Overall survival in patients with EGFR mutation-positive NSCLC receiving sequential afatinib and osimertinib: updated analysis of the GioTag study

Maximilian J. Hochmair,[1] Alessandro Morabito,[2] Desiree Hao,[3] Cheng-Ta Yang,[4] Ross A. Soo,[5] James C-H Yang,[6] Rasim Gucalp,[7] Balazs Halmos,[7] Lara Wang,[8] Angela Märten,[9] Tanja Cufer[10]

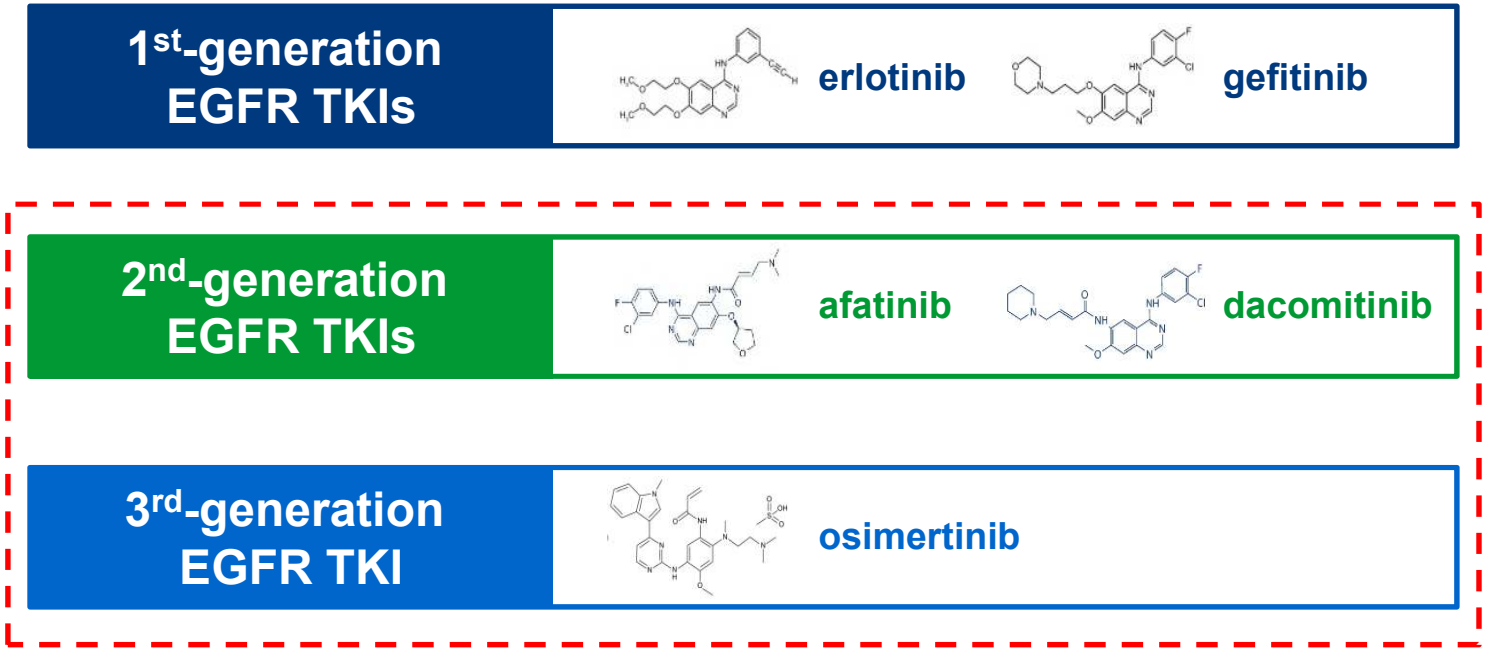
[1]Department of Respiratory and Critical Care Medicine, and Ludwig Boltzmann Institute of COPD and Respiratory Epidemiology, Vienna, Austria; [2]Thoracic Medical Oncology, Istituto Nazionale Tumori, "Fondazione G.Pascale"-IRCCS, Napoli, Italy; [3]Tom Baker Cancer Center, Cummings School of Medicine, University of Calgary, Calgary, Alberta, Canada; [4]Department of Thoracic Medicine, Chang Gung Memorial Hospital, Taoyuan, Taiwan; [5]Department of Haematology-Oncology, National University Hospital, Singapore [6]Department of Oncology, National Taiwan University Hospital and National Taiwan University Cancer Center, Taipei City, Taiwan; [7]Department of Oncology, Montefiore/Albert Einstein Cancer Center, New York, USA; [8]Boehringer Ingelheim Taiwan Limited, Taipei City, Taiwan; [9]Boehringer Ingelheim International GmbH, Germany; [10]University Clinic Golnik, University of Ljubljana, Ljubljana, Slovenia

