retrospective study, we have revealed that 55% of patients who received a second-line treatment following 1G/2G TKI were treated with osimertinib. For this population,

the median OS exceeded 3 years. Only 19% of the studied patients received osimertinib in first-line, given that this agent was only made available in France in 2019.

The strengths of this study are the large number (n=254) of treated patients exhibiting *EGFR* mutations, along with its multicenter design. Due to its retrospective design, there are missing data, particularly for molecular testing and ctDNA (method and results). The period of identification of *EGFR* mutation was rather large (2015 to 2019), including accessibility to osimertinib in second-line (2017) and first-line (2019) settings in France. It is important to note that cancer diagnosis could have been made prior to 2015.

The characteristics of the studied patients are in accordance with the known characteristics of *EGFR*-mutated patients, including a majority of never-smokers, women, and patients without comorbidities [13–15]. The proportion of patients with CNS metastasis at diagnosis (43%) was higher than in other real-life studies such as 24.4% in the Rangachari's cohort [16] and 25% in the Hendriks' cohort from the Netherlands [17]. Considering molecular biology characteristics at diagnosis, we have seen that 50% of patients displayed an exon 19 deletion, whereas Rosell et al. [18] and Riely et al. [19] reported a higher number of exon 19 deletions (60%).

At progression after a first-line treatment with 1G/2G TKI, only 41% of patients benefited from a new biopsy, with ctDNA analysis performed in 41% of patients. In another real-life cohort of *EGFR* and *ALK* patients [20], 46% of patients underwent re-biopsy at the time of acquired resistance. The low rate of tissue re-biopsy can be explained by a greater use of liquid biopsy. Indeed, over the last 5 years, ctDNA has become one of the standards enabling to identify a resistance mutation.

At progression after first-line treatment with 1G/2G TKI, the *T790M* mutation was identified in 46% of patients who benefited from a biopsy. In 2011, Sequist et al. [21] similarly reported a proportion of 49% of *T790M* mutations identified on tissue re-biopsy at progression, whereas this figure was even higher in the Yu et al. article [8], with 62.5% of patients benefiting from a new biopsy. The prescription of osimertinib concerned 55% (n=62) of patients eligible for a

second-line regimen after stopping 1G/2G TKI. This proportion is similar to the comparator group of the FLAURA study in which 47% of patients received osimertinib after first-line 1G/2G TKI [10]. In our cohort, for 12 out of 62 osimertinib-treated patients, osimertinib was prescribed in the absence of any T790M mutation. While the reasons for this prescription were not systematically recorded, this proportion appears to be consistent with that of another real-life study [22].

TTF with 1G/2G TKI as frontline was 11.2 months. This is similar to the PFS obtained in a prior study with these molecules, being 13.1 months with erlotinib [23], 10.8 months with gefitinib [5], and 11.1 months with afatinib [6]. TTF observed following 3G TKI group in first-line was 20.6 months, which is also similar to the PFS obtained in the FLAURA study, namely 18.9 months [2]. OS of 1G/2G TKI-treated patients in first-line was 31.4 months, whereas for osimertinib-treated patients in first-line, OS was not reached after a median 12.3-month follow-up. Similarly, in the FLAURA study, OS was 31.8 months in the comparator group, whereas median OS was 38.6 months in the osimertinib arm with a median 35.8-month follow-up [9]. In the French early access program for osimertinib cohort, the median OS subsequently to osimertinib initiation was 20.5 months [24]. TTF with osimertinib in second-line after 1G/2G TKI was similar to the PFS obtained in the AURA trial, consisting of 8.9 months in our cohort and 10.1 months in AURA trial [25]. However, we have revealed a better OS with the osimertinib in second-line in our cohort, consisting of 41.3 months vs. 26.8 months in the AURA trial. This is in line with other studies, particularly concerning a post-hoc analysis of LUX-Lung 7 in which 23 patients who received sequentially gefitinib and osimertinib displayed a median OS of 46.0 months [26].

