Quality of life (QoL) analysis from ENSURE, a phase 3, open-label study of first-line erlotinib versus gemcitabine/cisplatin (GP) in Asian patients with epidermal growth factor receptor (*EGFR*) mutation-positive non-small-cell lung cancer (NSCLC)

Yi-long Wu,[1] Caicun Zhou,[2] Gang Wu,[3] Xiaoqing Liu,[4] Zhaoyang Zhong,[5] Shun Lu,[6] Marie Cherry Lynn Fernando,[7] Chong-Kin Liam,[8] Meng Chen,[9] Yunxia Zuo[9]

[1]Guangdong Lung Cancer Institute, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangdong, China; [2]Department of Oncology, Affiliated Shanghai Pulmonary Hospital of Tongji University, Shanghai, China; [3]Department of Cancer, Union Hospital of Tongji Medical College, Wuhan, China; [4]Internal Medicine Tumor Department, 307 Hospital of the Academy of Military Medical Sciences, Beijing, China; [5]Cancer Centre, Research Institute of Surgery, Daping Hospital, Third Military Medical University, Chongqing, China; [6]Department of Lung Cancer, Shanghai Chest Hospital, Shanghai, China; [7]Manila Doctors Hospital, Manila, the Philippines; [8]Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; [9]Roche (China) Holding Ltd

Disclosures

- Yi-long Wu has received speaker fees from Roche, Eli Lilly, AstraZeneca and Sanofi
- Shun Lu has received speaker fees from Boehringer Ingelheim, AstraZeneca, Eli Lilly and Roche
- Meng Chen and Yunxia Zuo are employees of F. Hoffmann-La Roche Ltd
- Caicun Zhou, Gang Wu, Xiaoqing Liu, Zhaoyang Zhong, Marie Cherry Lynn Fernando and Chong-Kin Liam declare no conflicts of interest
- Support for third-party writing assistance was provided by F. Hoffmann-La Roche Ltd

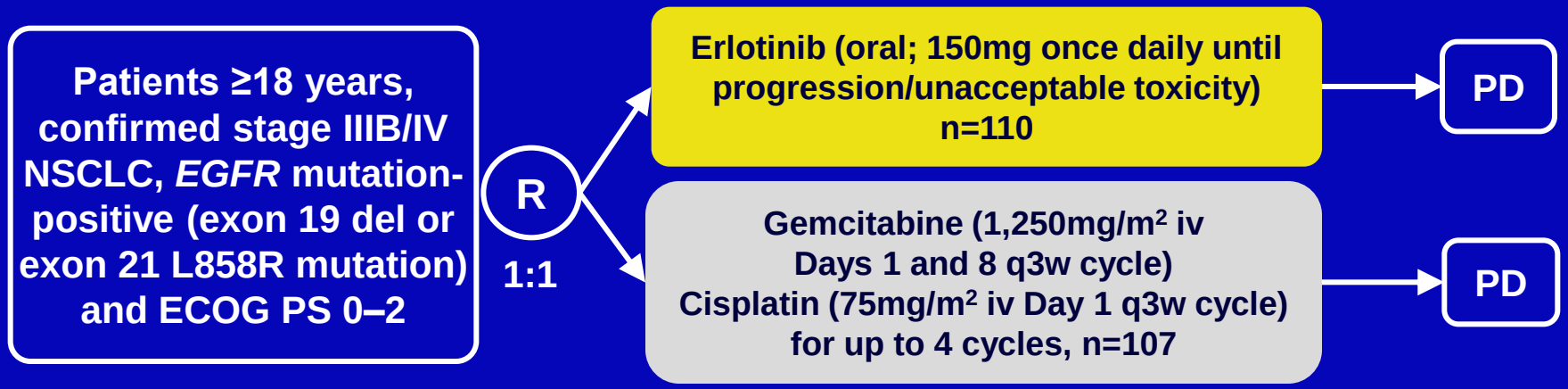
Background

- Erlotinib is an EGFR TKI with proven efficacy in advanced NSCLC,[1] providing superior first-line efficacy to chemotherapy for patients whose tumours harbour activating *EGFR* mutations[2,3]
- The phase 3, randomised, open-label ENSURE study evaluated first-line erlotinib versus GP in patients from China, Malaysia and the Philippines with *EGFR* mutation-positive NSCLC
- Patients with confirmed *EGFR* mutation-positive NSCLC were randomised 1:1 to receive erlotinib or GP
  - patients were stratified by mutation type, ECOG PS, gender and country
- Primary endpoint: PFS
- Secondary endpoints: ORR, DCR, OS, safety and QoL