Presented at the Latin America Conference on Lung Cancer (LALCA 2019), Mexico City, Mexico, October 17–19, 2019

Introduction

EGFR TKIs in NSCLC

- Three generations of EGFR TKIs are now widely available for the treatment of *EGFR* mutation-positive NSCLC

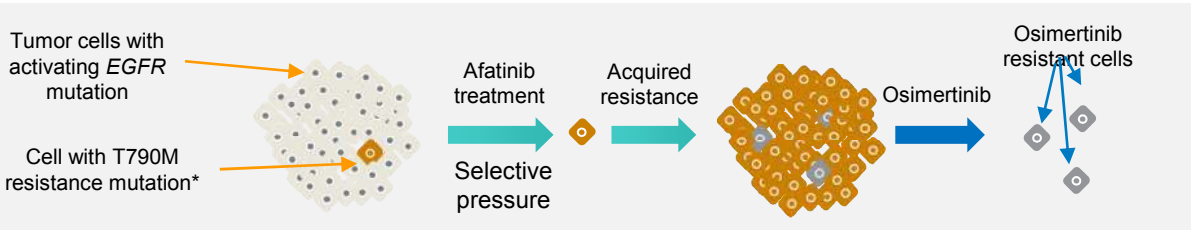


EGFR TKIs, epidermal growth factor receptor tyrosine kinase inhibitors; NSCLC, non-small cell lung cancer

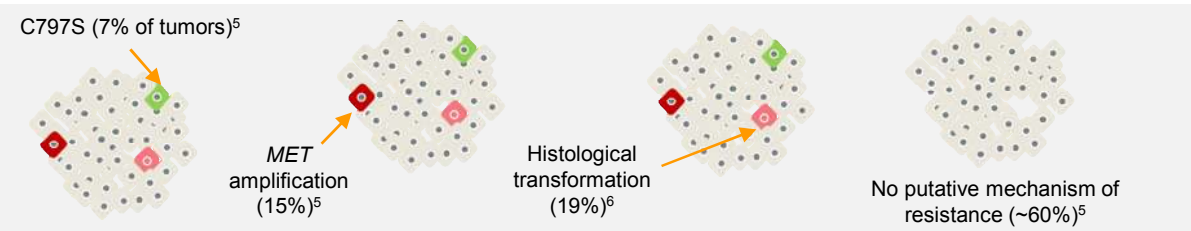
Introduction (cont'd)

- 2nd- (afatinib and dacomitinib)[1,2] and 3rd-generation (osimertinib)[3] EGFR TKIs have demonstrated superior PFS over 1st-generation EGFR TKIs based on independent blinded review
- However, the best 1st-line treatment choice and treatment sequence to maximize OS for patients with *EGFR* mutation-positive NSCLC is currently unknown
- Resistance mechanisms to afatinib are more homogenous than those for osimertinib

Afatinib
T790M-positive acquired resistance in around 60–75% of cases, facilitating second-line treatment with osimertinib[4]



Osimertinib
Heterogeneous resistance mechanisms[5,6]: no clear targeted treatments post osimertinib but some agents have shown promise in early phase trials[7,8]