In our cohort, 75 patients had at least three treatment lines. In accordance with published real-world evidence studies, 24% of patients did not receive any subsequent systemic treatment [27]. After osimertinib in second-line, almost all the patients who received a third-line were, in fact, treated using chemotherapy. While a lot of resistance mechanisms have been well described to

date, in about 40–50% of cases in first- or second-line settings, the resistance mechanism is unknown. The most common resistance mechanisms described are the loss of T790M mutation (49–68%), *Met* amplification (15–20%), C797S mutation (7% in first line up to 26% in second line), *HER2* amplification (2–5%), PIK3CA mutation/amplification (4%), as well as BRAFV600E mutation (3%) [22,28–31].

In addition, multiple co-existing molecular alterations have been observed in a considerable percentage of patients. Thus, developing an efficient treatment strategy to bypass resistance mechanisms proves to be a major challenge. Currently, many studies are evaluating drugs that could counteract tumor progression, especially concerning the *Met* amplification bypass pathway. To illustrate, savolitinib, which is a c-Met inhibitor, is being tested along with osimertinib in the TATTON study [32]. An association of amivantanab (EGFR-MET bispecific antibody) and lazertinib (third-generation EGFR TKI that targets T790M mutation while activating EGFR mutations) is also being tested in the MARIPOSA study [33]. There is also a renewed interest concerning the HER3 involvement in acquired resistance. Patritumumab and deruxtecan (antibody directed to HER3 attached to a topoisomerase I inhibitor) demonstrated antitumor activity across various EGFR TKI resistance mechanisms in pretreated patients in a phase I study, with a pivotal phase II study already initiated [34].

5. Conclusions

In a real-life setting, around half of *EGFR* mutated patients that had been 1G/2G TKI-pre-treated benefited from osimertinib in second-line, with a median OS of 3.5 years. TKI sequencing in the setting of *EGFR* mutant NSCLC is thus highly feasible. The challenge is to better understand resistance mechanism to osimertinib in second line and, even more so in first line, in order to develop new therapeutic options.

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Figures and Table

Fig. 1. Study population: flow-chart.