DCR = disease control rate; ECOG PS = European Cooperative Oncology Group performance status; ORR = objective response rate
OS = overall survival; PFS = progression-free survival
TKI = tyrosine-kinase inhibitor

1. Shepherd F, et al. NEJM 2005
2. Rosell R, et al. Lancet Oncol 2012
3. Zhou C, et al. Lancet Oncol 2011

Methods

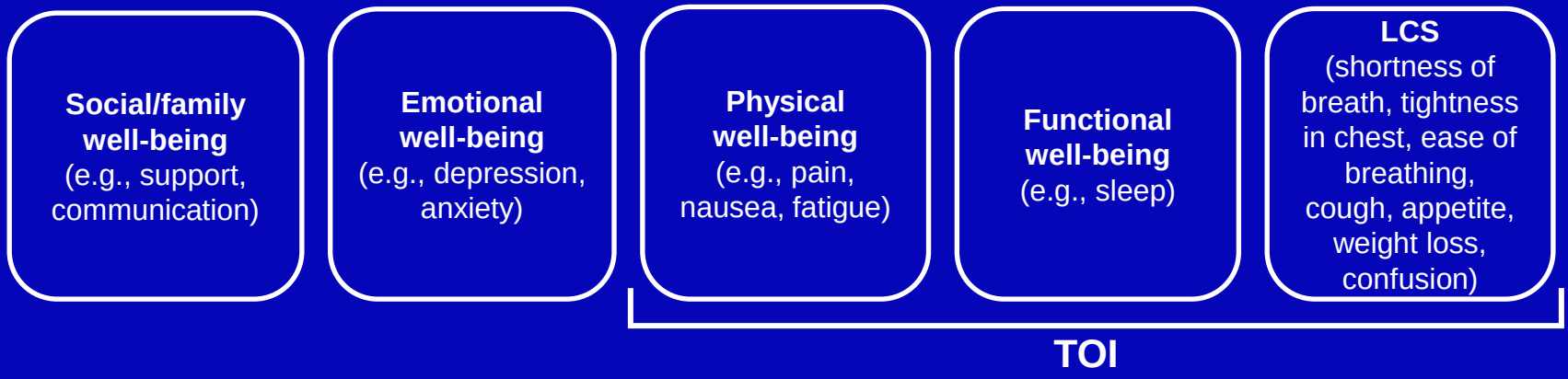


- Stratification factors: mutation type, ECOG PS, gender and country
- QoL was assessed using FACT-L every 6 weeks until Week 25, then every 12 weeks until PD
- The FACT-L questionnaire results were used to calculate
  - time to symptomatic progression (≥3-point decline in LCS score from baseline)
  - time to deterioration in TOI (≥6-point decline in TOI from baseline: LCS score plus physical and functional scores)
  - time to deterioration in QoL (≥6-point decline in QoL from baseline: TOI score plus social and emotional scores)
- Data cut-off for the QoL analysis was 19 November 2012

FACT-L = functional assessment of cancer therapy-lung; LCS = lung cancer subscale
iv = intravenously; PD = disease progression; R = randomised; TOI = trial outcome index; q3w = every 3 weeks

Quality of life

- QoL is important in assessing treatment benefit: it examines the balance between efficacy and tolerability, and the impact on patients' daily lives
- Many oncologists are unwilling to prolong survival at the expense of worsening QoL, especially in advanced disease where the palliative aspect of treatment is an important consideration
- In advanced disease, treatment benefit may not only be an improvement in symptoms, but also a delay in the progression of symptoms
  – time to symptomatic progression is part of QoL analyses
- QoL in NSCLC can be assessed by the FACT-L questionnaire, comprising domains assessing the impact on daily life in addition to lung cancer-specific symptoms