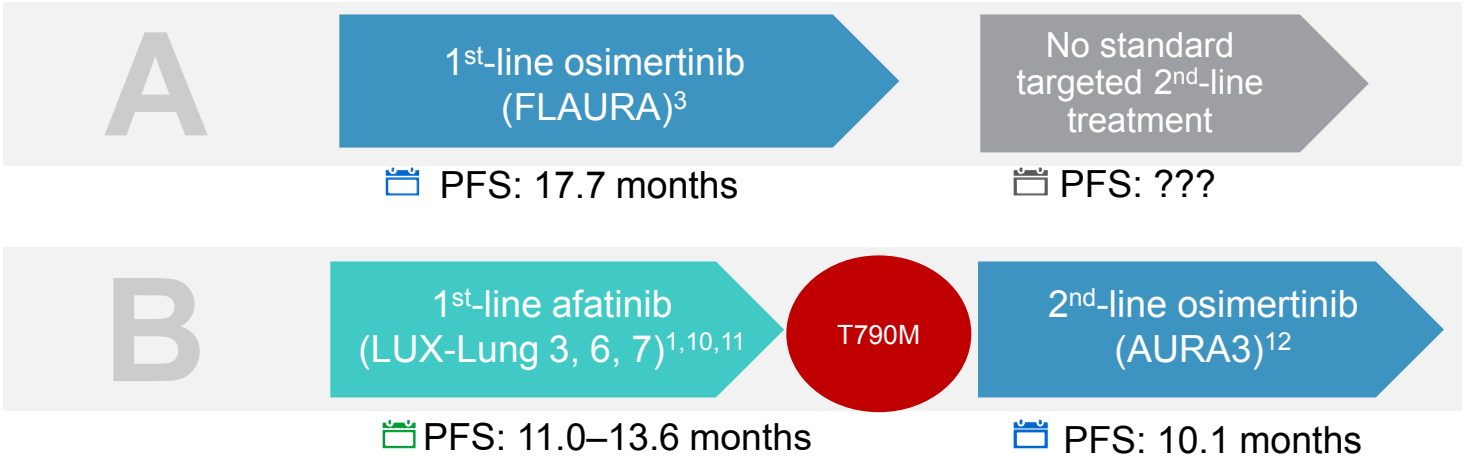
*T790M cells can be present in small numbers prior to treatment and can also emerge during treatment[9]

OS, overall survival

Introduction (cont'd)

Rationale for sequential afatinib and osimertinib

- Most patients progressing on afatinib will be eligible for 2nd-line osimertinib
- Osimertinib has shown 1st- and 2nd-line (T790M) activity
- There is no standard targeted treatment for patients progressing on osimertinib



Hypothesis: Clinical outcomes with B > A??

PFS, progression-free survival

Introduction (cont'd)

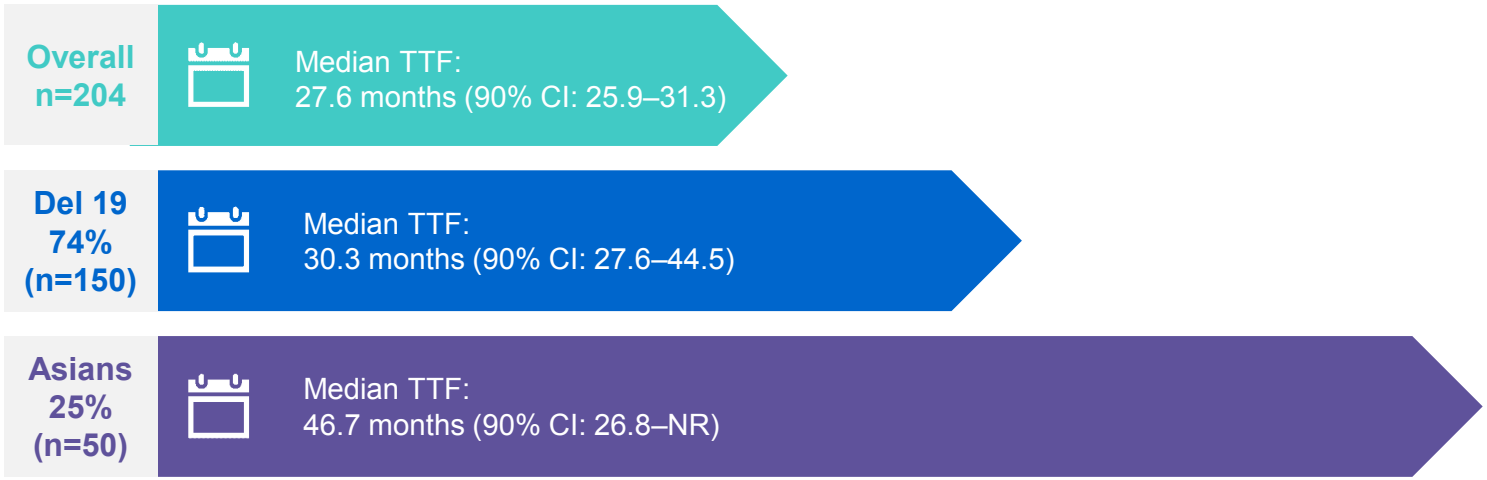
The GioTag study: original analysis

- GioTag is a global observational study assessing clinical outcomes in patients treated with 1st-line afatinib and 2nd-line osimertinib after detection of T790M