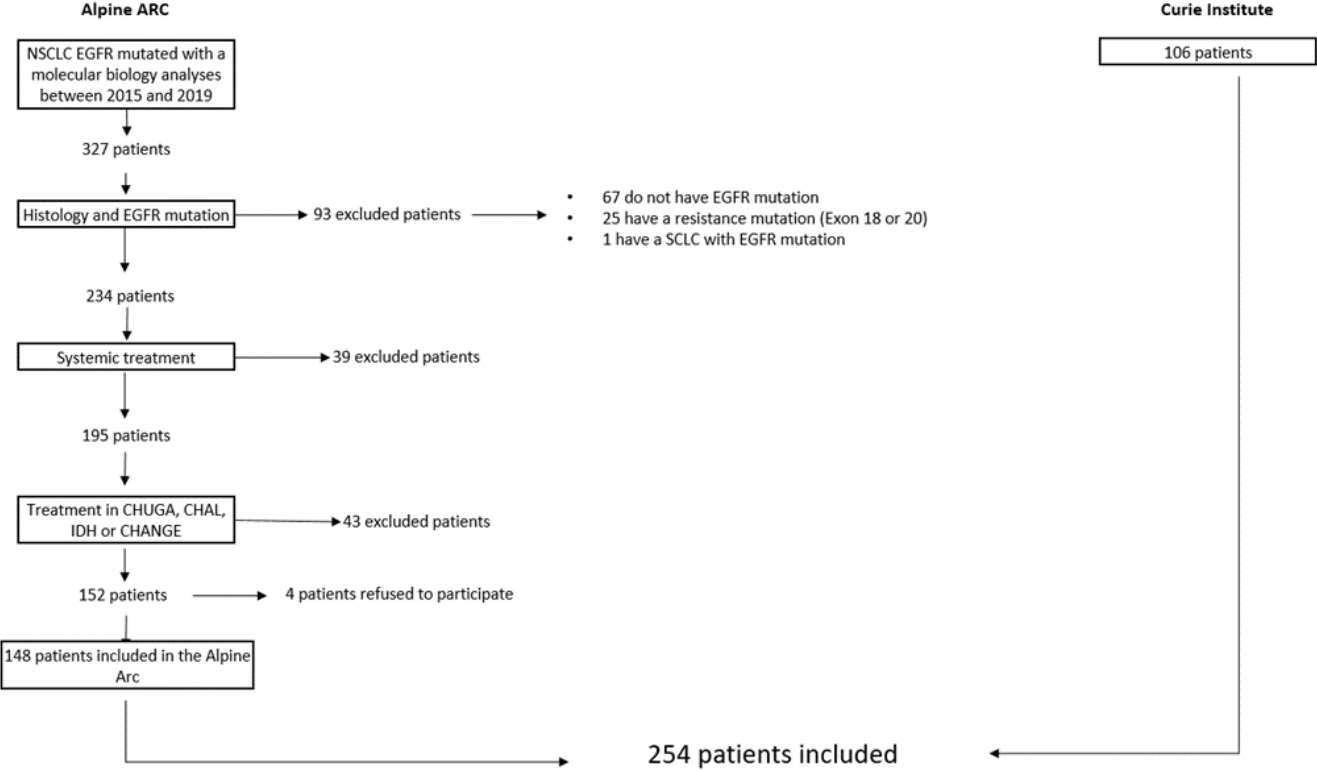
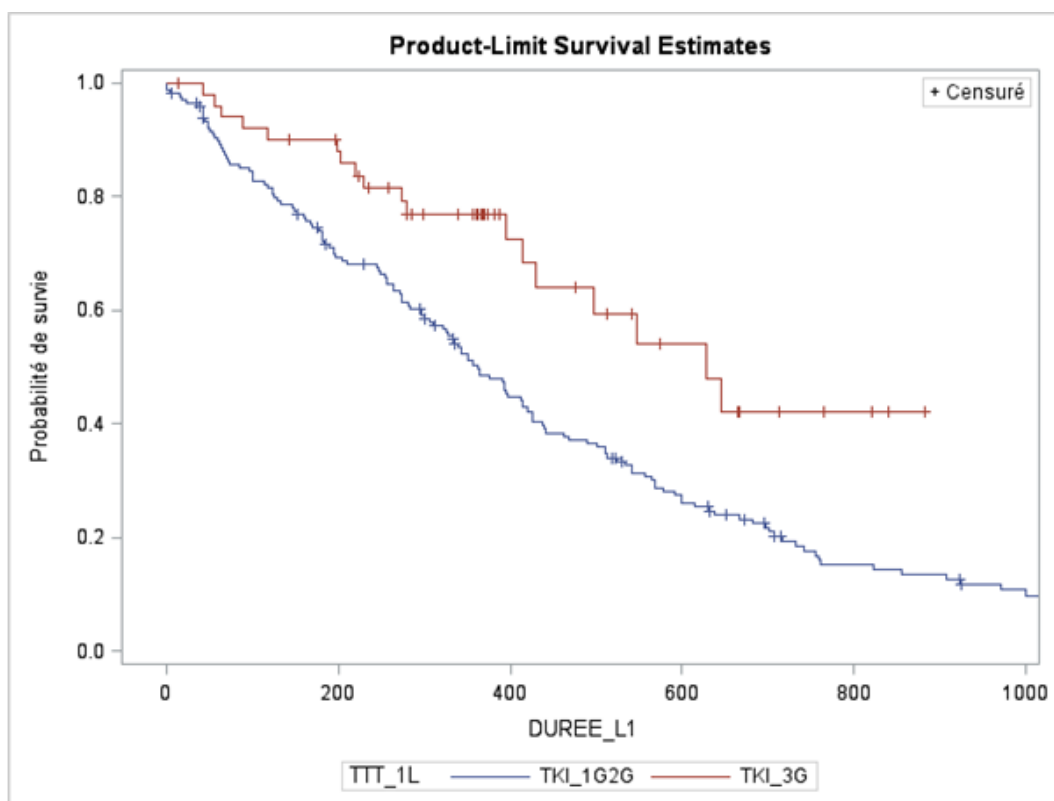


Fig. 2. Time to treatment failure according to first-line tyrosine kinase inhibitor.

