

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

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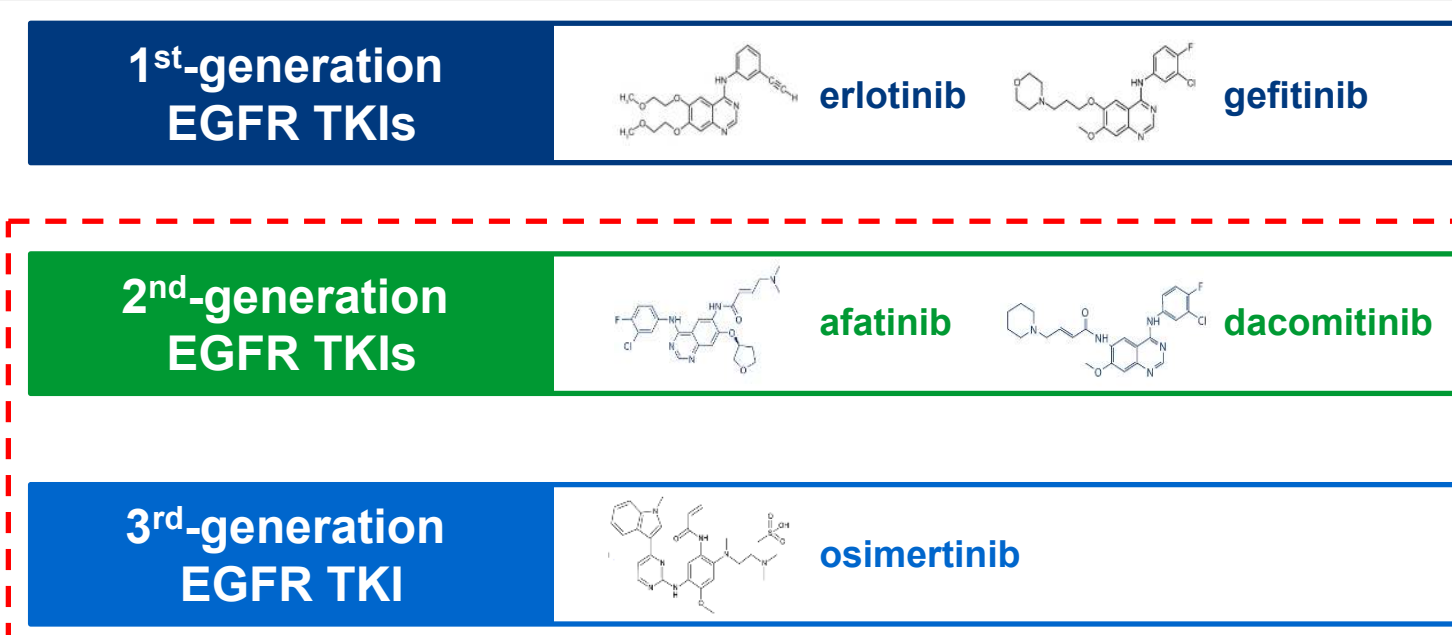
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Introduction

