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Effectiveness of afatinib in clinical practice - first results of the GIDEON trial: a prospective non-interventional study in *EGFR*-mutated NSCLC in Germany

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Introduction

- Afatinib irreversibly inhibits signalling via all homo- and hetero-dimers formed by receptors of the ERBB family[1]
- Afatinib is approved for the treatment of EGFR tyrosine kinase inhibitor (TKI)-naïve patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating *EGFR* mutation(s)[2]
- Numerous randomized clinical trials (RCTs) have shown significantly improved efficacy outcomes with afatinib compared with chemotherapy or other EGFR TKIs, and a manageable safety profile[3–6]
- While RCTs are essential for determining the efficacy and safety of a drug, the conditions/recruitment strategy in these studies is usually stringent and may differ from those in real-world clinical practice
- Non-interventional studies (NIS) are important to learn about various aspects of drug use under real-life conditions, including effectiveness, safety and tolerability[7]
- Here we report the first interim analysis of the GIDEON NIS, which was initiated to investigate the effectiveness and tolerability of first-line afatinib treatment in routine clinical use in Germany

Methods

- Recruitment into the GIDEON NIS was initiated following launch of afatinib in Germany in February 2014
  - First patient in: April 2014
  - Last patient in: December 2016
- 160 patients were recruited at 49 centres across Germany (Fig. 1)
- Patient inclusion criteria:
  - Confirmed *EGFR* mutation
  - EGFR TKI-naïve

Figure 1. Patient recruitment centres.

Endpoints

Primary	• Progression-free survival at 12 months
Key Secondary	• PFS • OS • Objective response rate (CR+PR) • Disease control rate (CR+PR+SD)

CR, complete response; *EGFR*m+, *EGFR* mutation-positive; NIS, non-interventional study; OS, overall survival; PFS, progression-free survival; PR, partial response; RCT, randomised clinical trial; SD, stable disease; TKI, tyrosine kinase inhibitor

Results

Patient demographics and baseline characteristics

- 160 patients were recruited, 151 of whom received the study drug and were included in the analysis (Table 1)
- Patients were mostly female (68%); the median age was 67 years
- Patients mostly had Stage IV disease (84.1%), ECOG PS 0–1 (94.7%)
- *EGFR* mutation analysis revealed that:
  - The majority of patients (64.9%) had a deletion in Exon 19 (del19)
  - 21.8% had tumours harbouring L858R mutations; 13.2% had other *EGFR* mutations in exons 18–21; no patient had a *de novo* T790M

Table 1. Patient demographics and baseline characteristics

		GIDEON NIS (n=151)
Gender (n, %)	Female	103 (68.2%)
Age, years; median (range)		67.0 (38–89)
Age groups/years; n (%)	<65	60 (39.7%)
	≥65	91 (60.3%)
	≥70	67 (44.4%)
	≥75	43 (28.5%)
Stage (baseline); n (%)	IIIB	22 (14.6%)
	IV	127 (84.1%)
	Missing	2 (1.3%)
ECOG PS; n (%)	0–1	136 (90.1%)
	>1	7 (4.6%)
	Missing	8 (5.3%)
***EGFR* mutation; n (%)**	Del19	98 (64.9%)
	L858R	33 (21.8%)
	Others* (Exon 18–21)	20 (13.2%)

*No T790M mutations were present.

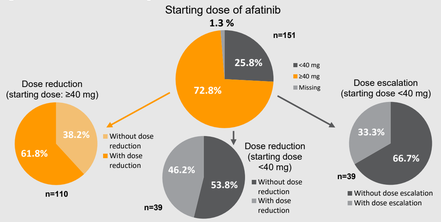
Afatinib starting dose and dose modifications (Fig. 2)

- The majority of patients (72.8%) started at ≥40 mg, and 25.8% started at <40 mg
- Among patients starting at ≥40 mg:
  - 61.8% had a dose reduction
- Among patients starting at <40 mg:
  - 46.2% had a dose reduction
  - 33.3% had a dose increase

ECOG PS, Eastern Cooperative Oncology Group performance status

Results

Figure 2. Afatinib starting dose and dose modification



ORR and DCR

- ORR was 73% and DCR was 90% (Fig. 3)
- There was little variability in ORR (65–83%) and DCR (89–93%) between patient subgroups (Fig. 4)
  - Both ORR and DCR were similar in patients with different types of mutations (Del19, L858R, or uncommon), with or without baseline brain metastases, and with a starting dose of 40 mg or <40 mg

Figure 3. Best response to afatinib, by investigator assessment.

