# Treatment of EGFR mutant advanced NSCLC

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CANCER RESEARCH UK | LUNG CANCER CENTRE OF EXCELLENCE

# Outline

Data on first-line

Overcoming T790M mutation

Conclusion

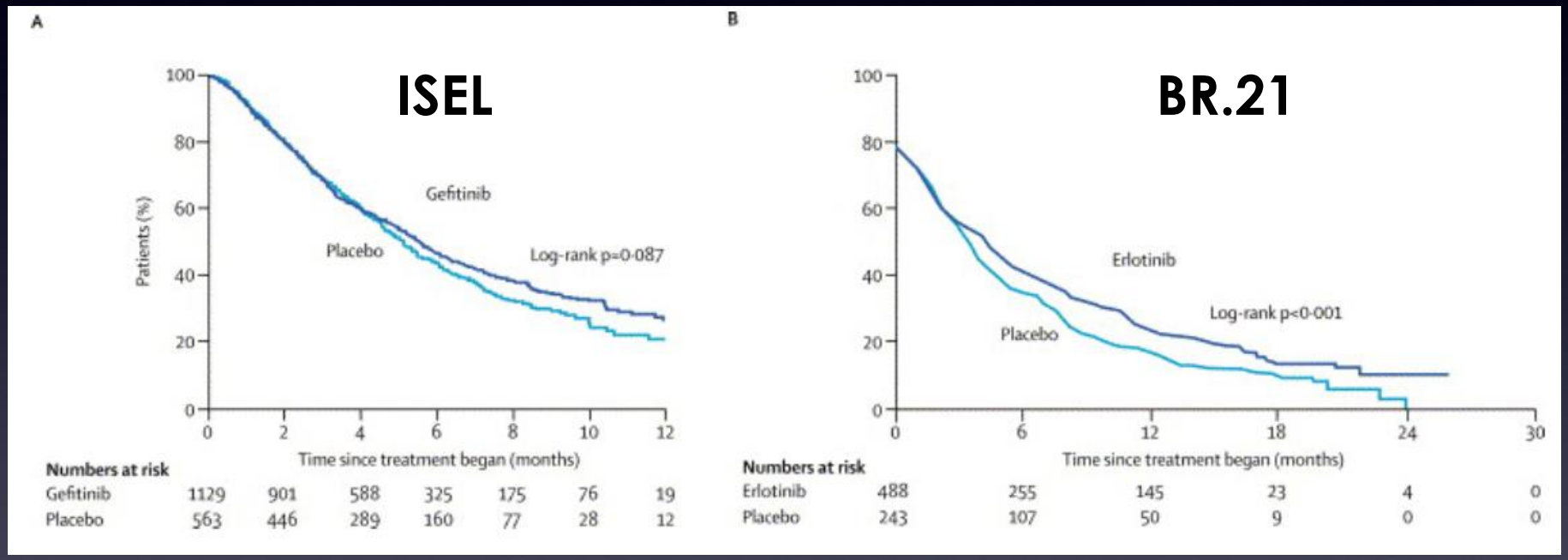
# First-line treatment NSCLC

Histological sub-type

EGFR/ALK/PD-L1 status

# NSCLC with EGFR activating mutation

# EGFR-TKIs in pretreated NSCLC patients




*Thatcher et al, Lancet 2005; Shepherd et al, NEJM 2005,*

# EGFR activating mutations

The NEW ENGLAND JOURNAL of MEDICINE

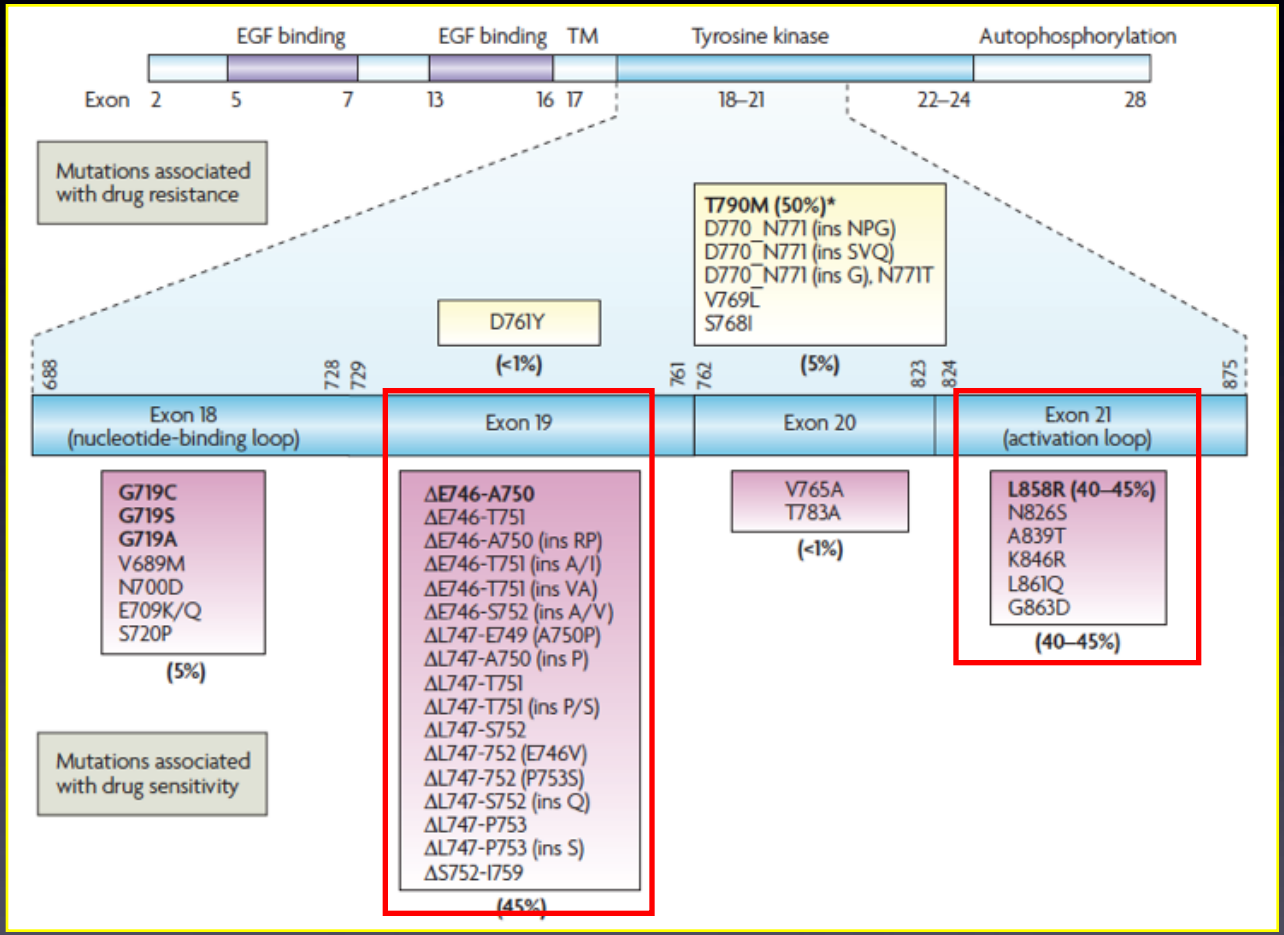
ESTABLISHED IN 1812 MAY 20, 2004 VOL. 350 NO. 21

## Activating Mutations in the Epidermal Growth Factor Receptor Underlying Responsiveness of Non–Small-Cell Lung Cancer to Gefitinib

Thomas J. Lynch, M.D., Daphne W. Bell, Ph.D., Raffaella Sordella, Ph.D., Sarada Gurubhagavatula, M.D., Ross A. Okimoto, B.S., Brian W. Brannigan, B.A., Patricia L. Harris, M.S., Sara M. Haserlat, B.A., Jeffrey G. Supko, Ph.D., Frank G. Haluska, M.D., Ph.D., David N. Louis, M.D., David C. Christiani, M.D., Jeff Settleman, Ph.D., and Daniel A. Haber, M.D., Ph.D.