EGFR TKIs in NSCLC

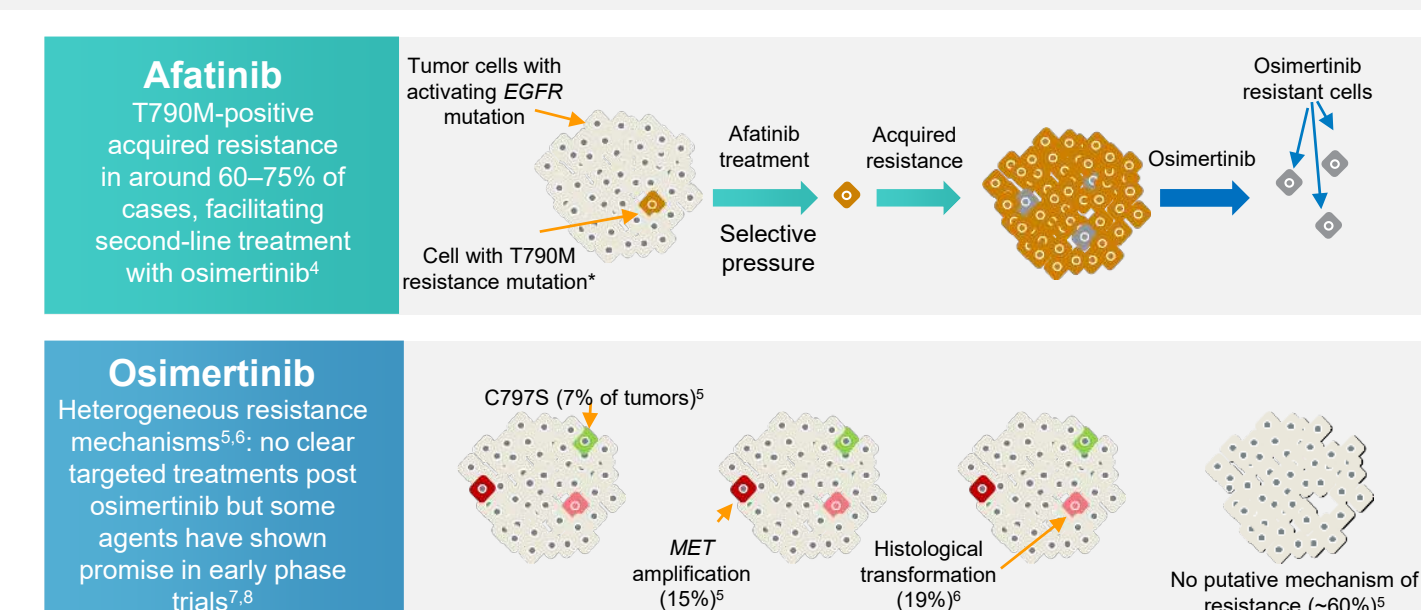
- Three generations of EGFR TKIs are now widely available for the treatment of *EGFR* mutation-positive NSCLC

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



- 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

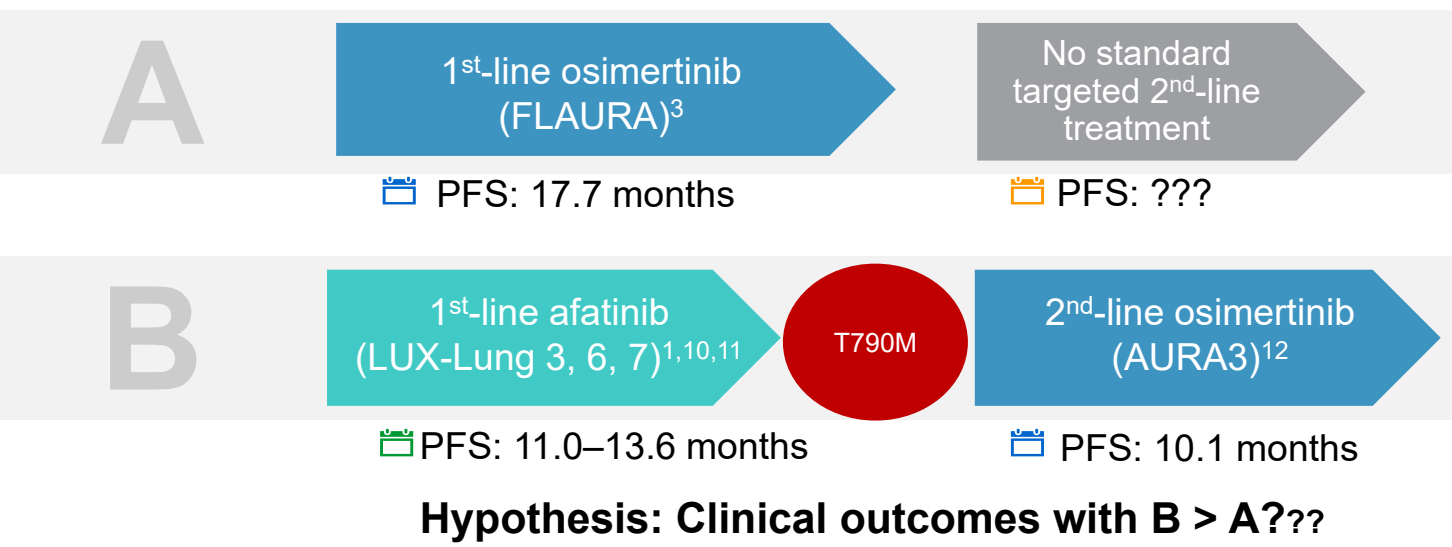
OS, overall survival



T790M cells can be present in small numbers prior to treatment and can also emerge during treatment