- In the original analysis of the GioTag study, promising time to treatment failure (TTF) was reported in patients treated with afatinib and sequential osimertinib in everyday clinical practice[13]
- Outcomes were particularly promising in Asian patients and patients with tumors harboring a Del19 mutation

NR, not reached; TTF, time to treatment failure

Introduction (cont'd)



- However, in the original analysis of GioTag, OS data were immature

Objective

- To conduct an updated analysis of OS and TTF of patients treated in GioTag

Methods

- GioTag is a global observational study across 10 countries (Austria, Canada, Israel, Italy, Japan, Singapore, Slovenia, Spain, Taiwan and the USA)[13]
- A maximum of 15 consecutive patients were enrolled from each site

The first global, observational study to evaluate outcomes of patients who received 1st-line afatinib followed by osimertinib (NCT03370770)

- Medical charts (38%) and electronic health records (62%) of consecutive patients treated in real-world practice were retrospectively reviewed
- Patients had *EGFR* mutation-positive (Del19/L858R) TKI-naïve advanced NSCLC and were treated with 1st-line afatinib, developed T790M-mediated acquired resistance, and received 2nd-line osimertinib treatment
- **Primary outcome: TTF**
- **Exploratory outcome: OS**

- This interim updated analysis (database lock April 2019) was performed when 42% of patients had experienced an OS event

Results

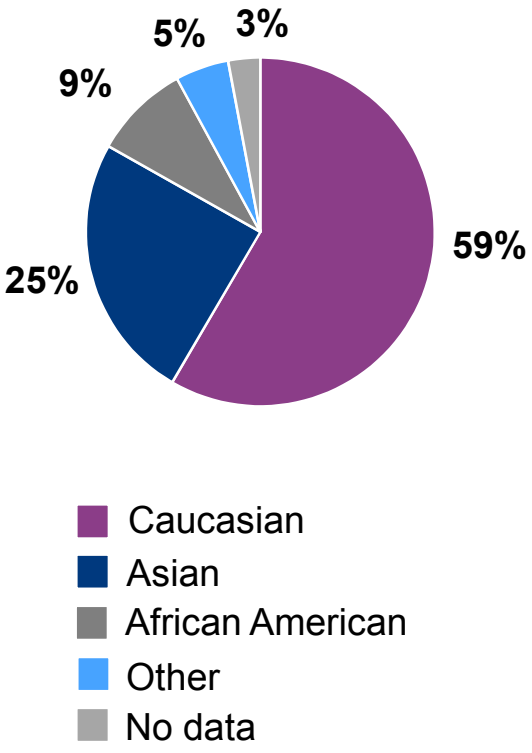
Patients

- Baseline characteristics have been described previously[13]

204*
patients treated with first-line afatinib and 2nd-line osimertinib

15%
of patients had ECOG PS of ≥2

10%
had stable brain metastases



Results (cont'd)

