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1532P

Afatinib followed by osimertinib in patients with *EGFR* mutation-positive (*EGFR*m+) advanced NSCLC: updated data from the GioTag real-world study

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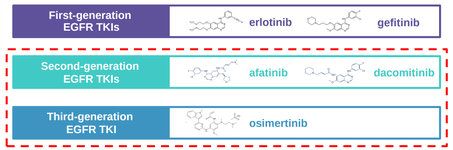
Introduction

EGFR TKIs in NSCLC

- EGFR TKIs are first-line treatment of choice for patients with *EGFR*m+ NSCLC
- Three generations of EGFR TKI are now widely available

EGFRm+, EGFR mutation-positive; TKI, tyrosine kinase inhibitor

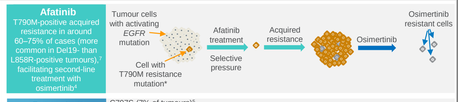


- Second- (afatinib and dacomitinib)[1,2] and third-generation (osimertinib)[3] EGFR TKIs have demonstrated superior PFS over first-generation EGFR TKIs
- However, the best first-line treatment choice and treatment sequence to maximise OS for patients with *EGFR*m+ NSCLC is currently unknown

Acquired resistance to EGFR TKIs

- The gatekeeper *EGFR* T790M mutation is a common resistance mechanism to first- and second-generation EGFR TKIs[4]
- Multiple mechanisms for resistance to osimertinib are reported, but no putative resistance mechanism has been detected in ~60% of cases[5,6]

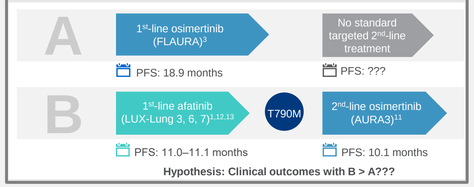
OS, overall survival; PFS, progression-free survival



*T790M cells can be present in small numbers prior to treatment and can also emerge during treatment[10]

Rationale for sequential afatinib and osimertinib

- Most patients progressing on afatinib will be eligible for second-line treatment with osimertinib
- Osimertinib has shown first- and second-line (against T790M) activity[3,11]
- There is currently no standard targeted treatment for patients progressing on osimertinib



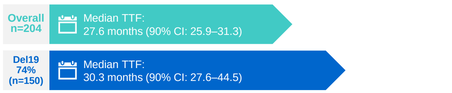
Hypothesis: Clinical outcomes with B > A???

Introduction (cont'd)

The GioTag study: original analysis

- GioTag is a global observational study assessing clinical outcomes in patients treated with first-line afatinib and second-line osimertinib after detection of T790M

- In the original analysis of the GioTag study, promising TTF was reported in patients treated with afatinib and sequential osimertinib in everyday clinical practice[14]
- Outcomes were particularly promising in Asian patients and patients with tumours harbouring a Del19 mutation



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

CI, confidence interval; NR, not reached; TTF, time to treatment failure

Objective

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

Methods

- The GioTag study is a global observational study across 10 countries (Austria, Canada, Israel, Italy, Japan, Singapore, Slovenia, Spain, Taiwan and the USA)[14]
- A maximum of 15 consecutive patients were enroled from each site

The first global, observational study to evaluate outcomes of patients who received first-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*m+ (Del19/L858R) TKI-naïve advanced NSCLC and were treated with first-line afatinib, developed T790M-mediated acquired resistance, and received second-line osimertinib treatment
- **Primary outcome:** TTF
- **Exploratory outcome:** OS

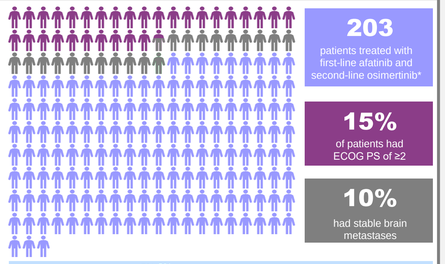
- This interim updated analysis (database lock April 2019) was performed when 42% of patients had experienced an OS event. TTF was also reanalysed
- Updated data were collected from available electronic health records from 94 patients (all from the USA)
- Final analysis, incorporating manual chart reviews from an additional 29 patients, is anticipated in early 2020