Targeted therapies can improve QoL versus chemotherapy

- Improved QoL was seen for first-line erlotinib versus GP in Chinese *EGFR* mutation-positive patients in the OPTIMAL trial[1]
  - patients receiving erlotinib experienced clinically relevant improvements in QoL versus GP in total FACT-L, TOI and LCS ($p<0.0001$)[1]
- Improved QoL was also seen in Asian patients treated with first-line gefitinib versus carboplatin/paclitaxel in the IPASS[2] trial
  - improved QoL ($p=0.01$) and TOI ($p<0.0001$) in the overall population
  - improved QoL ($p<0.0001$), TOI ($p<0.0001$) and LCS ($p=0.0003$) in the *EGFR* mutation-positive subgroup
- Improved QoL for erlotinib versus placebo ($p<0.0001$) has also been shown in the second-line setting using the EORTC QoL questionnaire[3]
- Here, the QoL analyses for first-line ENSURE are presented

EORTC = European Organisation for Research and Treatment of Cancer

1. Chen G, et al. Ann Oncol 2013
2. Mok T, et al. NEJM 2009
3. Bezjak A, et al. J Clin Oncol 2006

Baseline demographics of the ENSURE patient population

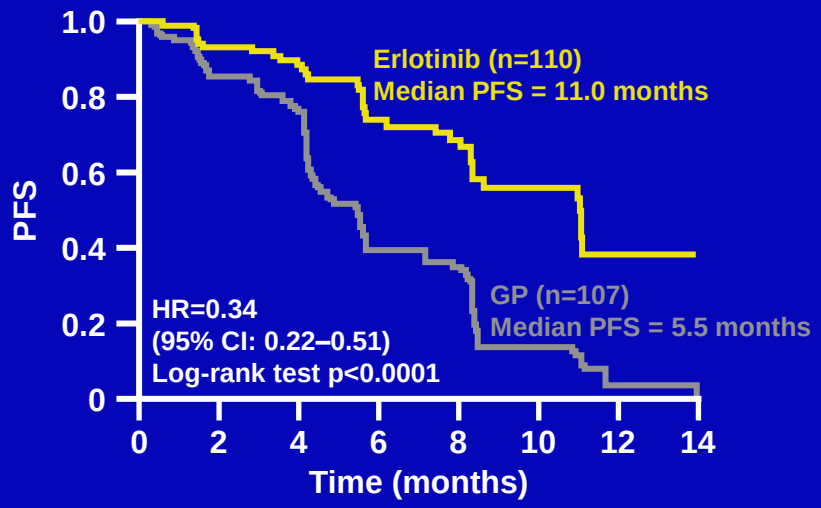
Characteristic	Erlotinib (n=110)*	GP (n=107)*
Age		
Median years (range)	57.5 (33–79)	56.0 (30–78)
<65 years, %	79.1	79.4
≥65 years, %	20.9	20.6
Gender, %		
Male	38.2	39.3
Female	61.8	60.7
ECOG PS, %	(n=109)	(n=104)
0	14.7	14.4
1	78.9	79.8
2	6.4	5.8
Smoking status, %		
Current	24.5	29.0
Former	3.6	1.9
Never	71.8	69.2
Stage, %		
IIIB	9.1	6.5
IV	90.9	93.5
Histology, %		
Adenocarcinoma	94.5	94.4
Squamous-cell carcinoma	1.8	1.9
Other	3.6	3.6
***EGFR* mutation type, %**	(n=109)	(n=107)
Exon 19 deletion	52.3	57.0
Exon 21 L858R mutation	47.7	43.0