Overall survival

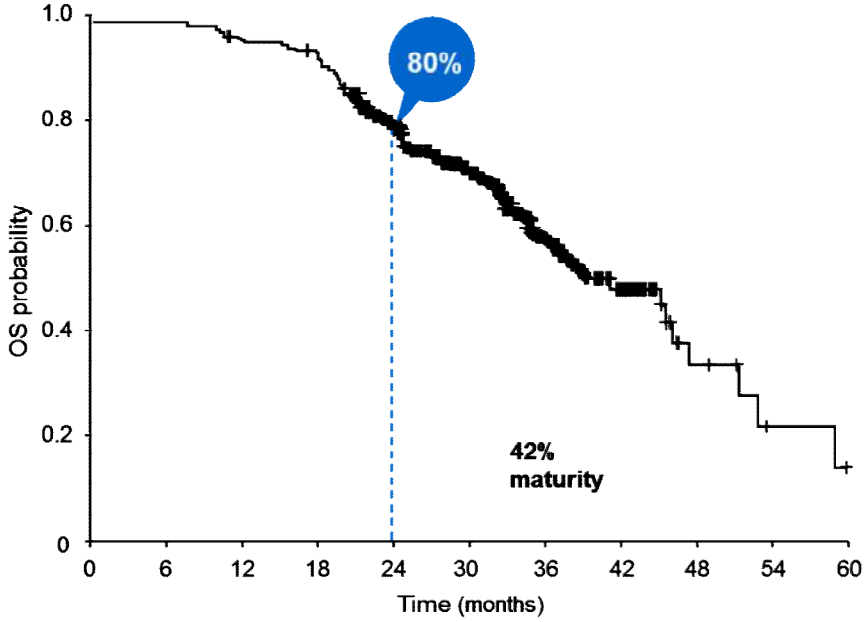
- Median follow-up was 30.3 months (interquartile range 24.0–36.8)
- Four in five patients were still alive after 2 years
- In patients who received the approved 40 mg/day dose of afatinib, median OS was 45.3 months (90% CI 37.6–47.6)
- Median OS was almost 3 years in patients with L858R-positive tumors

CI, confidence interval

Results (cont'd)

OS: overall dataset

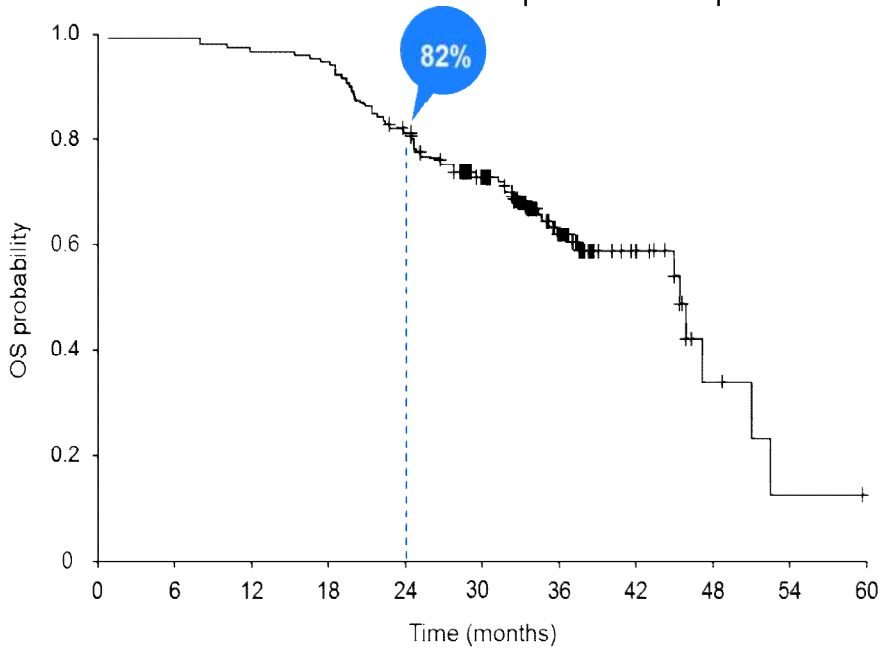
Afatinib followed by osimertinib	N=203
Events	85
Median OS, months (90% CI)	41.3 (36.8–46.3)



Patients at risk	203	203	194	186	153	107	63	23	8	3	2

OS: patients with Del19-positive tumors

Afatinib followed by osimertinib	Del19 (N=149)	L858R (N=53)
Events	58	27
Median OS, months (90% CI)	45.7 (45.3–51.5)	35.2 (32.0–39.1)