*Lynch et al, NEJM 2004*

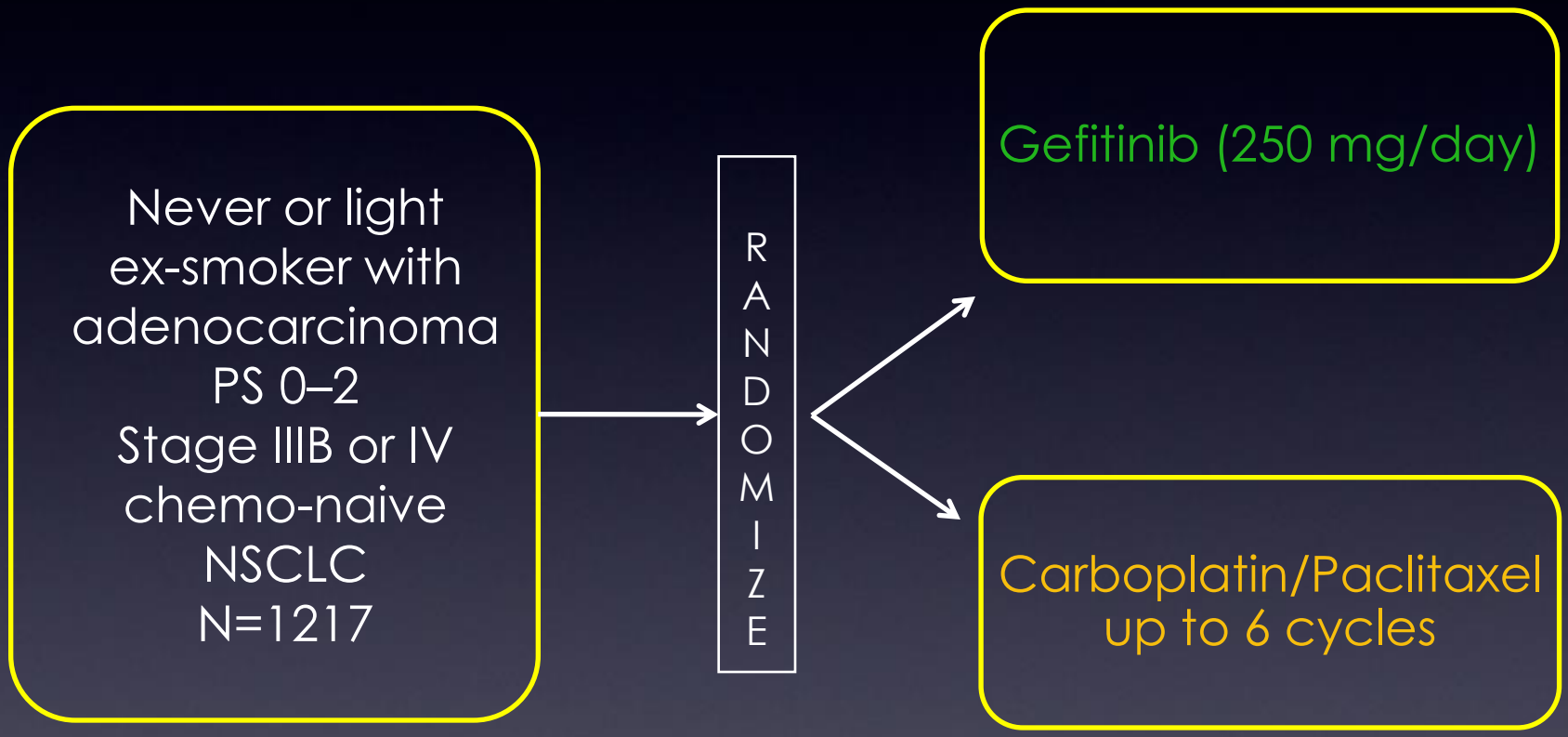
# EGFR activating mutations




*Sharma et al, Nat Rev Cancer 2007*

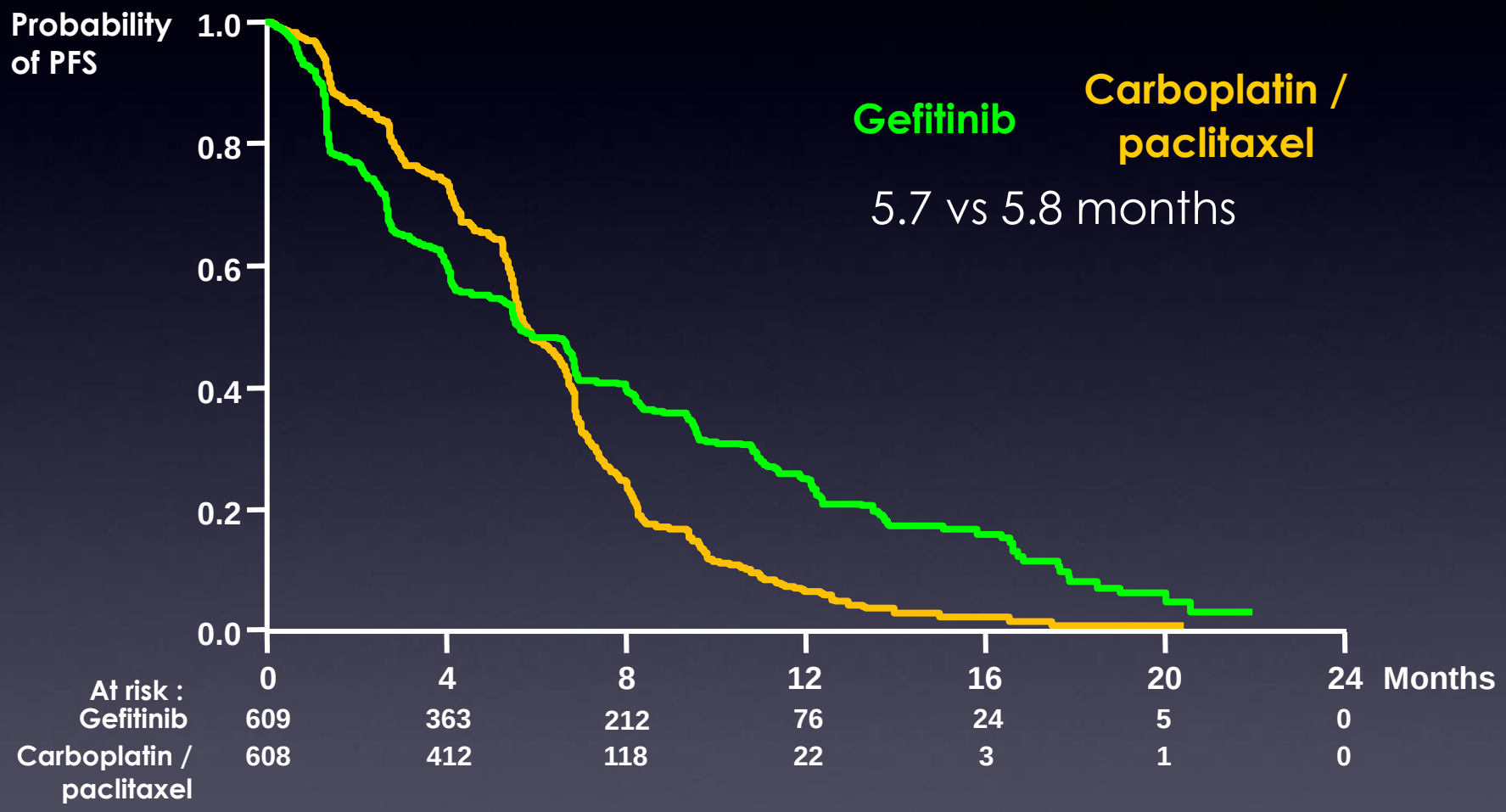
# Gefitinib

# IPASS Trial

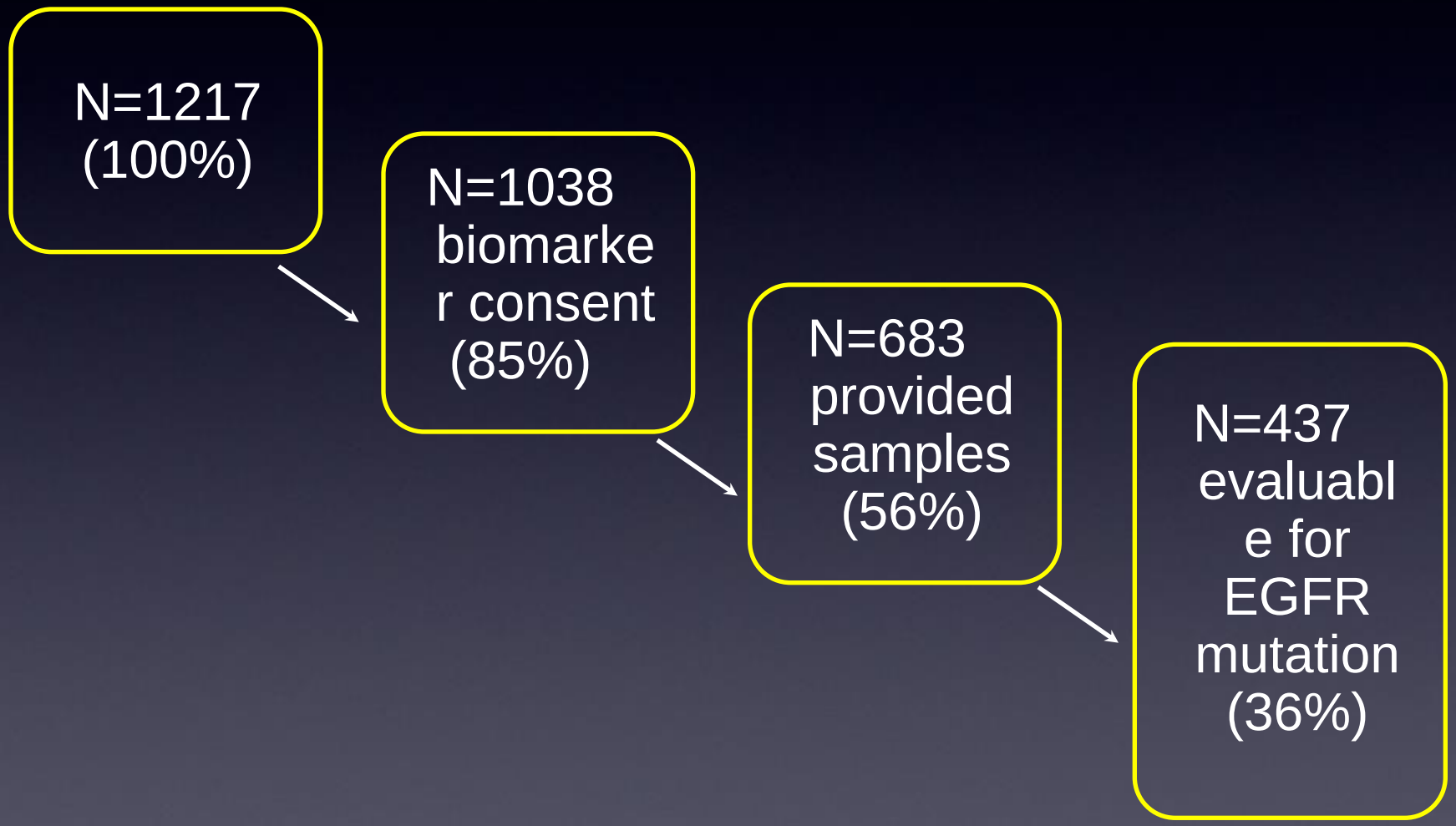