*Unless otherwise specified

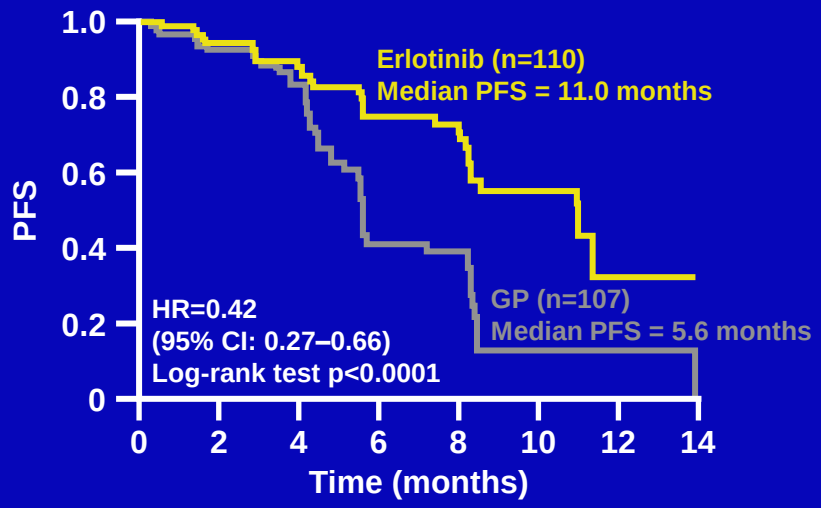
ENSURE primary endpoint

- **ENSURE met its primary endpoint of improved PFS with erlotinib versus GP**
  - **preplanned interim analysis (20 July 2012)**
    - **median PFS 11.0 vs 5.5 months (HR=0.34, 95% CI: 0.22–0.51; p<0.0001)**
    - **IRC-assessed median PFS 11.0 vs 5.6 months (HR=0.42, 95% CI: 0.27–0.66; p<0.0001)**