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



PFS, progression-free survival

The GioTag study: original analysis

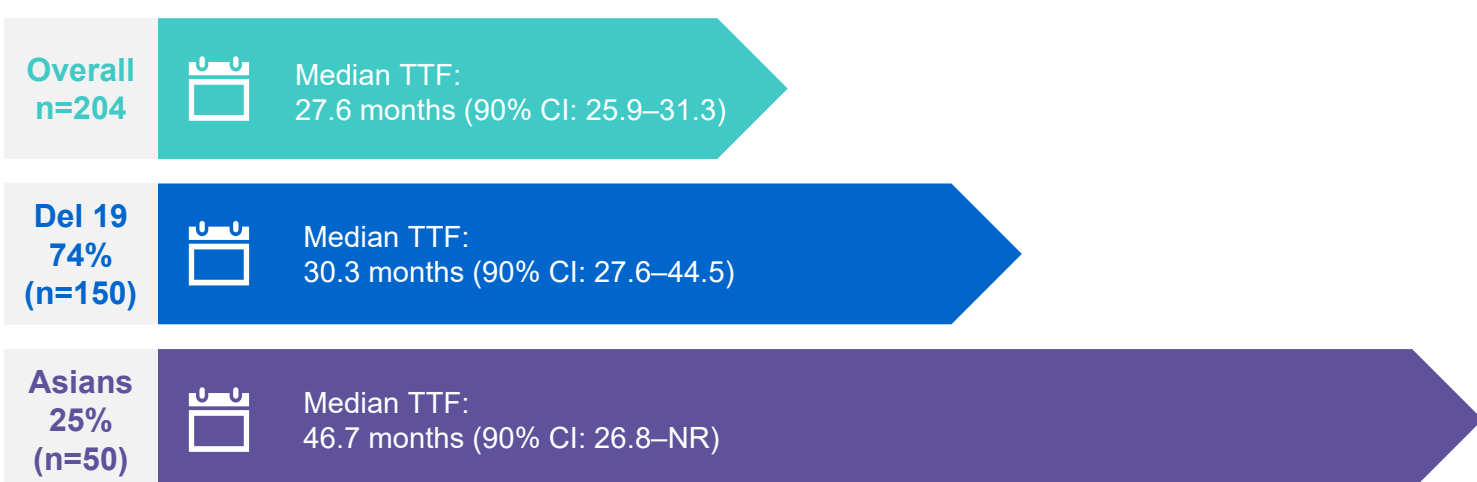
- GioTag is a global observational study assessing clinical outcomes in patients treated with 1st-line afatinib and 2nd-line osimertinib after detection of T790M



NR, not reached

- 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 practice¹³
- Outcomes were particularly promising in Asian patients and patients with tumors harboring a Del19 mutation

TTF, time to treatment failure



- 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)