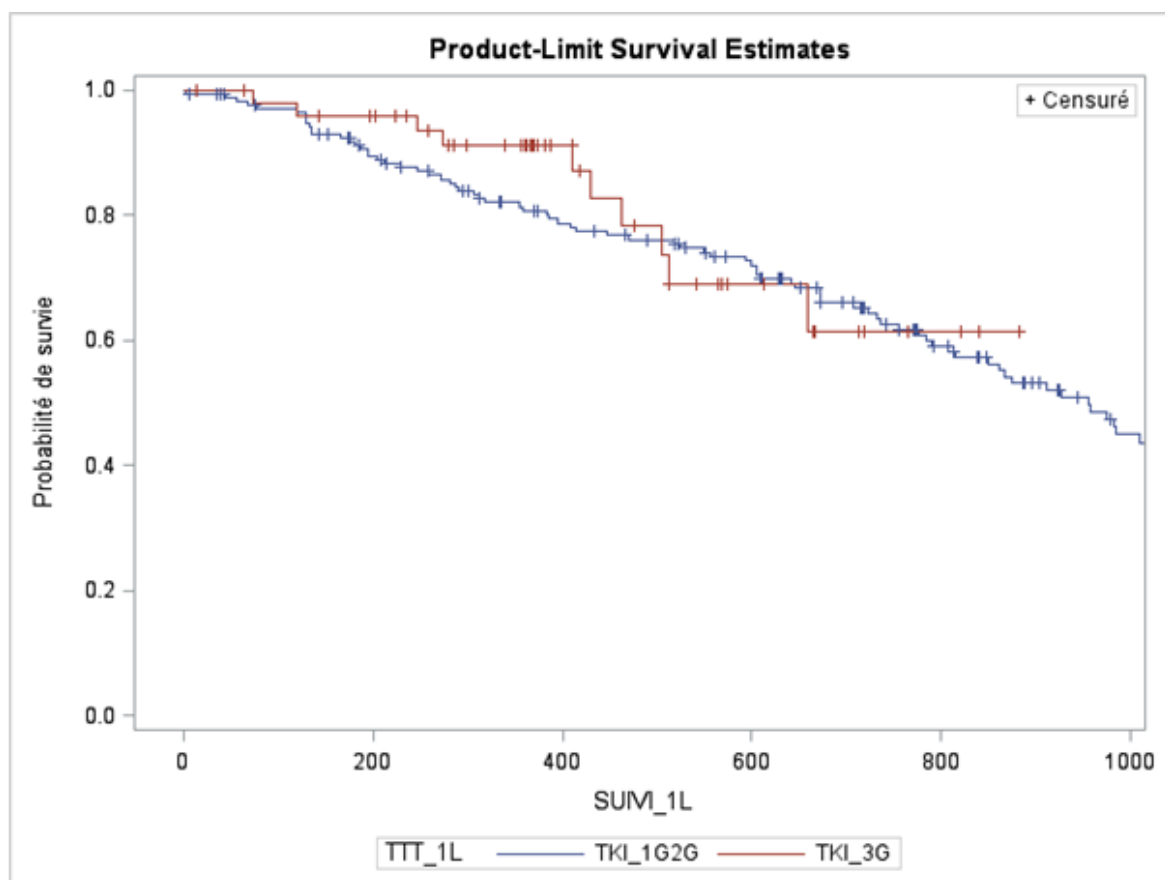
1G/2G: first- and second-generation; 3G: third-generation; TKI: tyrosine kinase inhibitor.



	Time-to-treatment failure (months)	P -value= 2.10^{-3} (Log rank test)
1G/2G TKI	11.2 [IQR 25%–75%, 5.5–20.8]	
3G TKI	20.6 [IQR 25%–75%, 13–NR]	

Fig. 3. Overall survival according to first-line tyrosine kinase inhibitor.

1G/2G: first- and second-generation; 3G: third generation; TKI: tyrosine kinase inhibitor.