Investigator-assessed PFS



IRC-assessed PFS

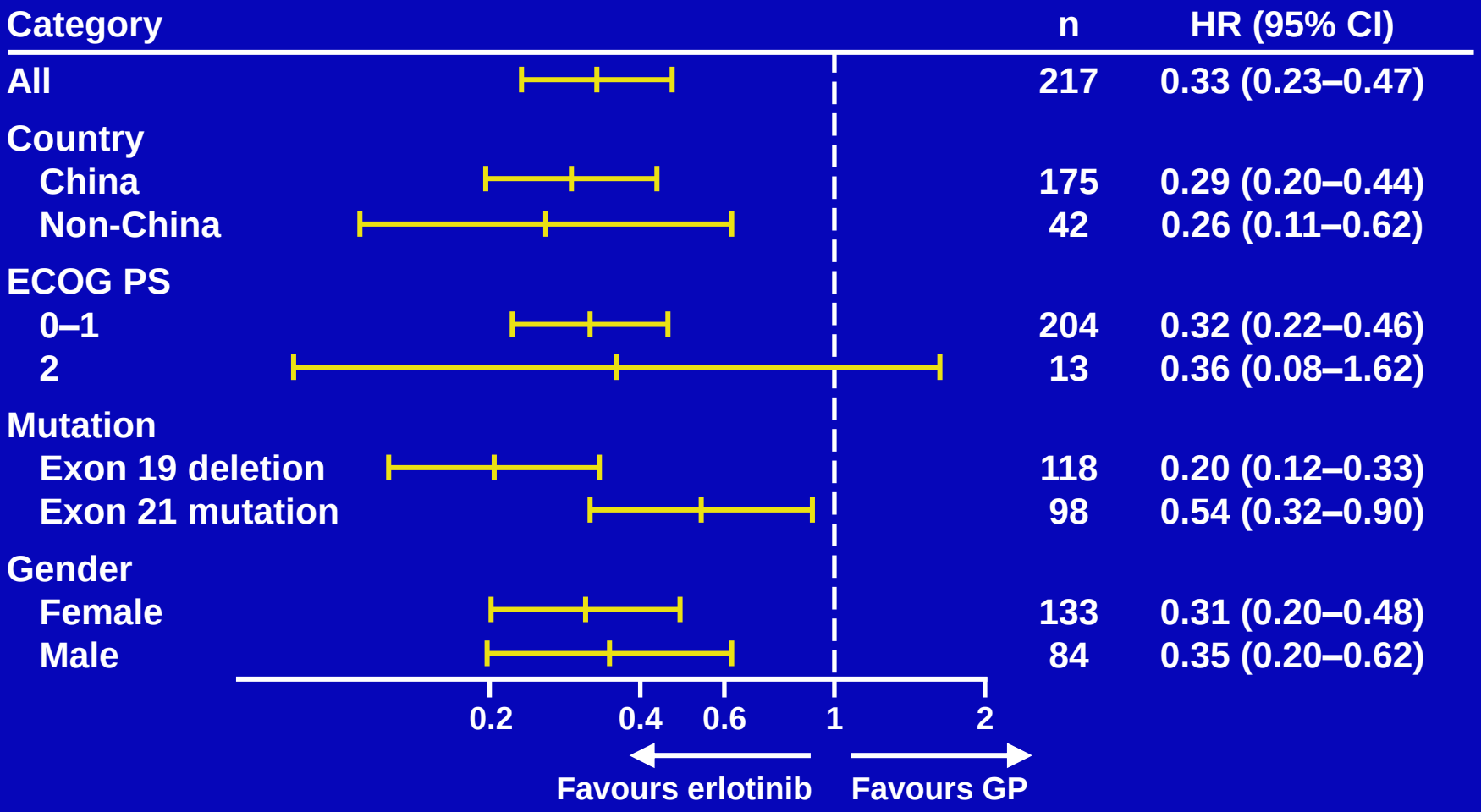


  - **updated analysis (19 November 2012): median PFS 11.0 vs 5.5 months (HR=0.33, 95% CI: 0.23–0.47; p<0.0001)**

CI = confidence interval; HR = hazard ratio; IRC = independent review committee

