Scan the QR code for an electronic copy of the poster and supplementary material

Afatinib versus erlotinib as second-line treatment of patients with advanced squamous cell carcinoma of the lung: final analysis of the global Phase III LUX-Lung 8 trial

1442P

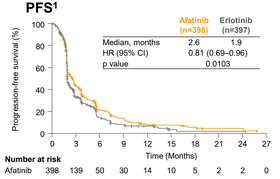
Glenwood D Goss[1*], Manuel Cobo[2], Shun Lu[3], Konstantinos Syrigos[4], Ki Hyeong Lee[5], Erdem Göker[6], Vassilis Georgoulias[7], Dolores Isla[8], Alessandro Morabito[9], Young J Min[10], Andrea Ardizzoni[11], Agnieszka Cseh[12], Shaun Bender[13], Enriqueta Felip[14]

[1]University of Ottawa, Ottawa, Canada; [2]Hospital Carlos Haya, Malaga, Spain; [3]Shanghai Chest Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China; [4]Athens School of Medicine, Athens, Greece; [5]Chungbuk National University College of Medicine, Cheongju, South Korea; [6]Ege University Faculty of Medicine, Izmir, Turkey; [7]University Hospital of Heraklion, Heraklion, Crete, Greece; [8]Hospital Lozano Blesa, Zaragoza, Spain; [9]Istituto Nazionale Tumori – IRCCS "Fondazione G. Pascale", Naples, Italy; [10]Ulsan University Hospital, Ulsan, South Korea; [11]Policlinico S. Orsola, Bologna, Italy; [12]Boehringer Ingelheim RCV GmbH & Co. KG, Vienna, Austria; [13]Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, USA; [14]Vall d'Hebron University Hospital, Barcelona, Spain

Background

- In the primary analysis of LL8 (data cut-off: April 2015), second-line afatinib improved outcomes vs erlotinib in patients with SCC of the lung[1]

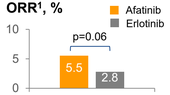
PFS[1]



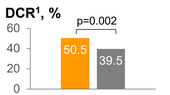
	Afatinib (n=398)	Erlotinib (n=397)
Median, months	2.6	1.9
HR (95% CI)	0.81 (0.69–0.96)	
p value	0.0103	

Number at risk										
Afatinib	398	139	50	30	14	10	5	2	2	0
Erlotinib	397	99	34	17	10	2	1	1	1	0

ORR[1], %



DCR[1], %

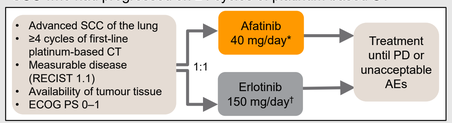


- Based on these findings, afatinib is approved for the treatment of patients with locally advanced or metastatic NSCLC of squamous histology progressing on or after platinum-based CT
- PFS and OS benefits on afatinib appeared even greater for pts with ErbB mutation-positive tumours vs ErbB wild-type tumours[2]
- Afatinib was also associated with improvements in PROs and symptoms versus erlotinib[3]
- Here we present the final analysis of OS and safety data
  - Other key efficacy endpoints had already been met[1] and in order to reduce time to trial closure, were not included in the final analysis
  - As of April 2015, only 9 (1%) pts remained on treatment, so minimal changes would be expected

CT, chemotherapy; DCR, disease control rate; HR, hazard ratio; LL8, LUX-Lung 8; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PROs, patient-reported outcomes; SCC, squamous cell carcinoma

Methods[1]

- This open-label, Phase III trial enrolled patients with stage IIIB/IV lung SCC who had progressed on ≥4 cycles of platinum-based CT



- Primary endpoint: PFS (independent review); key secondary endpoint: OS; other endpoints included ORR, DCR and safety
- Clinical outcomes for patients with long-term disease control were assessed based on:
  - Tumour genetic analysis (frequency of mutations in individual genes)
  - The VeriStrat®[4,5] serum protein test (used to assign a VeriStrat-Good [VS-G] or VeriStrat-Poor [VS-P] classification to each sample)

AE, adverse event; ECOG PS, Eastern Cooperative Oncology Group performance status; PD, progressive disease; RECIST, Response Evaluation Criteria in Solid Tumours
*Dose escalation to 50 mg and reduction to 30 or 20 mg permitted. †Dose reduction to 100 or 50 mg permitted