Patients at risk	149	149	145	141	119	82	50	18	4	1	1

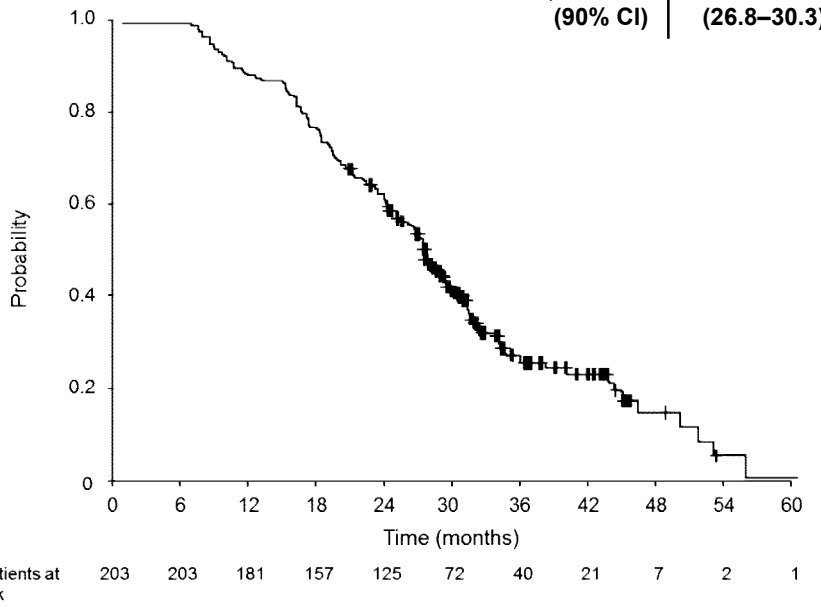
Results (cont'd)

Time to treatment failure

- Median TTF was slightly increased compared with the original analysis

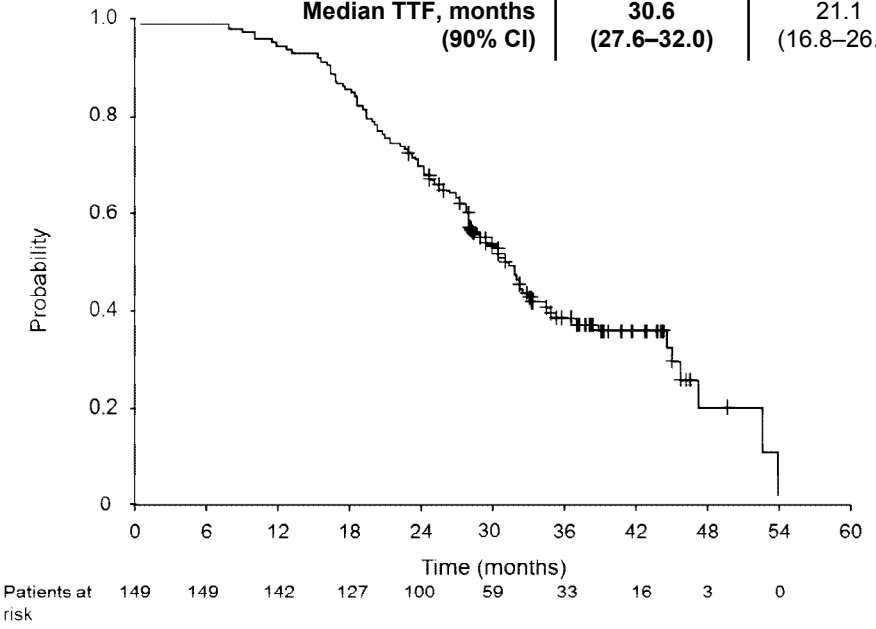
TTF: overall dataset

Afatinib followed by osimertinib	N=203
Events	140
Median TTF, months (90% CI)	28.1 (26.8–30.3)