PFS benefit across subgroups

- The PFS benefit for erlotinib was consistent across predefined subgroups (updated analysis)



FACT-L questionnaire completion rates

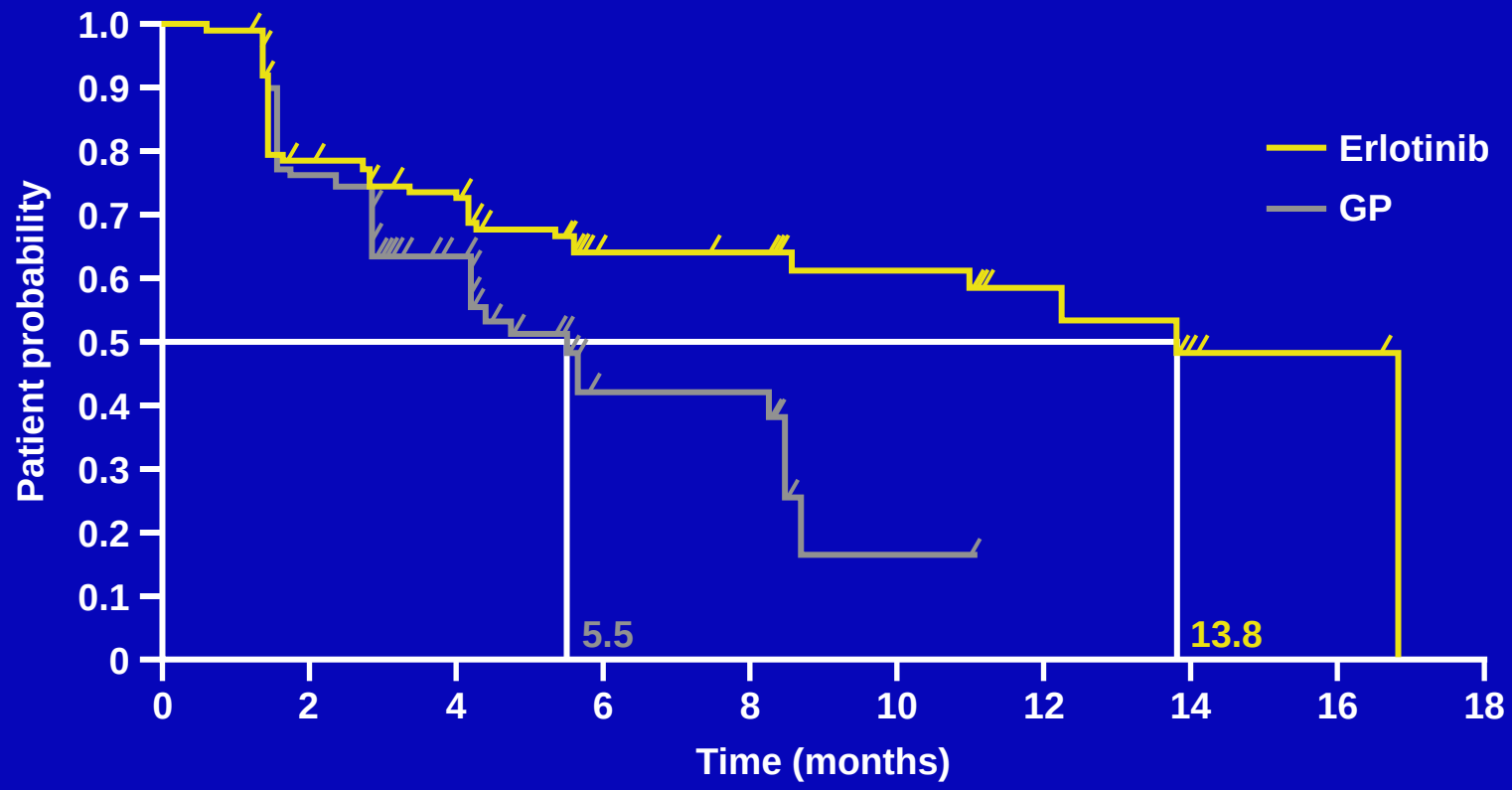
- FACT-L completion rates were 99% for erlotinib and 98% for GP at baseline