Results

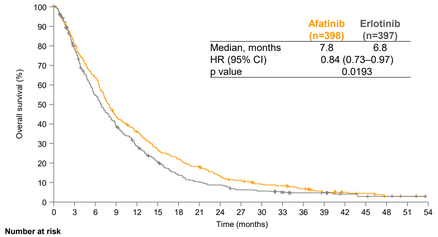
Baseline characteristics[1]

- 795 patients were included (398 on afatinib; 397 on erlotinib)
- Baseline characteristics were well balanced between arms

Efficacy

- Updated OS (data cut-off: March 2018) was significantly longer for afatinib than erlotinib (Fig. 1 and 2)

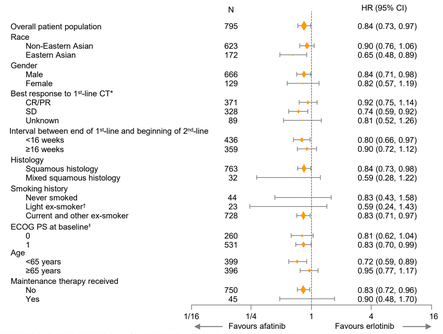
Figure 1: Overall survival



	Afatinib (n=398)	Erlotinib (n=397)
Median, months	7.8	6.8
HR (95% CI)	0.84 (0.73–0.97)	
p value	0.0193	

Number at risk																												
Afatinib	398	317	250	170	138	103	85	68	49	40	31	29	22	13	8	6	2	2	0									
Erlotinib	397	305	210	150	108	75	51	37	32	22	19	15	11	10	5	3	2	0	0									

Figure 2: Overall survival by subgroup



*Seven patients had a best response of PD; †<15 pack years + stopped >1 year before diagnosis; ‡Four patients had ECOG PS of 2 at baseline (protocol violations)

Results

Safety

- Overall AE profile was comparable between arms (afatinib vs erlotinib):
  - AEs ≥ Grade 3 (G3): 57.4% vs 57.5%
  - Serious AEs: 44.4% and 44.3%
- Incidence of drug-related ≥G3 diarrhoea and stomatitis was higher on afatinib, rash/acne was higher on erlotinib (Table 1)
- Proportion of patients with AEs leading to dose reduction was higher for afatinib (26.5 vs 14.2%)
- AEs leading to treatment discontinuation were comparable across arms (20.4 vs 16.7%)
  - AEs leading to ≥1% discontinuation: diarrhoea (4.1 vs 1.5%), rash/acne‡ (2.6 vs 2.0%), malignant neoplasm progression (1.8 vs 0.5%), pneumonia (1.5 vs 0.3%), dyspnoea (1.3 vs 1.5) and stomatitis‡ (1.0 vs 0%)

Table 1. Drug-related AEs (>10%)

	Afatinib n=392, %		Erlotinib n=395, %	
AE category	All	≥Grade 3*	All	≥Grade 3†
Total with related AEs	93	28	82	18
Diarrhoea	70	10	34	3
Rash/acne‡	67	6	68	10
Stomatitis‡	28	4	8	0
Fatigue‡	8	1	7	1
Decreased appetite	13	1	10	1
Nausea	13	1	7	1
Paronychia‡	10	1	4	<1

*Six patients (1.5%) in the afatinib group had drug-related fatal AEs: interstitial lung disease (two patients) and pneumonia, respiratory failure, acute renal failure and general physical health deterioration (one patient each); †Five patients (1.3%) in the erlotinib group had drug-related fatal AEs: interstitial lung disease, intestinal obstruction, pneumonia, pneumonitis and peritonitis (one patient each); ‡Grouped terms

Patients with long-term disease control (≥12 months' treatment) on afatinib: n=21

- Baseline characteristics were similar to the overall LL8 afatinib-treated population
- Tumour genetic analysis indicated certain aberrations, particularly ErbB family, were more common than in the overall afatinib-treated population (Fig. 3 and 4)
- At data cut-off, all patients had discontinued study treatment
  - No discontinuations were due to AEs
- 6/21 patients dose-reduced to 30 mg; three further reduced to 20 mg
- The frequency of dose-reductions due to diarrhoea (19.0%), rash/acne (4.8%), and stomatitis (4.8%) was similar to the overall afatinib-treated population