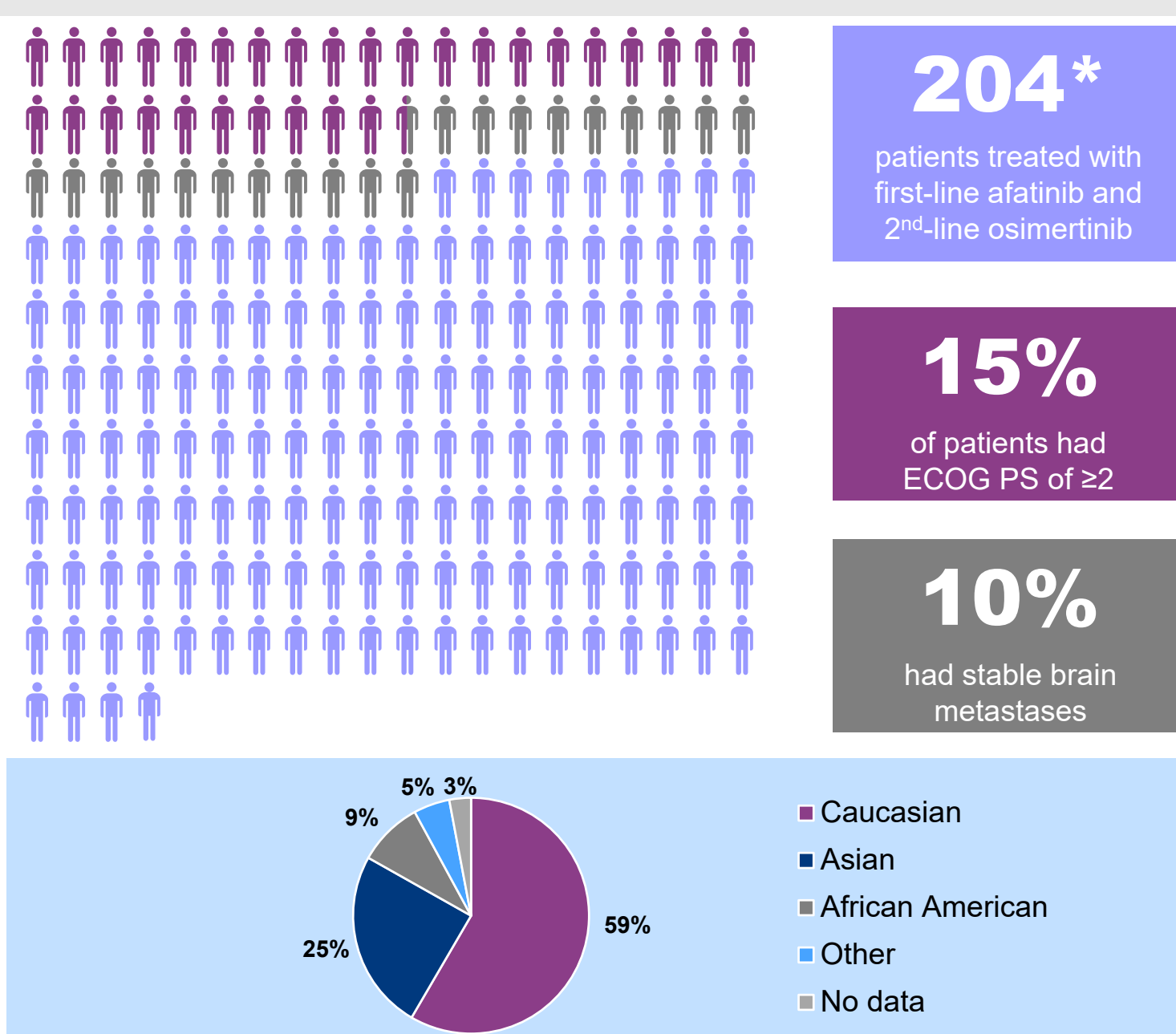
- Medical charts (62%) and electronic health records (38%) of consecutive patients treated in real-world practice were retrospectively reviewed
- Patients had *EGFR* mutation-positive (Del19/L858R) TKI-naïve advanced NSCLC and were treated with 1st-line afatinib, developed T790M-mediated acquired resistance, 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 previously¹³