Timepoint	Erlotinib, n (%)*	GP, n (%)*
Baseline	109 (99)	102 (98)
Week 6	107 (99)	89 (92)
Week 12	99 (98)	80 (95)
Week 18	96 (100)	65 (89)
Week 24	89 (100)	42 (88)
Week 36	56 (92)	29 (100)
Week 48	37 (100)	7 (78)
Week 60	19 (95)	0 (0)
Week 72	8 (89)	0 (0)
Week 84	1 (100)	0 (0)

*Percentages are based on the number of patients who completed the questions at that visit

Time to symptomatic progression

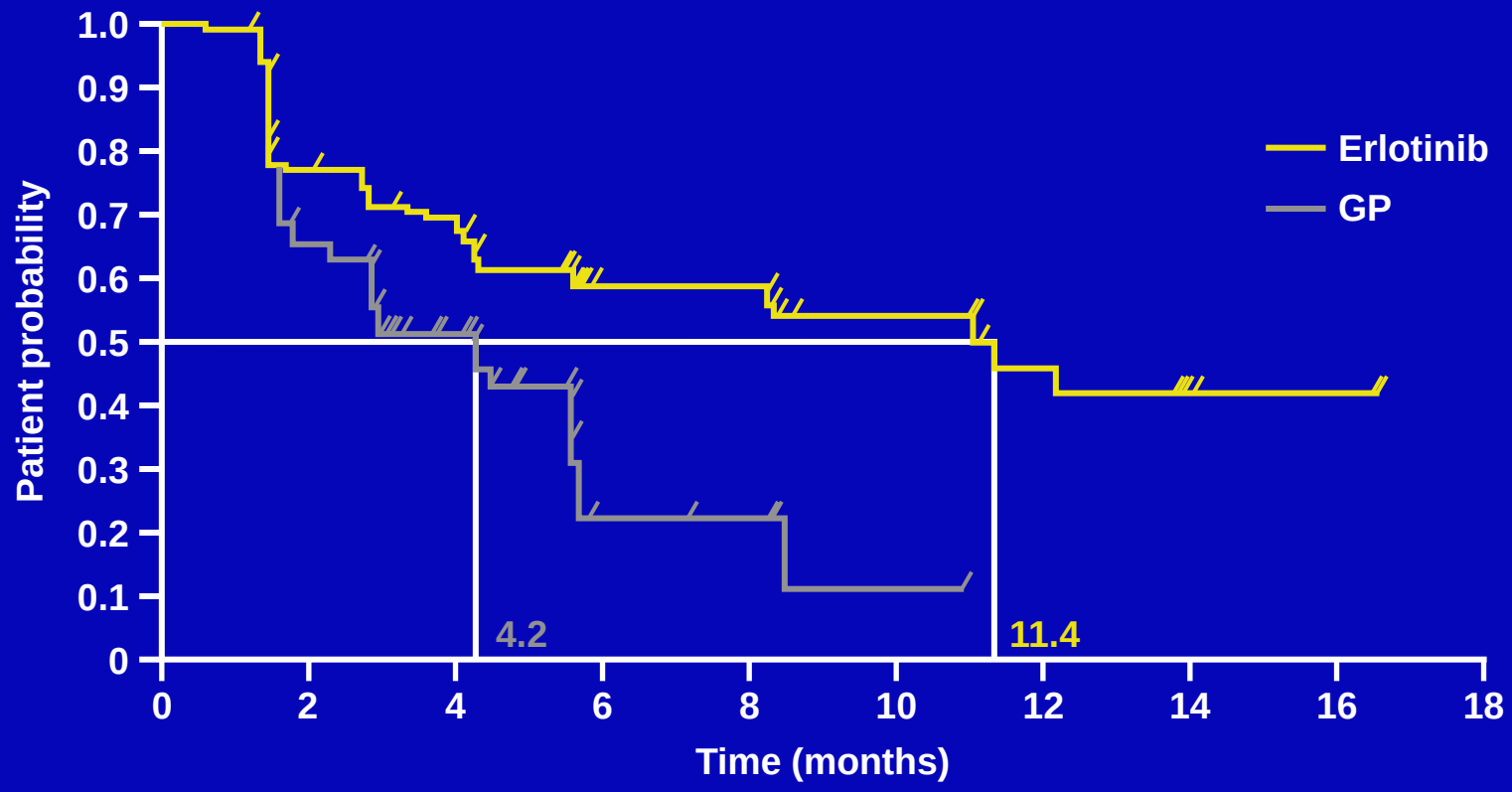
- Median time to symptomatic progression was 13.8 vs 5.5 months for erlotinib and GP, respectively (HR=0.56, 95% CI: 0.36–0.87; p=0.0076)



Number at risk:										
Erlotinib	108	83	76	35	34	20	12	4	3	0
GP	92	65	41	11	11	2	0	0	0	0

Time to deterioration in TOI

- Median time to deterioration in TOI was 11.4 months for erlotinib and 4.2 months for GP (HR=0.51, 95% CI: 0.34–0.76; p=0.0006)