Scan the QR code below for additional content: Afatinib dose over time in patients with long-term disease control

Figure 3. ErbB family short variant mutations

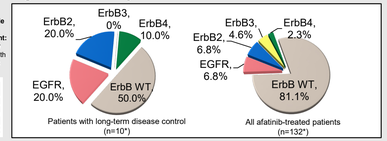
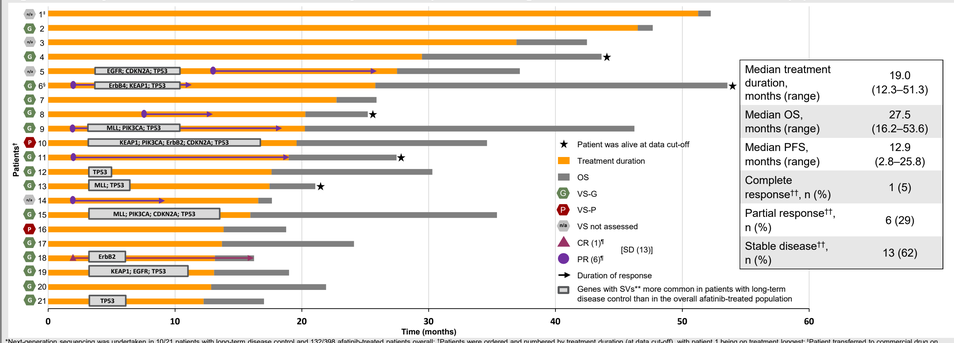


Figure 4. Efficacy outcomes and biomarkers more commonly observed in patients with long-term disease control than in the overall LL8 population



Median treatment duration, months (range)	19.0 (12.3–51.3)
Median OS, months (range)	27.5 (16.2–53.6)
Median PFS, months (range)	12.9 (2.8–25.8)
Complete response††, n (%)	1 (5)
Partial response††, n (%)	6 (29)
Stable disease††, n (%)	13 (62)

*Next-generation sequencing was undertaken in 10/21 patients with long-term disease control and 132/398 afatinib-treated patients overall; †Patients were ordered and numbered by treatment duration (at data cut-off), with patient 1 being on treatment longest; ‡Patient also had rearrangements in two genes; §First observed response at time of tumour measurement; **≥1 SV present in at least 3/10 patients with long-term disease control, or part of the ErbB family (EGFR, ErbB2, ErbB3, ErbB4); ††One patient was not evaluable
SV, short variant; WT, wild-type

Summary

- Results from the final analysis of LL8 are consistent with those previously reported
- Updated OS was significantly longer with afatinib than erlotinib
  - Median 7.8 vs 6.8 months (HR 0.84, p=0.019)
- The tolerability profile was comparable across arms and AEs were manageable
- Twenty-one patients had long-term disease control (≥12 months)
  - Median treatment duration: 19.0 months
  - Median OS: 27.5 months
- ErbB family mutations were more frequent in patients with long-term disease control

Conclusions

- These data position afatinib as a treatment option for patients with SCC of the lung progressing on chemotherapy, particularly those with ErbB family genetic aberrations
- Afatinib has a well established, predictable tolerability profile, which is manageable with supportive care and tolerability-guided dose reductions, and long-term treatment is well tolerated

References

1. Soria JC, et al. Lancet Oncol 2015;16:897–907.
2. Goss GD, et al. JAMA Oncol 2018;4:1189–97.
3. Felip E, et al. Clin Lung Cancer. 2018;19:74-83.e11.
4. Gregorc V, et al. Lancet Oncol 2014;15:713–21.
5. Taguchi F, et al. J Natl Cancer Inst 2007;99:838–46.

Scan the QR code for an electronic copy of the poster and supplementary content†

†These materials are for personal use only and may not be reproduced without written permission of the authors and the appropriate copyright permissions

Presented at the European Society For Medical Oncology (ESMO) congress, Munich, Germany, October 19–23, 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 Christina Jennings, of GeoMed, an Ashfield company, part of UDG Healthcare plc, during the development of this poster.
*Corresponding author email address: ggoss@toh.ca