*Mok et al, NEJM 2009*

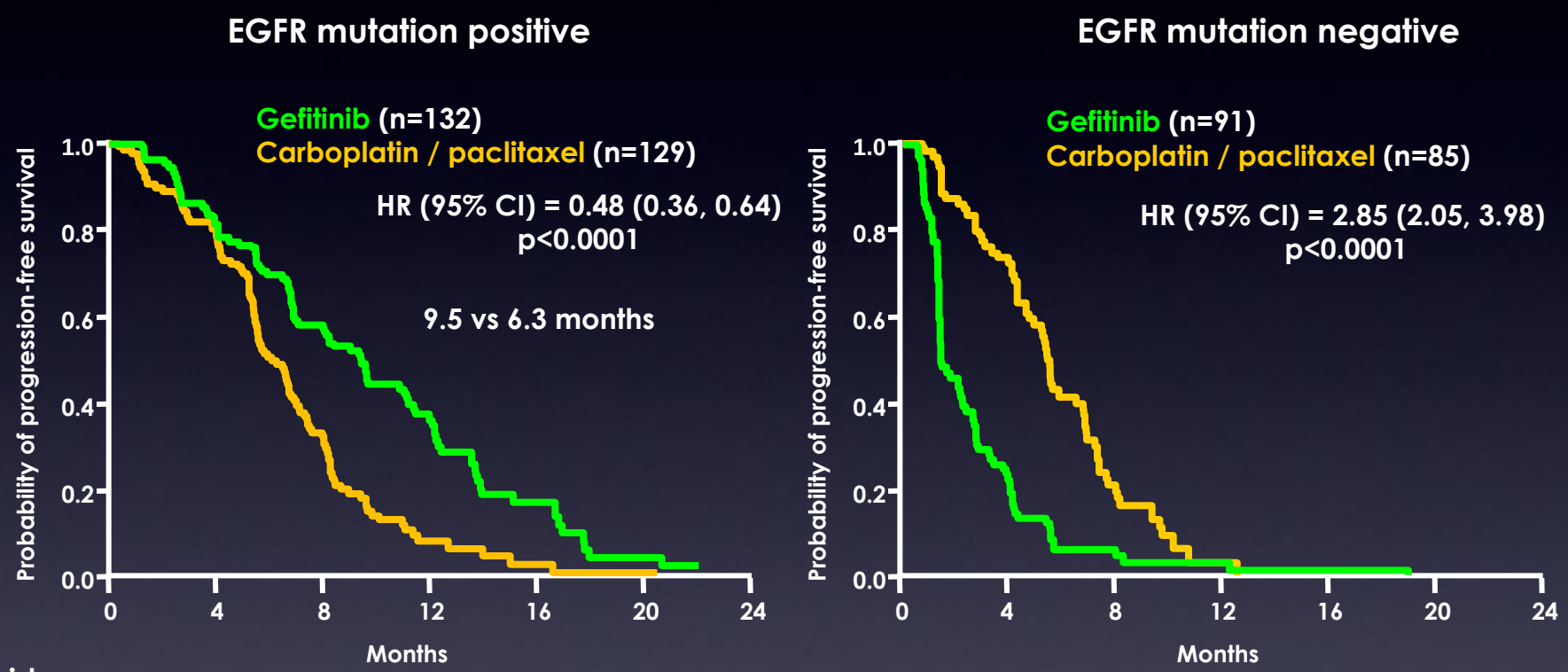
# PFS in ITT population



# IPASS - Biomarker analysis



# PFS in EGFR M+ and M-



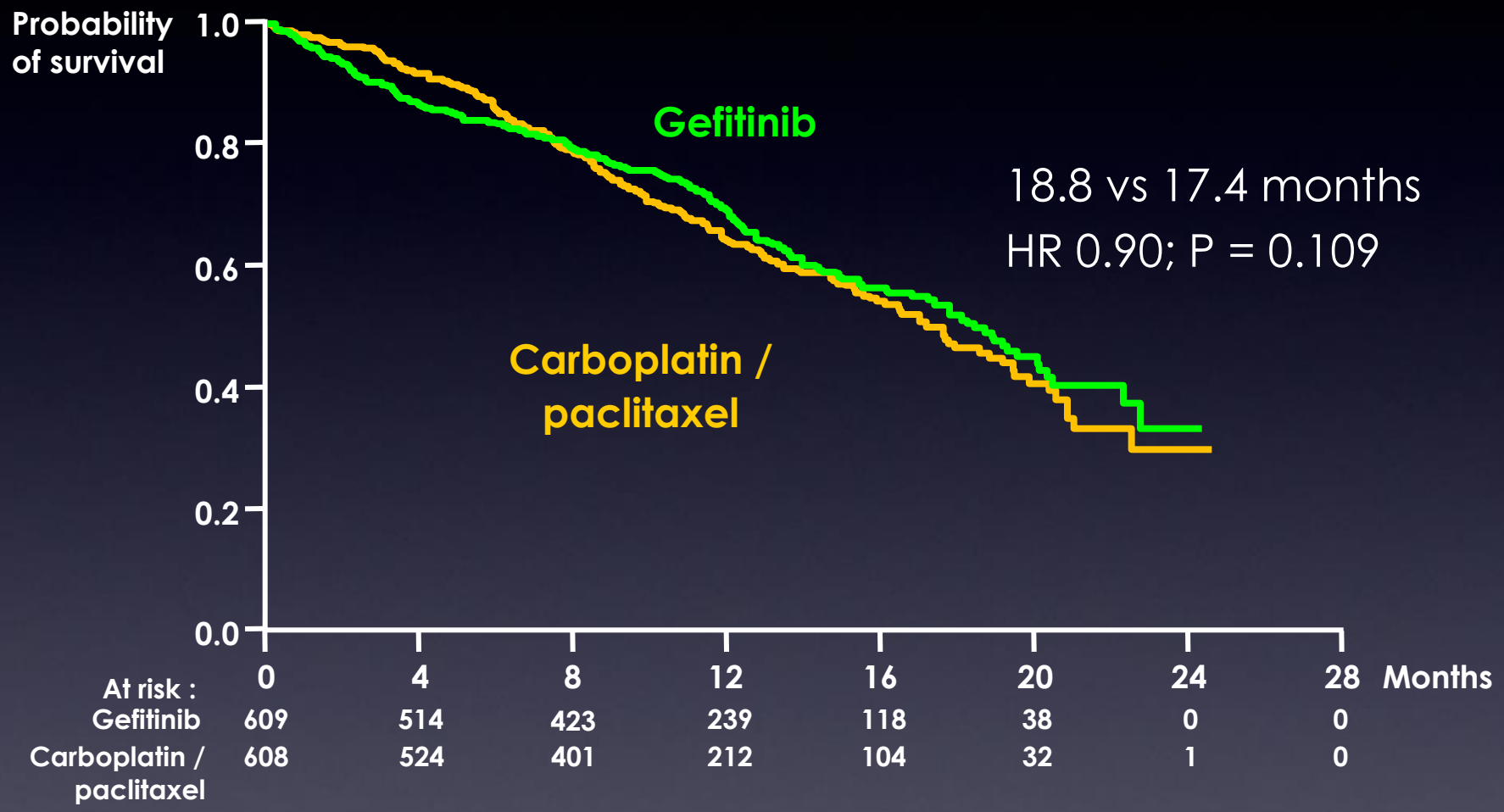

At risk :

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Gefitinib | 132 | 108 | 71 | 31 | 11 | 3 | 0 | 91 | 21 | 4 | 2 | 1 | 0 | 0 |
| C / P | 129 | 103 | 37 | 7 | 2 | 1 | 0 | 85 | 58 | 14 | 1 | 0 | 0 | 0 |

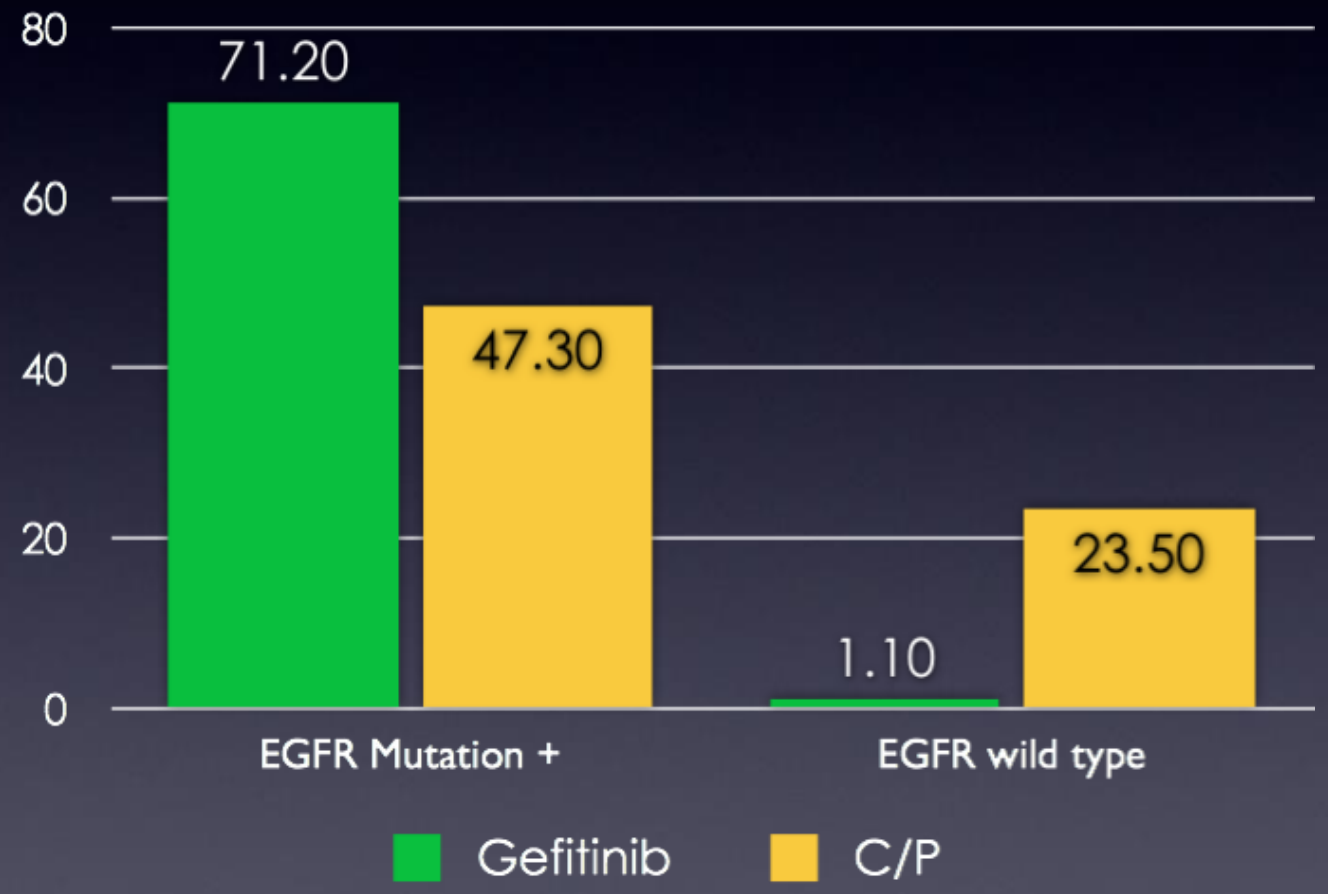
**Treatment by subgroup interaction test, p<0.0001**

