Named patient use program for afatinib in advanced NSCLC with progression on prior therapy: experience from Asian centers

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Background

- Afatinib, an irreversible ErbB family inhibitor, is approved in several countries worldwide for patients with non-small-cell lung cancer (NSCLC) with sensitizing *EGFR* mutations[1,2]
- A global named-patient-use (NPU) program for afatinib in patients with advanced/metastatic NSCLC took place between 2010 and 2016
  - The main objective was to provide compassionate access to treatment for patients with no other options
  - Data were provided on a voluntary basis without onsite monitoring or data cleaning
- 5636 patients from 49 countries received afatinib; results were previously published for 3966 patients (omitting data for Taiwan)
  - Median time-to-treatment-failure (TTF) was 4.4 months (n=2862)
  - Objective response rate (ORR) was 23% (267/1141)[3]
- Here we summarize treatment outcomes for patients who received afatinib in the NPU program at centers in 10 Asian countries

Methods

Patients

- The study design has been described previously[3]
- Patients were eligible for inclusion if they had advanced/metastatic NSCLC, had progressed after achieving clinical benefit (≥stable disease [SD] lasting ≥6 months) during erlotinib/gefitinib therapy and/or had an activating *EGFR* or *HER2* mutation, had exhausted other treatment options, and were ineligible for afatinib trials

Afatinib dose

- The recommended starting dose was 50 mg oral afatinib once daily
  - Lower starting doses (30/40 mg once daily) were allowed, at the discretion of the treating physician
  - Tolerability-guided dose modifications were allowed (10 mg steps: maximum 50 mg/day, minimum 30 mg/day)
  - Afatinib treatment was continued as long as deemed beneficial by the treating physician

Methods

Outcome measures

TTF	Time from initiation of afatinib to discontinuation, switch to another drug, death or end of available data (whichever occurred first)
ORR	Patients with CR or PR (as a proportion of the total number of patients with a recorded response)
DCR	Patients with CR, PR, or SD (as a proportion of the total number of patients with a recorded response)
Safety	At minimum, serious AEs, AEs leading to discontinuation, and drug-related AEs

AEs, adverse events; CR, complete response; DCR, disease control rate; ORR, objective response rate; PR, partial response; SD, stable disease; TTF, time to treatment failure.

Data capture & analysis

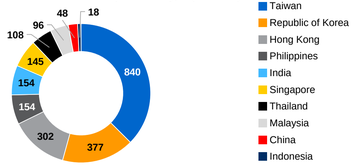
- Information collected by participating physicians: age, gender, comorbidities, disease stage, prior therapies, *EGFR* mutation status (including the presence of common [del19 or L858R], uncommon [ex20ins, L861Q, G719X, T790M, or S768I] and *HER2* mutations
- Data were analyzed using SAS® (Version 9.4, SAS Institute, Inc., NC, USA)

Results

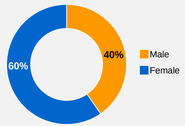
Patients

- Data for this analysis were derived from 2242 NSCLC patients from 10 Asian countries (data cut-off, 18 January 2016)

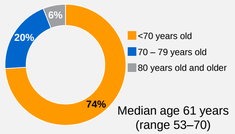
Patients enrolled per country, n (N=2242)



Gender (%) (N=2220)



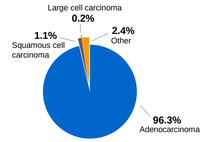
Age (%) (N=2192)



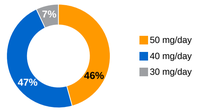
Median age 61 years (range 53–70)

Results

Histology (%) (N=1924)



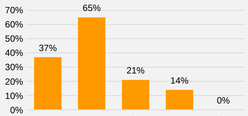
Starting dose (%) (N=1333)



Previous therapies

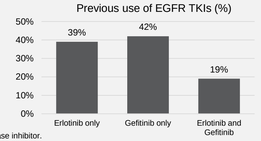
- 99% (2223/2242 patients) had received previous lines of therapy

Previous lines of systemic therapy (%)



- Median = 3 lines (IQR 2–4)
- 99% (2202/2223) had previously been treated with erlotinib or gefitinib

Previous use of EGFR TKIs (%)

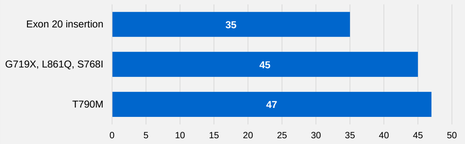


IQR, interquartile range; TKI, tyrosine kinase inhibitor.