	Overall survival (months)	<i>P</i> -value=0.6 (Log rank test)
1G/2G TKI	31.4 [IQR 25%–75%, 17.3–69.2]	
3G TKI	NR [IQR 25%–75%, 16.6–NR]	

Table 1

Demographic and clinical patient characteristics at diagnosis.

Patient characteristics	N=254
Male gender	65 (26)
Age – year	70 (63-77)
Charlson comorbidity score (MD=14)	0 (0-0)
Smoking status (MD=13)	
- Never	155 (64)
- Current	23 (9)
- Former	63 (26)
If current or former smoker (pack-year) (MD=13)	23 [15-40]
If former smoker, smoking cessation delay (year) (MD=12)	21 [10-31]
WHO performance status (MD=22)	
- 0	83 (36)
- 1	102 (44)
- 2-4	47 (20)
Cancer characteristics	
Metastases	
- CNS metastases	109 (43)
- Hepatic metastases	63 (25)
Histology	
- Adenocarcinoma	243 (96)
- Other	11 (4)
	Including 4 SCC
EGFR mutation*	
- Exon 19 (deletion)	128 (50)
- Exon 21 (L858R)	123 (49)
- Other	3 (1)

Qualitative variables are expressed as n (%) and quantitative variables as median (IQR, 25%–75%).

* Co-mutation in *EGFR* gene in 10 patients.

MD: missing data; WHO: World Health Organization; CNS: central nervous system; EGFR: epidermal growth factor receptor; SCC: squamous cell carcinoma.

Table 2. Characteristics of first line treatment

	1G/2G TKI 177 (70)	3G TKI 51 (19)	Chemo and/or ICI 26 (10)
Response	N=162	N=49	Not recorded
Response	106 (65)	38 (78)	
Stable disease	49 (30)	11 (22)	
Progression	7 (4)	0 (0)	
1st line ongoing	27 (15)	33 (65)	0 (0)
Reason of discontinuation	N=124/143	N=13/18	Not recorded
Progression	104 (84)	10 (77)	
Toxicity	20 (16)	2 (15)	
End of clinical trial	0 (0)	1 (8)	
Duration of treatment (months)			
If ongoing	17 (6.1-22.8)	12.1 (9.2-17.8)	...
If stopped	10.7 (4.8-17.8)	9.1 (6.6-16.3)	1.2 (0.3-2.5)
2nd biopsy			
Tissue biopsy	62 (34)	12 (24)	1 (4)
- Time from 1st line initiation (months)	11.2 (7.6-19.7)	12.4 (8.6-16.6)	21.9
- T790M	29	0	
ctDNA	62	2	0 (0)
- T790M	22	0	
After 1st line discontinuation	150 (85)	18 (35)	27 (100)
No treatment	38 (24)	8 (44)	0 (0)
- died in the next month	30 (79)	6 (75)	
- palliative care	8 (21)	2 (25)	
2nd line	112 (63)	10 (20)	26 (100)
- Other TKI 1/2G	15 (13)	1 (10)	21 (81)
- TKI 3G	62 (55)	2 (20)	4 (15)
- Chemo +/- ICI	35 (31)	7 (70)	1 (4)

TKI: tyrosine kinase inhibitor; ICI: immune checkpoint inhibitor; 1/2G: first- or second-generation; 3G: third-generation.