TTF: patients with Del19-positive tumors

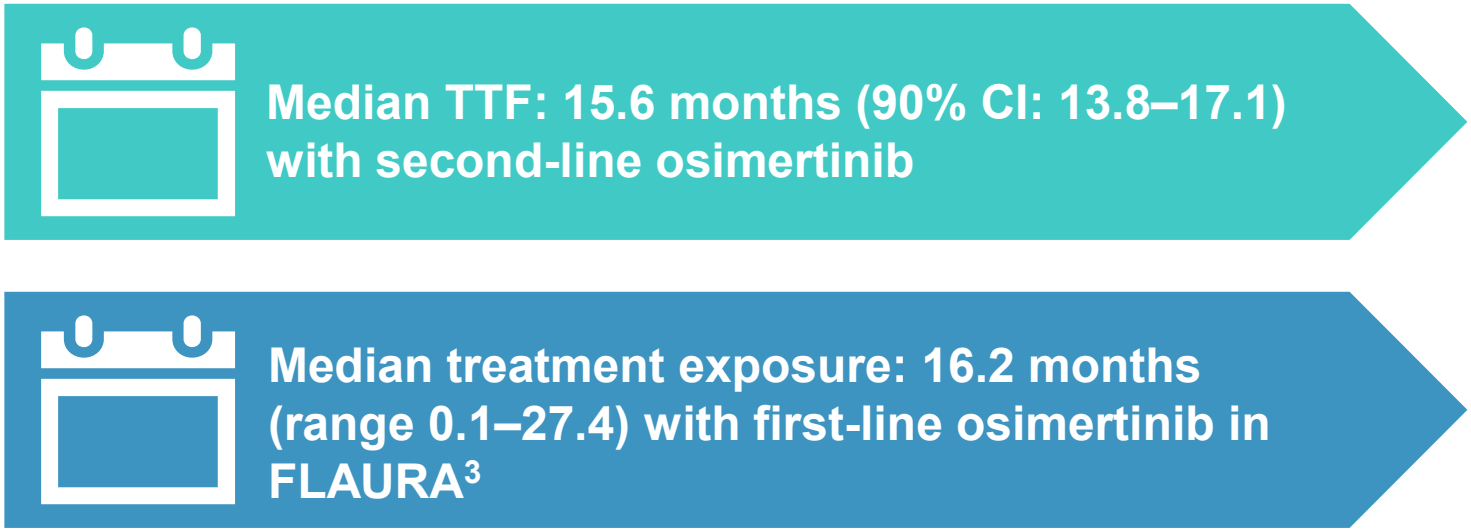
Afatinib followed by osimertinib	Del19 (N=149)	L858R (N=53)
Events	92	47
Median TTF, months (90% CI)	30.6 (27.6–32.0)	21.1 (16.8–26.3)



Results (cont'd)

Treatment with osimertinib

- Prior treatment with afatinib did not appear to preclude prolonged TTF with 2nd-line osimertinib



Key findings and conclusions

- In this updated analysis of GioTag, median OS was ~3.5 years and the 2-year OS rate was 80%
- In patients with Del19-positive tumors at the onset of treatment, median OS was ~4 years
- Overall, the median TTF was 28.1 months
- Median TTF with osimertinib was 15.6 months, indicating that substantial clinical benefit with osimertinib can be achieved in a 2nd-line setting following afatinib
- These data, along with high rate of emergence of T790M in patients treated with afatinib, especially those with Del19-positive disease (~75%),[14] indicate that sequential afatinib followed by osimertinib is potentially a feasible therapeutic strategy
- Prospective data are required to evaluate the OS of patients treated with different EGFR TKIs, and sequential regimens, in patients with *EGFR* mutation-positive NSCLC

References

1. Park K, et al. Lancet Oncol 2016;17:577–89
2. Wu YL, et al. Lancet Oncol 2017;18: 1454–66
3. Soria JC, et al. N Engl J Med 2018;378:113–25
4. Hochmair MJ, et al. Target Oncol 2019;14:75–83
5. Ramalingam SS, et al. Ann Oncol 2018;29 (suppl): LBA50
6. Schoenfeld AJ, et al. J Clin Oncol 2019;37:9028
7. Haura EB, et al. J Clin Oncol 2019;37:9009
8. Janne PA, et al. J Clin Oncol 2019;37:9010
9. Hata AN, et al. Nat Med 2016;22:262–9
10. Sequist LV, et al. J Clin Oncol 2013;31:3327–34
11. Wu YL, et al. Lancet Oncol 2014;15:213–22
12. Mok TS, et al. N Engl J Med. 2017;376:629–40
13. Hochmair MJ, et al. Future Oncol 2018;14:2861–74
14. Jenkins S, et al. J Thorac Oncol 2017;12:1247–56

Acknowledgments

- This study was funded by Boehringer Ingelheim. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development and have approved the final version
- Medical writing assistance, supported financially by Boehringer Ingelheim, was provided by Lynn Pritchard, of GeoMed, an Ashfield company, part of UDG Healthcare plc, during the development of this poster
- Data were originally presented: WCLC 2019.

- Corresponding author email address: Maximilian.Hochmair@wienkav.at.
- Presented by: Jose Waingarten