Mutation status

- 97% of 1281 patients for whom information was available had an *EGFR* mutation
- Of those with specified mutations (n=1101), 93.9% had common mutations (del19, L858R) and 10.6% had uncommon mutations (some had multiple mutations)
- 12 patients had *HER2* mutations (none of these patients had *EGFR* mutations)
- All patients with specified *HER2* mutations (n=7) had p.A775_G776insYVMA

Uncommon *EGFR* mutations, n (N=117)



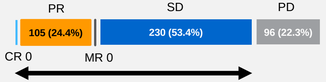
Data are numbers of patients with uncommon mutations (multiple uncommon mutations were reported in some patients)
EGFR, epidermal growth factor receptor.

Results

Response to afatinib

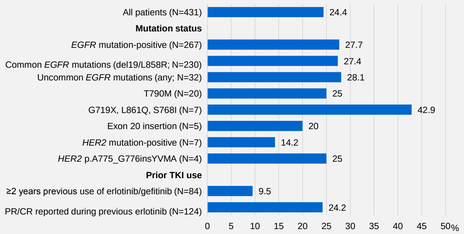
- ORR was 24.4% overall

Response to afatinib,* n (%)



*Based on 431 patients with response information available.
CR, complete response; DCR, disease control rate; MR, mixed response; PD, progressive disease; PR, partial response; SD, stable disease.

ORR by subgroup (%)



Data are number of responders, expressed as a % of the number of patients with response data in each subgroup.
CR, complete response; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; ORR, overall response rate; PR, partial response; TKI, tyrosine kinase inhibitor.

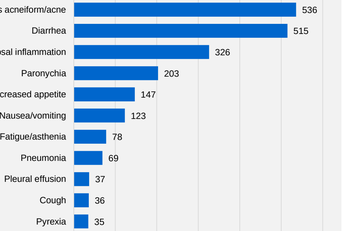
Time-to-treatment-failure (TTF)

	N	Median TTF, months (IQR)
Total	1550	7.6 (2.6–24.3)
Mutation status		
EGFR mutation-positive	834	7.2 (2.5–22.6)
Specified *EGFR* mutation (common or uncommon)	740	6.5 (2.3–22.4)
Common *EGFR* mutations (del19 or L858R)	692	6.4 (2.3–22.4)
Uncommon *EGFR* mutations (any)	83	8.4 (1.9–22.4)
T790M	35	5.9 (1.9–10.8)
G719X, L861Q, S768I	28	7.8 (0.8–25.4)
Exon 20 insertion	23	18.9 (8.5–27.4)
HER2 mutation-positive	12	12.2 (2.6–25.2)
p.A775_G776insYVMA	7	12.4 (4.0–15.8)
Prior TKI use		
≥2 years previous erlotinib/gefitinib	338	10.2 (3.5–26.5)
Any previous erlotinib	922	8.7 (2.8–25.2)
PR/CR during previous erlotinib	383	8.2 (2.6–23.5)

CR, complete response; EGFR, epidermal growth factor receptor; IQR, interquartile range; PR, partial response; TKI, tyrosine kinase inhibitor; TTF, time to treatment failure.

Results

Most common adverse events, n (N=2242)



Data are numbers of patients with each adverse event.

Conclusions

- This analysis of outcomes for Asian countries in the afatinib NPU program revealed clinically meaningful ORRs and TTF in this heavily pre-treated and resistant/refractory NSCLC population
  - Including activity in patients with both common and uncommon *EGFR* mutations
- After failure on prior EGFR TKIs, TTF with afatinib was numerically longer in patients with uncommon *EGFR* mutations and *HER2* mutations, compared with common *EGFR* mutations
- The safety profile of afatinib was consistent with that reported from non-Asian centers

References

1. Boehringer Ingelheim Pharmaceuticals, Inc. Gilotrif® Full Prescribing Information. January 2018.
2. Boehringer Ingelheim Pharmaceuticals, Inc. Giotrif® Summary of Product Characteristics. July 2018.
3. Cappuzzo F, et al. Future Oncol 2018;14:1477–86.

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https://tinyurl.com/y77fnbnl

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