ITT population
Cox analysis with covariates

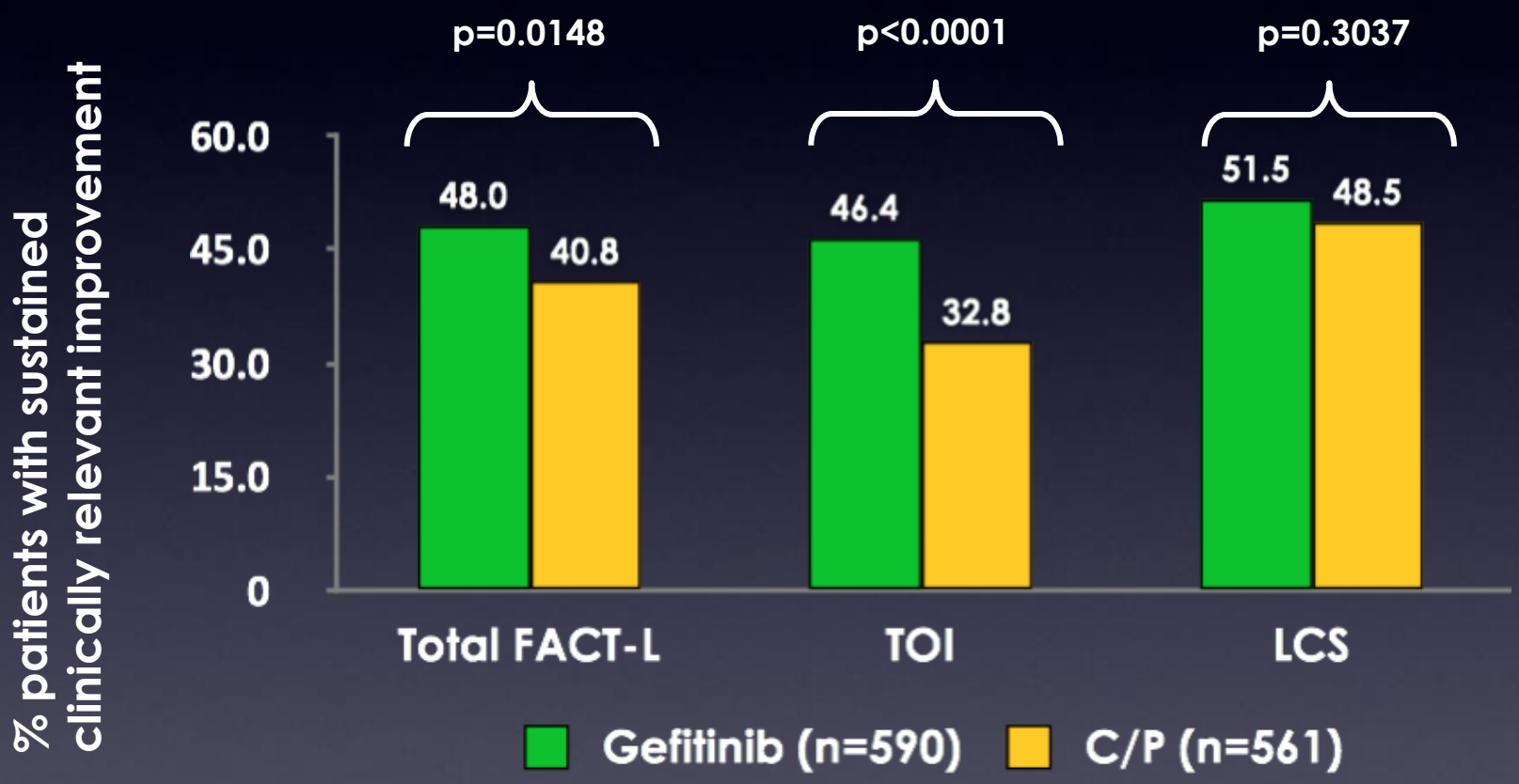
# Overall Survival



# ORR in EGFR M+ and WT



# Quality of life



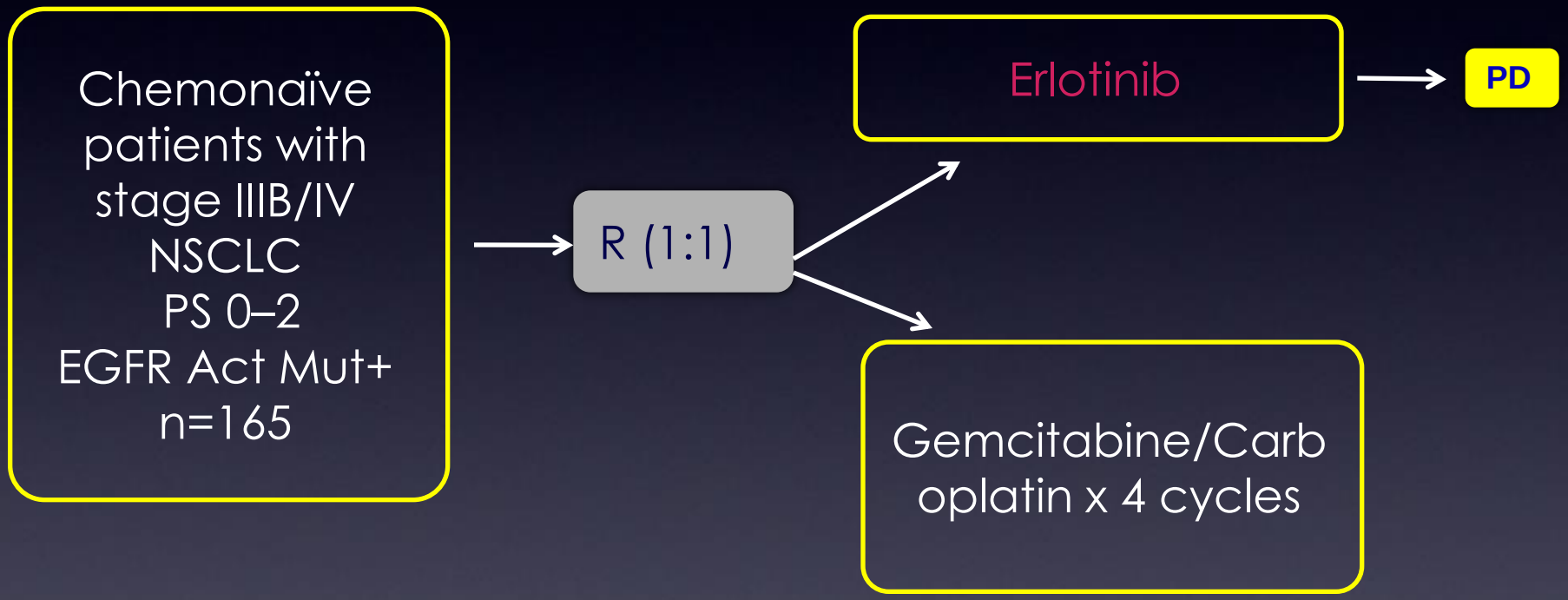
# Gefitinib in Asian Studies EGFR M+

| Study | N | Regimen | RR (%) | PFS | HR |
|---|---|---|---|---|---|
| NEJ002 | 230 | G | 73.7 | 10.8 | 0.30 |
| | | C/P | 30.7 | 5.4 | |
| WJTOG 3405 | 177 | G | 62.1 | 9.2 | 0.48 |
| | | C/D | 32.2 | 6.3 | |