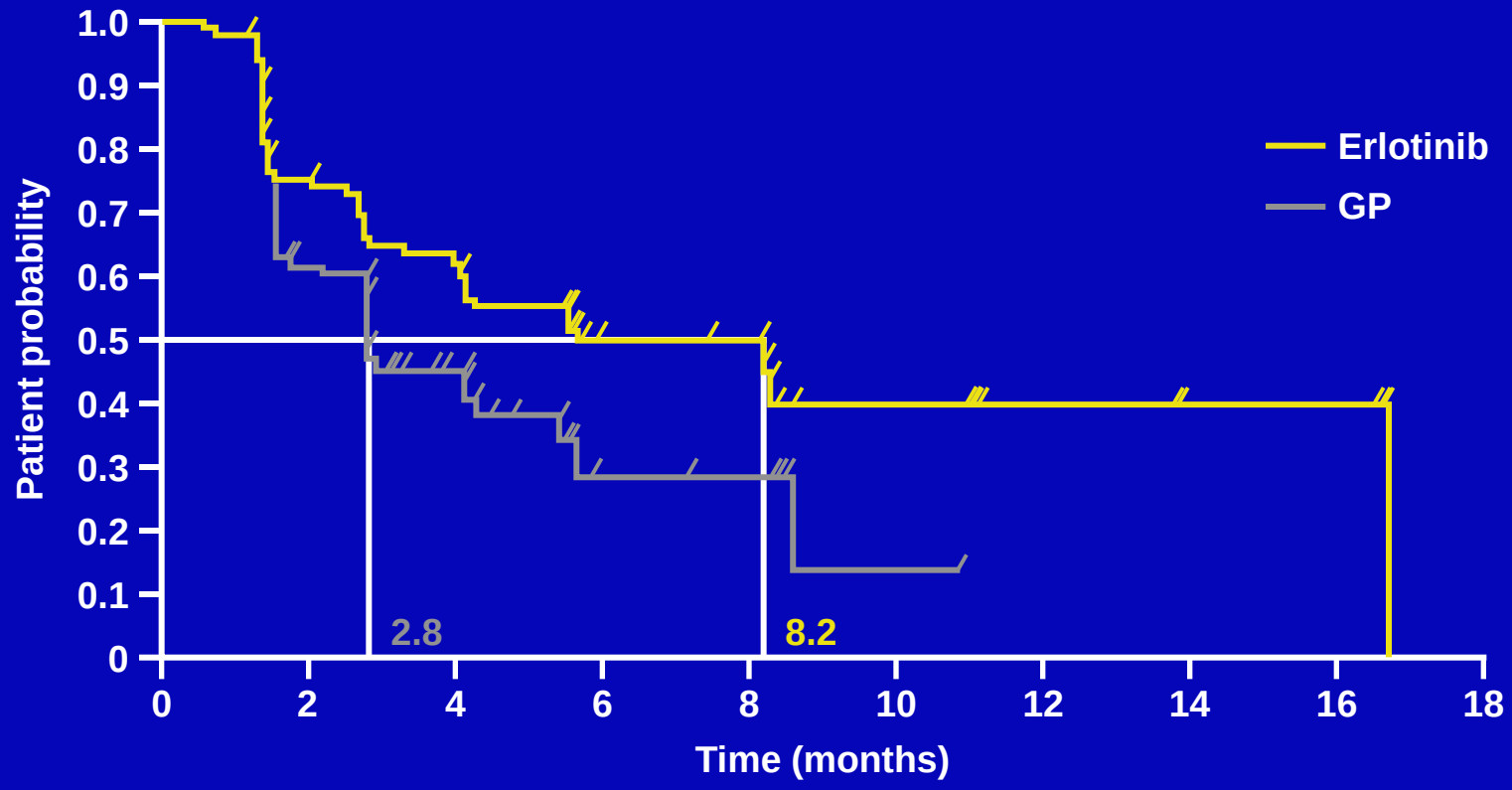


Number at risk:

Erlotinib	109	82	71	36	36	21	11	4	3	0
GP	92	56	31	5	4	1	0	0	0	0

Time to deterioration in QoL

- Median time to deterioration in QoL was 8.2 months for erlotinib and 2.8 months for GP (HR=0.64, 95% CI: 0.44–0.93; p=0.0168)



Number at risk:

Erlotinib	109	79	66	33	32	14	7	4	4	0
GP	92	51	27	7	6	1	0	0	0	0

Conclusions

- **In addition to improved PFS, erlotinib was associated with better outcomes compared with GP across all FACT-L assessments, including a significant delay in time to symptomatic progression and time to deterioration in TOI and QoL**
  - **this provides further support for the use of first-line erlotinib rather than chemotherapy for Asian patients who have *EGFR* mutation-positive NSCLC**
  - **these results were also in line with the QoL benefit seen in the OPTIMAL trial[1]**

1. Chen G, et al. Ann Oncol 2013

Acknowledgements

- The authors would like to thank all patients who participated in the study and all clinical personnel involved in data collection