Table 3. Characteristics of second-line treatment

	1G/2G TKI 37 (25)	3G TKI 68 (46)	Chemo +/- ICI^a 43 (29)
If TKI in 1st line	16 (43)	64 (94)	42 (98)
Response	N=11	N=53	N=34
Response	2 (18)	25 (47)	14 (41)
Stable disease	7 (63)	20 (38)	10 (29)
Progression	2 (18)	8 (15)	10 (29)
If no TKI in 1st line	21 (57)	4 (6)	1 (2) ^b
Response	N=19	N=3	N=1
Response	12 (63)	2 (67)	0 (0)
Stable disease	6 (32)	1 (33)	1 (100)
Progression	1 (5)	0 (0)	0 (0)
2nd line ongoing	3 (8)	26 (38)	8 (19)
Duration of 2nd (months)			
If ongoing	26 5.4-39.2)	5.4 (0.9-13.8)	3.4(2.2-3.7)
If stopped	7.2 (3-9.8)	9.4 (5-14)	2.1(1-5)
3rd biopsy			
Tissue biopsy	11 (30)	22 (32)	6 (14)
- Time from 2nd line initiation (days)	249 (190-321)	233 (157-420)	155 (111-173)
- T790M +/- with C797S / loss of T790M	5 / 0 / 0	... / 1 / 6	...
After 2nd line discontinuation	34 (92)	42 (62)	35 (81)
No treatment	7 (19)	15 (22)	14 (36)
- died in the next month	5 (71)	8 (53)	9 (65)
- palliative care	2 (29)	7 (47)	5 (35)
3rd line	27 (73)	27 (40)	21 ^c (48)
- Other TKI 1/2G	5 (19)	2 (7)	6 (29)
- TKI 3G	10 (37)	0 (0)	8 (38)
- Chemo +/- ICI	12 (44)	25 (93)	6 (29)

^a Two patients with a chemotherapy-ICI combination within a clinical trial.

^b Metastatic lung cancer was diagnosed in 2009, with first molecular analysis performed in 2010.

^c Including 1 patient treated with lapatinib in third line.

TKI: tyrosine kinase inhibitor; ICI: immune checkpoint inhibitor; 1/2G: first- or second-generation; 3G: third-generation.

Conclusion

THÈSE SOUTENUE PAR : BERARDI Giulia

TITRE : SEQUENCE THERAPEUTIQUE EN VRAIE VIE DES PATIENTS PRESENTANT UN CARCINOME BRONCHIQUE NON A PETITES CELLULES METASTATIQUE AVEC MUTATION ACTIVATRICE DE L'EGFR

CONCLUSION :

Dans cette étude multicentrique rétrospective, 254 patients présentant un cancer bronchique non à petites cellules avec une mutation de l'EGFR ont été inclus.

Les caractéristiques démographiques et cliniques des patients au diagnostic sont similaires aux données de la littérature : majoritairement des femmes, avec un âge médian de 70 ans, non fumeuses et avec peu de comorbidité.

A progression après une première ligne de traitement par inhibiteur de tyrosine kinase (ITK) de 1ère ou de 2ème génération la moitié des patients étaient traités par osimertinib. Un quart des patients ayant progressé après une première ligne ne recevaient pas de 2nd ligne. Un tiers des patients bénéficiaient d'au moins 3 lignes. Après osimertinib en 2ème ligne, 93% des patients traités recevaient de la chimiothérapie.

La médiane de survie globale des patients traités par ITK de 1ère ou 2ème génération puis par osimertinib était de 41,3 mois. Elle n'était pas atteinte pour les patients sous osimertinib en première ligne avec une durée de suivi médiane de 12.3 mois.

L'utilisation séquentielle des thérapies ciblées reste donc cliniquement faisable et pertinente chez les patients avec une mutation de l'EGFR. Le développement de nouveaux traitements pour contrôler les résistances à l'osimertinib devrait encore bouleverser les algorithmes de prise en charge de ces patients.

VU ET PERMIS D'IMPRIMER

Grenoble, le :

Le Doyen de l'UFR de Médecine

Pr. Patrice MORAND


LE DOYEN

Pr. Patrice MORAND

LE PRÉSIDENT DE LA THÈSE

Pr. MORO-SIBILOT

b 30/08/2020

Serment d'Hippocrate

“Au moment d’être admis(e) à exercer la médecine, je promets et je jure d’être fidèle aux lois de l’honneur et de la probité.

Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux.

Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J’interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l’humanité.

J’informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences.

Je ne tromperai jamais leur confiance et n’exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences.

Je donnerai mes soins à l’indigent et à quiconque me les demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admis(e) dans l’intimité des personnes, je tairai les secrets qui me seront confiés. Reçu(e) à l’intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs.

Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l’indépendance nécessaire à l’accomplissement de ma mission. Je n’entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J’apporterai mon aide à mes confrères ainsi qu’à leurs familles dans l’adversité.

Que les hommes et mes confrères m’accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonoré(e) et méprisé(e) si j’y manque.”