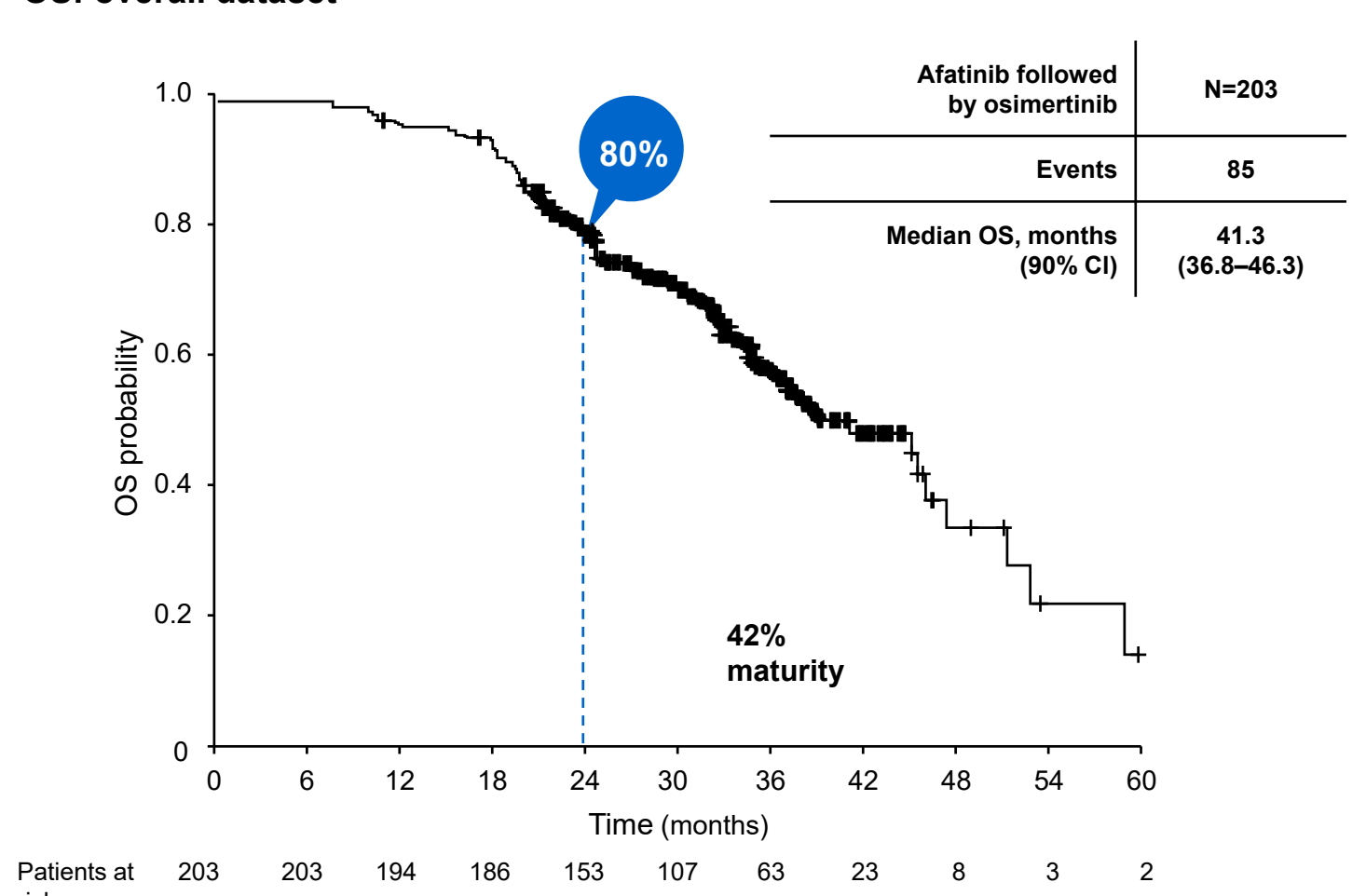


*One patient was not eligible for inclusion in the updated analysis of OS and TTP

Overall survival

- Median follow-up was 30.3 months (interquartile range 24.0-36.8)