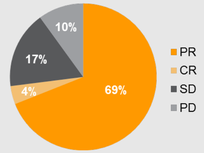
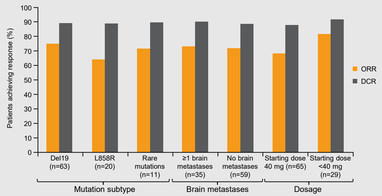


Figure 4. ORR and DCR in patient subgroups.



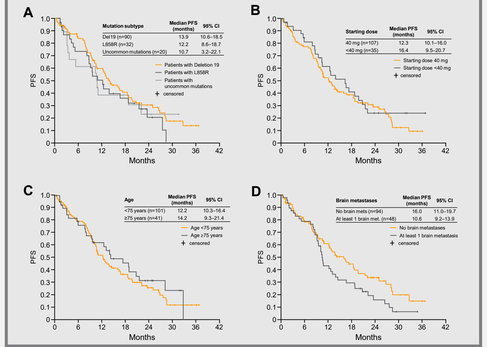
DCR, disease control rate; ORR, objective response rate; PD, progressive disease

Results

Progression-free survival

- The PFS rate at 12 months was 54.6%
- Overall median PFS was 12.9 months

Figure 5. PFS, by (A) mutation subtype, (B) starting dose, (C) age, and (D) baseline brain metastases.

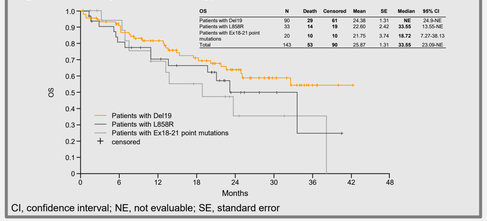


Preliminary OS results

OS by mutation subtype

- Preliminary OS data (median maturity: 23.36 months; 1-year maturity rate: 78.7%) show a median survival of over 33 months in the overall population; the median for Del19 patients has not been reached

Figure 6. OS, by mutation subtype.



CI, confidence interval; NE, not evaluable; SE, standard error

Safety

- The safety profile of afatinib was consistent with the known safety profile identified by the LUX-Lung 3, 6, and 7 clinical trials
- The most common grade 3/4 adverse events were diarrhoea (21%), dermatitis acneiform (9%), and stomatitis (3%)
- 11.6% of patients discontinued due to adverse drug reactions

Key findings and conclusions

- The first results of this prospective NIS confirm the robust clinical data for afatinib in the routine clinical setting, especially in the elderly population, which is underrepresented in clinical trials
- Although a high number of patients with brain metastases (~30%) and uncommon *EGFR* mutations (~13%) were included in GIDEON, afatinib showed robust response rates across all patient subgroups and with a median PFS of 12.9 months
- In selected patients, a starting dose of <40 mg afatinib does not seem associated with an inferior PFS compared with 40 mg
- ORR and DCR were similar to the values reported for afatinib in the LUX-Lung 3, 6, and 7 studies
- The safety profile of afatinib in this NIS was consistent with that determined in the LUX-Lung 3, 6, and 7 studies
- Preliminary OS analyses showed a median OS of 33 months in the overall population
- Final results are expected in 2019, including multivariate analyses and data for the TKI sequence of afatinib followed by osimertinib

References

1. Solca F, et al. J Pharmacol Exp 2012;343:342–50.
2. Boehringer Ingelheim Pharmaceuticals, Inc. Giotrif® Summary of Product Characteristics. May 2018.
3. Sequist LV, et al. J Clin Oncol 2013;31:3327–34.
4. Wu YL, et al. Lancet Oncol 2014;15:213–22.
5. Park K, et al. Lancet Oncol 2016;17:577–89.
6. Soria JC, et al. Lancet Oncol 2015;16:141–51.
7. Mishra D, Vora J. Perspect Clin Res 2010;1:128–33.

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Presented at the European Society of Medical Oncology (ESMO), Munich, Germany, 19–23 October 2018

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 Hashem Dbouk, of GeoMed, an Ashfield company, part of UDG Healthcare plc, during the development of this poster.
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