*Maemondo et al, NEJM 2010; Mitsudomi et al, Lancet Oncol 2010*

# Erlotinib

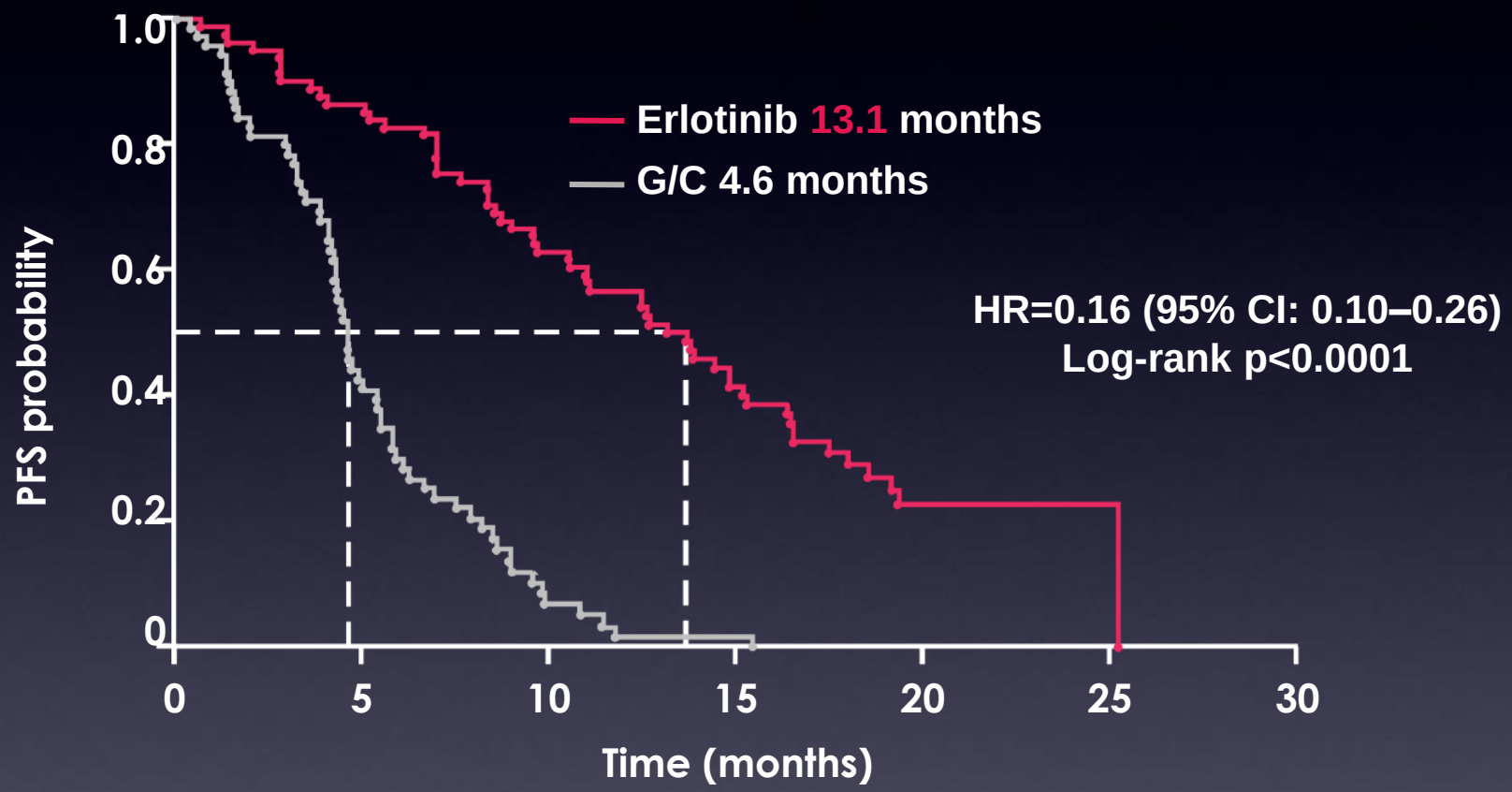
# OPTIMAL study design




Completed enrollment in <12 months

*Zhou et al, Lancet Oncol 2011*