Results

Patients

- Baseline characteristics of the GioTag patients have been described previously[14]
- Patients who are often excluded from clinical trials e.g. those with ECOG PS of ≥2, or those with brain metastases, were included
- Patients had diverse ethnicity; most patients were Caucasian, but the study included Asians and African Americans
- At the start of afatinib treatment, 74% of patients had *EGFR* Del19-positive tumours

ECOG PS, Eastern Cooperative Oncology Group performance status

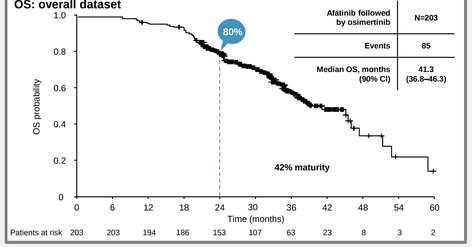


*One patient was excluded from the updated analysis due to reports of conflicting data

Overall survival

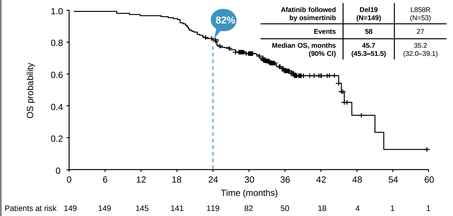
- Median follow-up was 30.3 months (interquartile range 24.0–36.8)
- In this broad patient population, median OS was almost 3.5 years
- 80% of patients were still alive after 2 years
- In patients who received the approved 40 mg/day dose of afatinib, median OS was 45.3 months (90% CI 37.6–47.6)

OS: overall dataset



Results (cont'd)

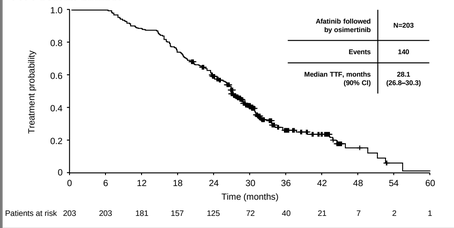
OS: patients with Del19-positive tumours



- Median OS was almost 4 years in patients with Del19-positive tumours
- In patients with Del19-positive tumours who received afatinib 40 mg/day, median OS was 45.7 months (90% CI 45.3–47.6)

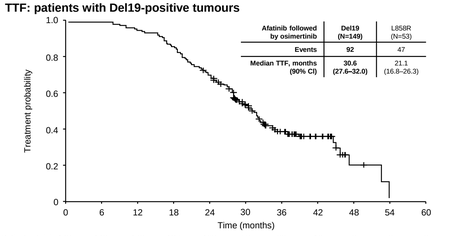
Time to treatment failure

TTF: overall dataset



- Median TTF was similar to that reported for the original analysis

TTF: patients with Del19-positive tumours



Results (cont'd)

Treatment with osimertinib

Median TTF: 15.6 months (90% CI: 13.8–17.1) with second-line osimertinib

Median treatment exposure: 16.2 months (range 0.1–27.4) with first-line osimertinib in FLAURA[3]

- Of note, prior treatment with afatinib did not appear to preclude prolonged TTF with second-line osimertinib (15.6 months)
- In the FLAURA trial, median exposure to osimertinib in a first-line setting was 16.2 months[3]

Key findings and conclusions

- In this updated analysis of GioTag, median OS was almost 3.5 years, and the 2-year OS rate was 80%
- In patients with Del19-positive tumours, median OS was almost 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 second-line setting following afatinib
- These data, along with high rate of emergence of T790M in patients treated with afatinib, especially in patients with Del19-positive disease (~75%),[7] 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*m+ NSCLC

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Data were originally presented in part at WCLC 2019; Hochmair et al. Poster P1.01-118. *Corresponding author email address: Maximilian.Hochmair@wienkav.at