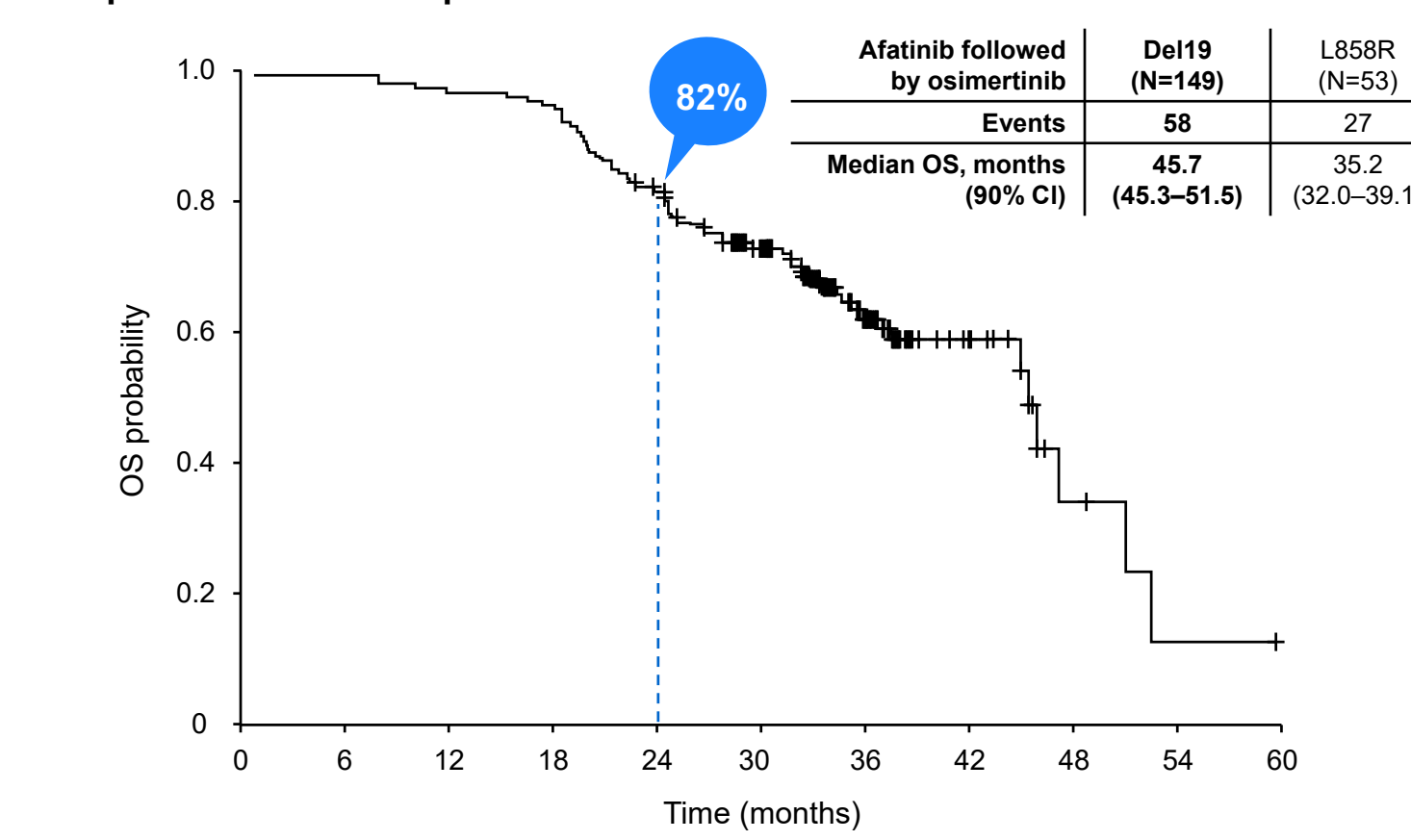
OS: overall dataset



- 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)