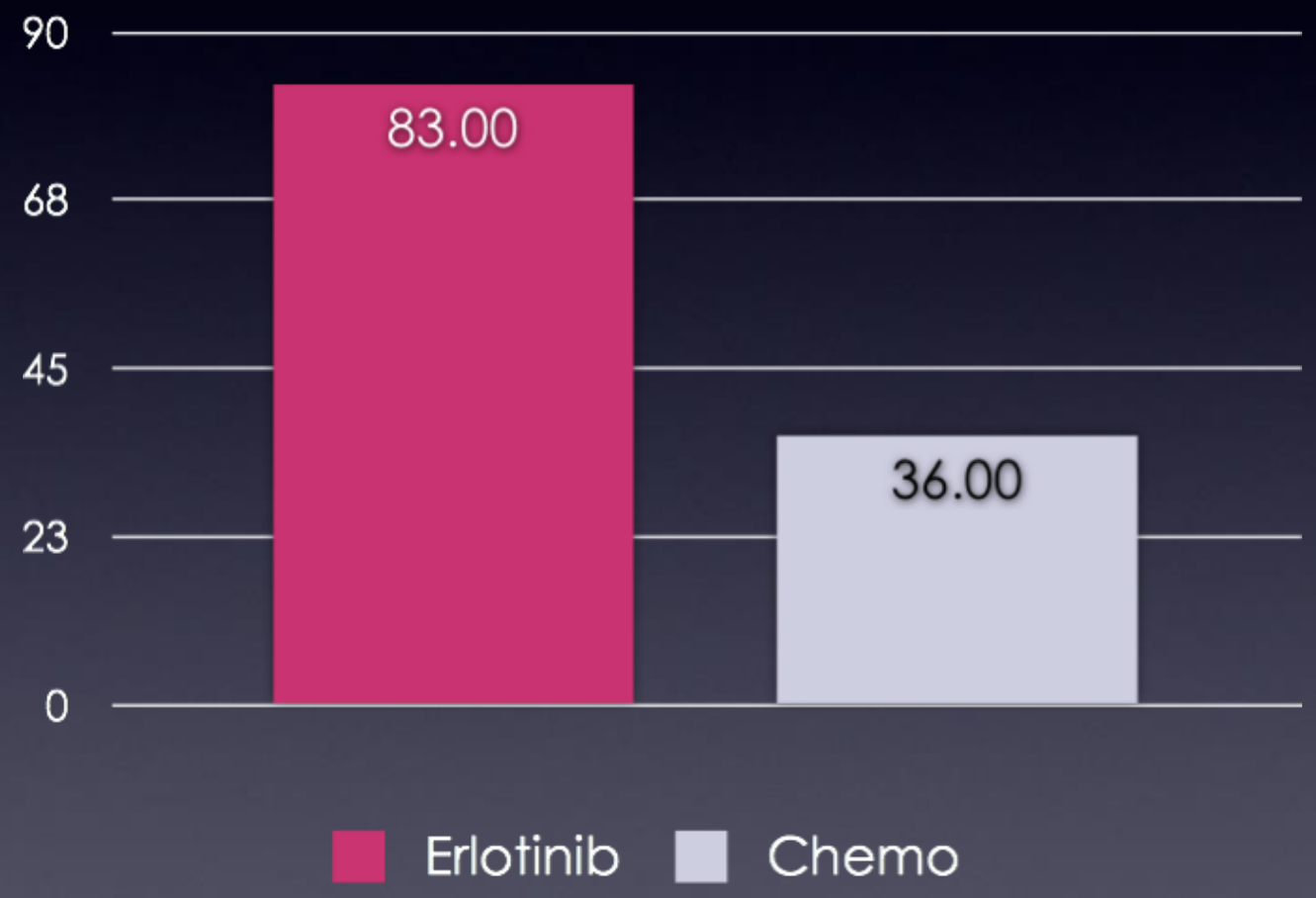
# OPTIMAL - PFS



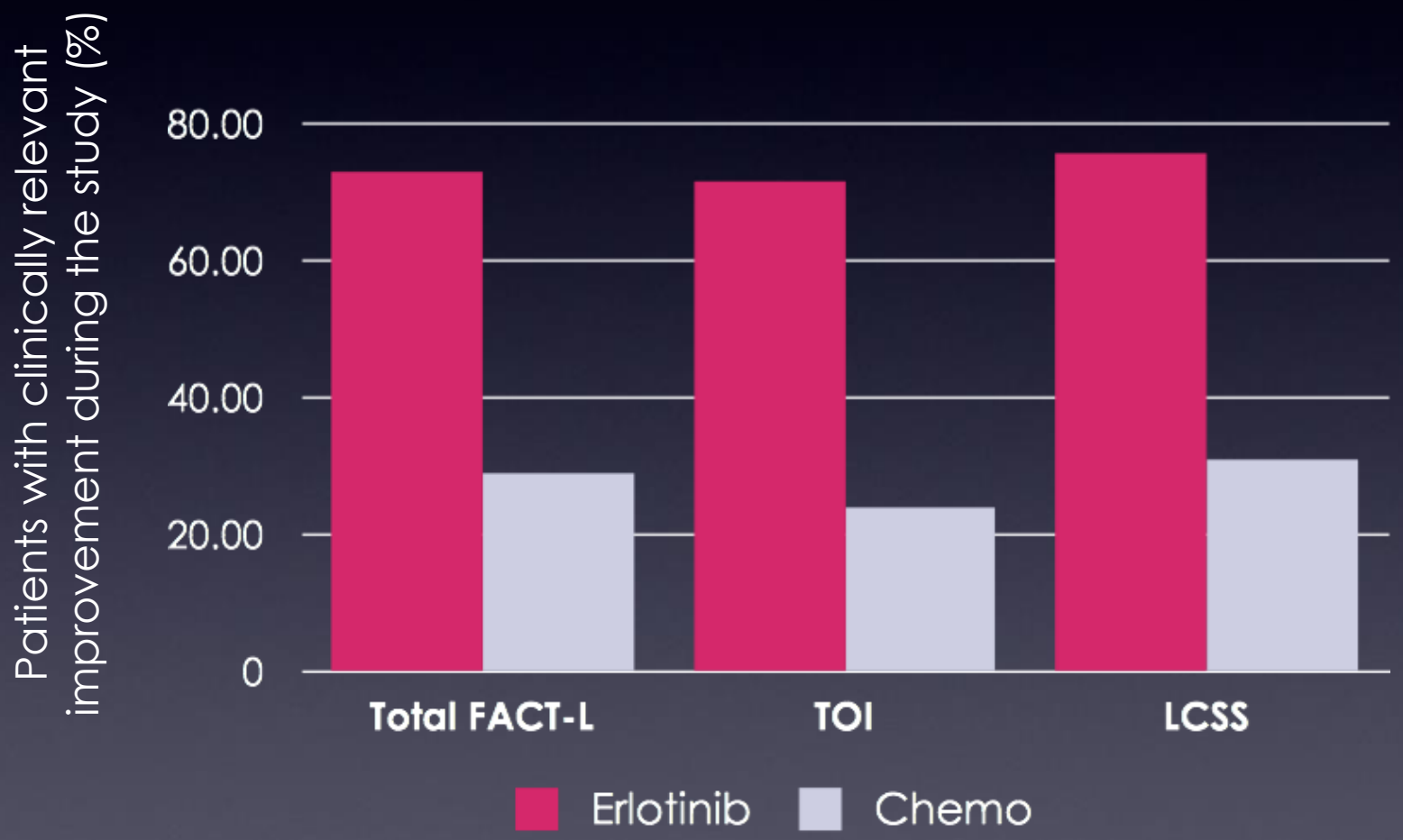

Patients at risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Erlotinib | 82 | 70 | 51 | 29 | 8 | 2 | 0 |
| G/C | 72 | 26 | 4 | 1 | 0 | 0 | 0 |