CI, confidence interval

OS: patients with Del19-positive tumors



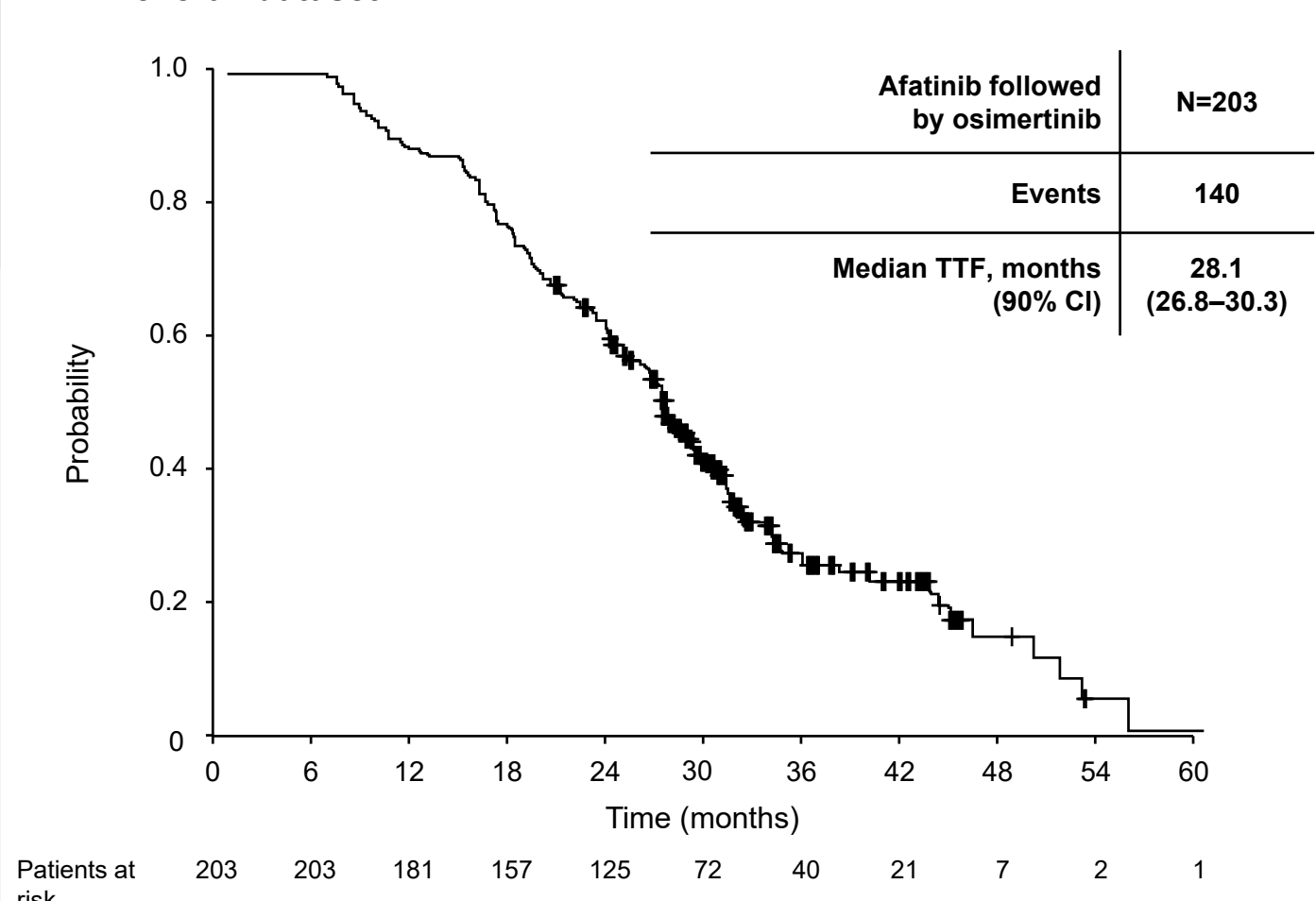
- Median OS was almost 3 years in patients with L858R-positive tumors

Results (cont'd)

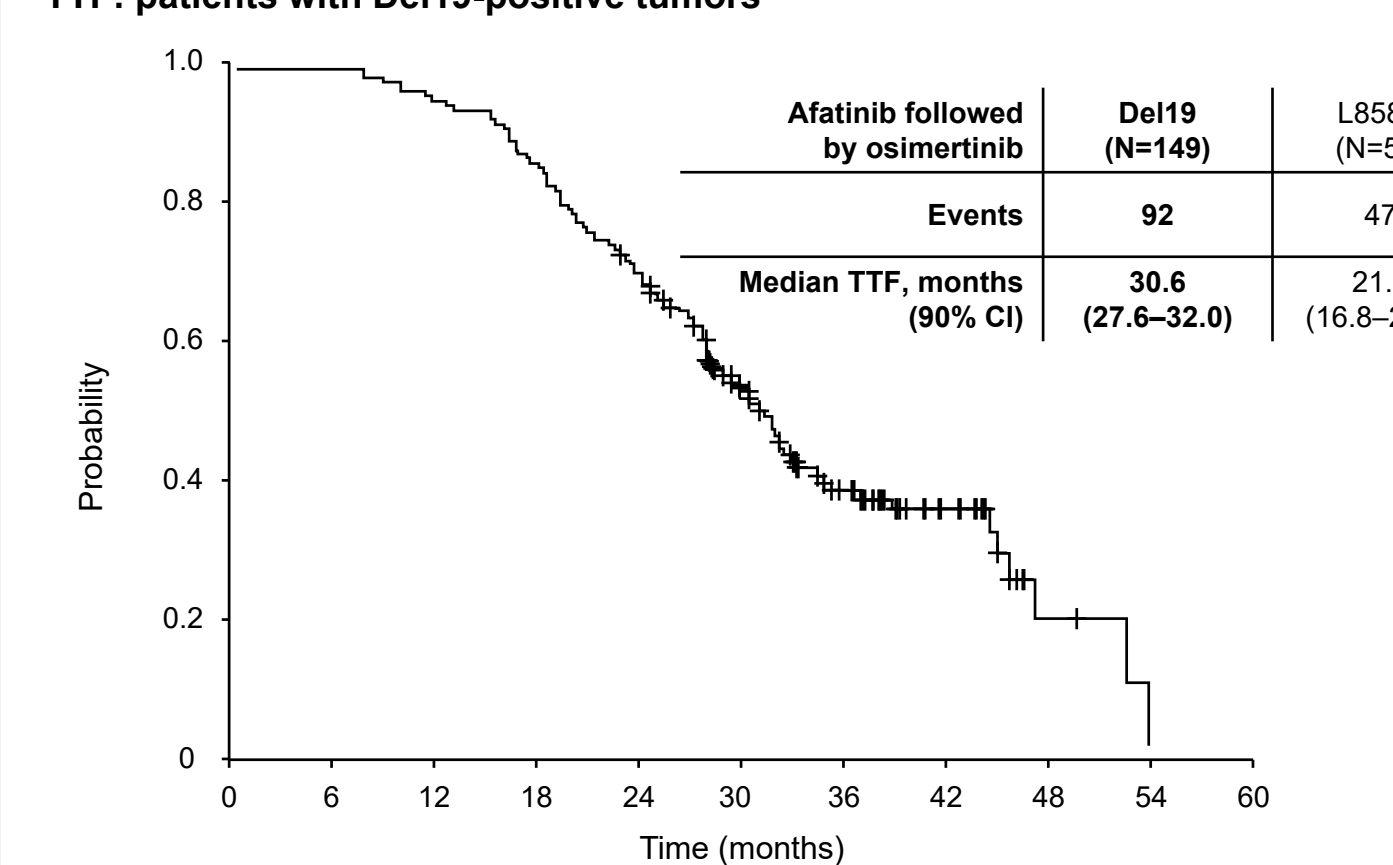
Time to treatment failure

- Median TTF was slightly increased compared with the original analysis

TTF: overall dataset

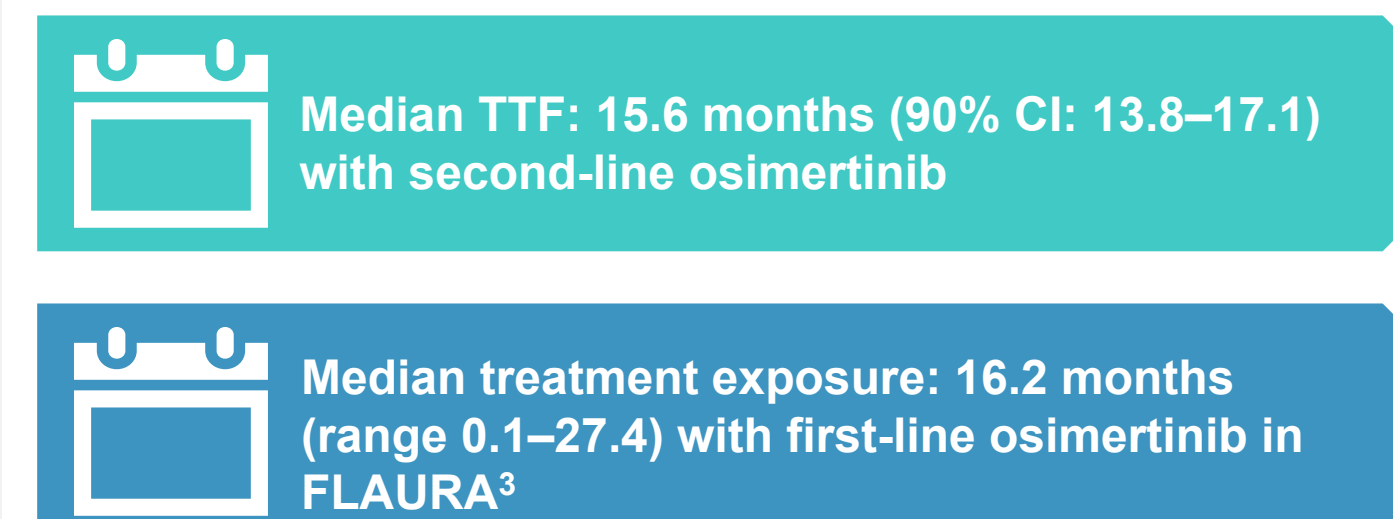


TTF: patients with Del19-positive tumors



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

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