# Overall Response Rate



# Quality of Life



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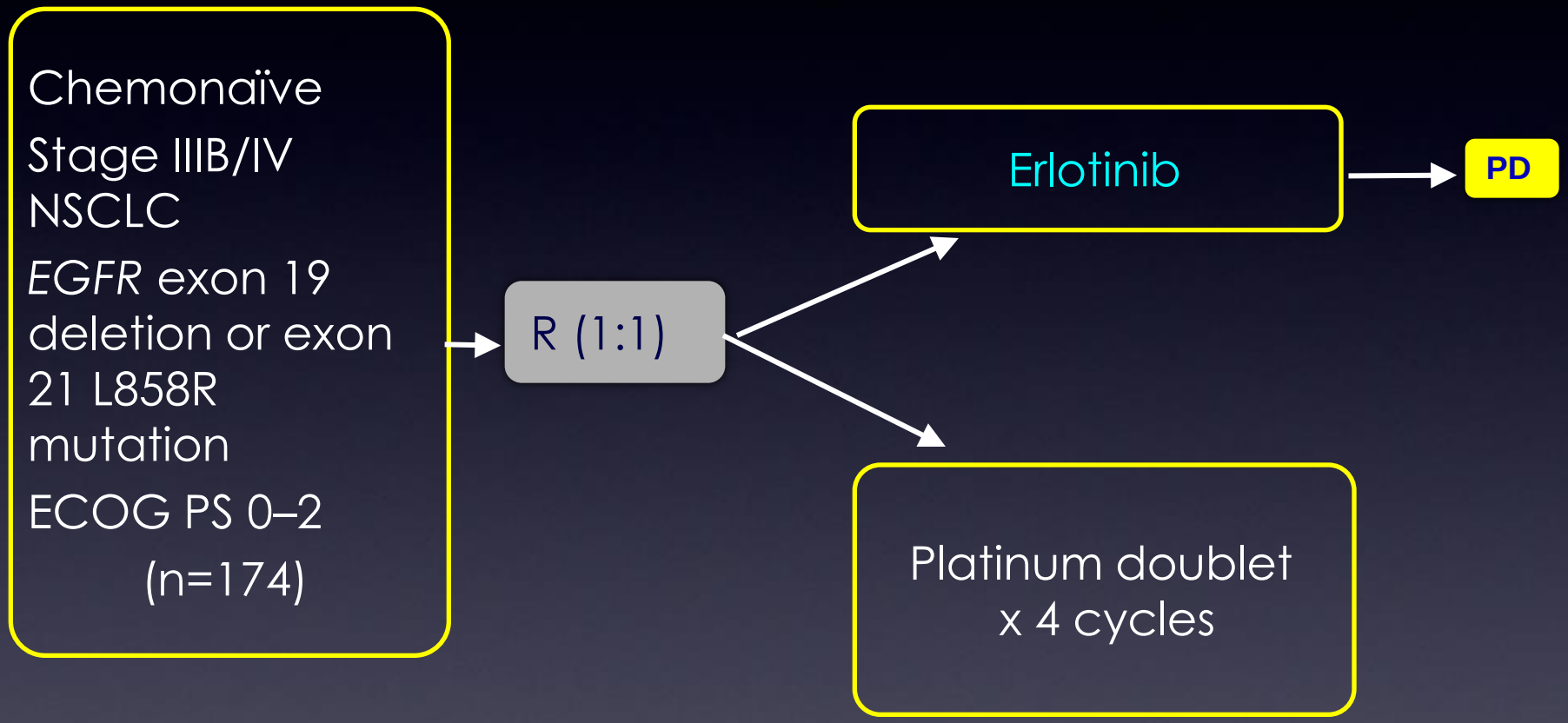
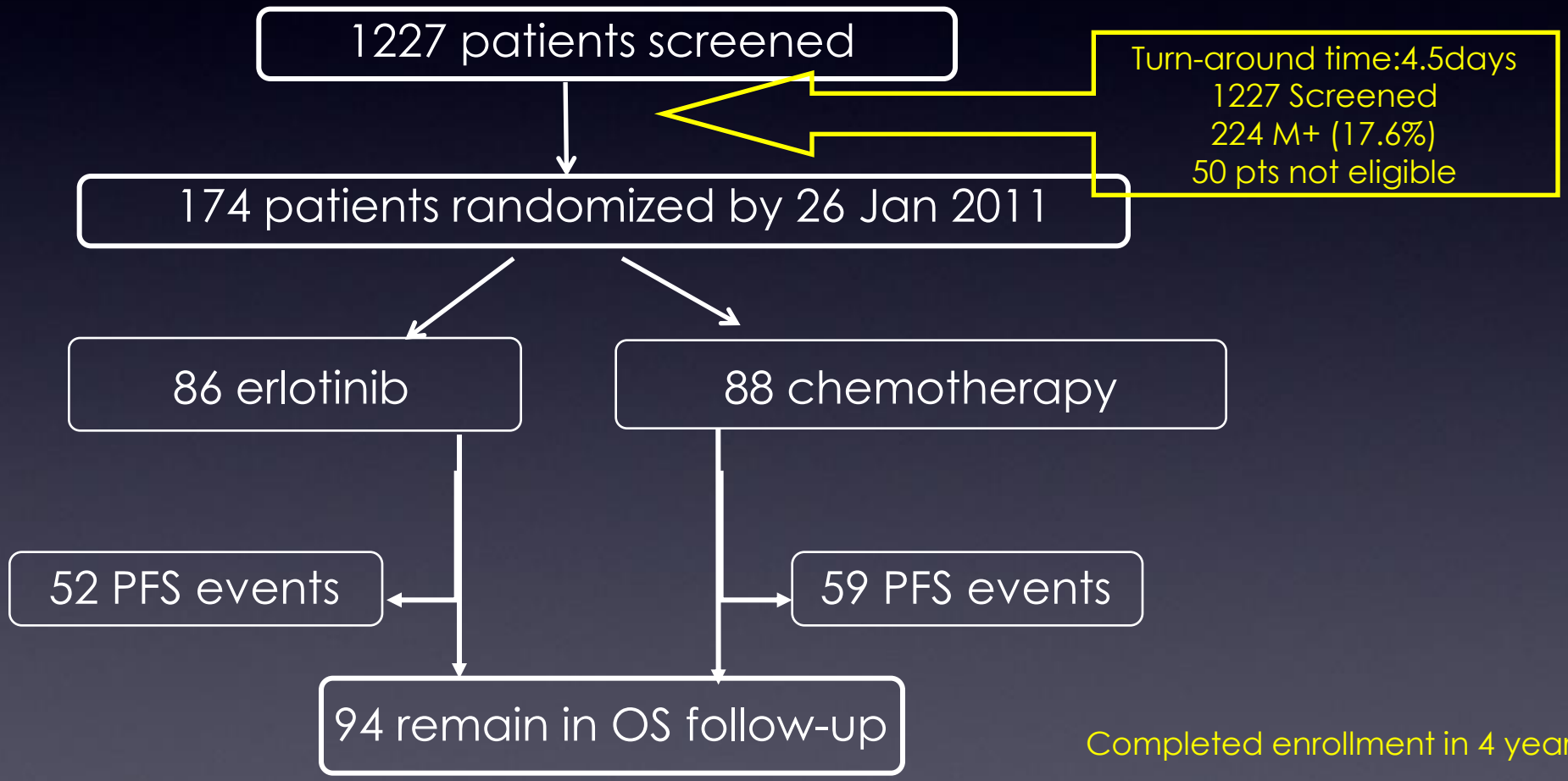
# EURTAC



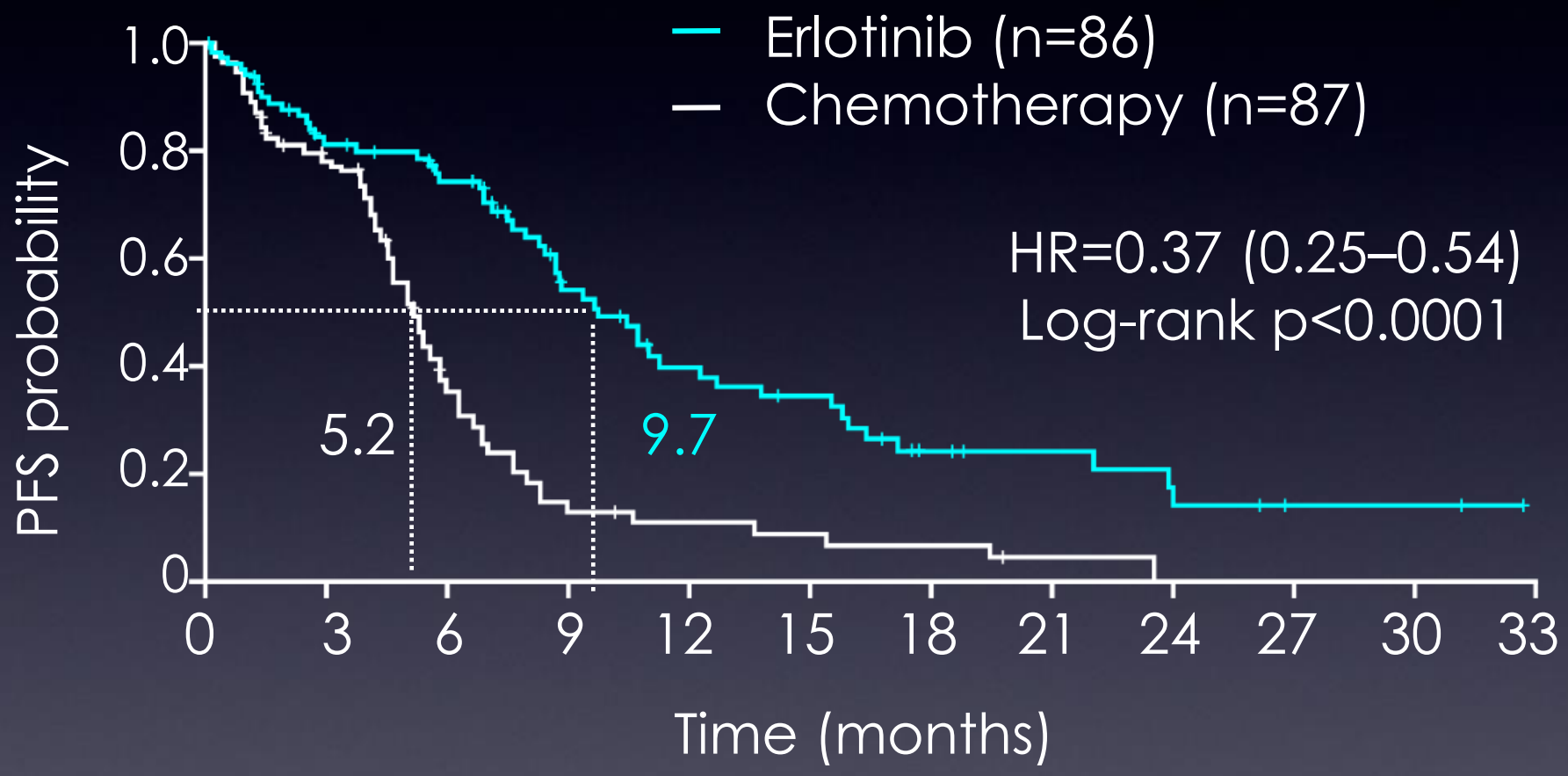

*Rosell et al, Lancet Oncol 2012*

# Study profile




Completed enrollment in 4 years

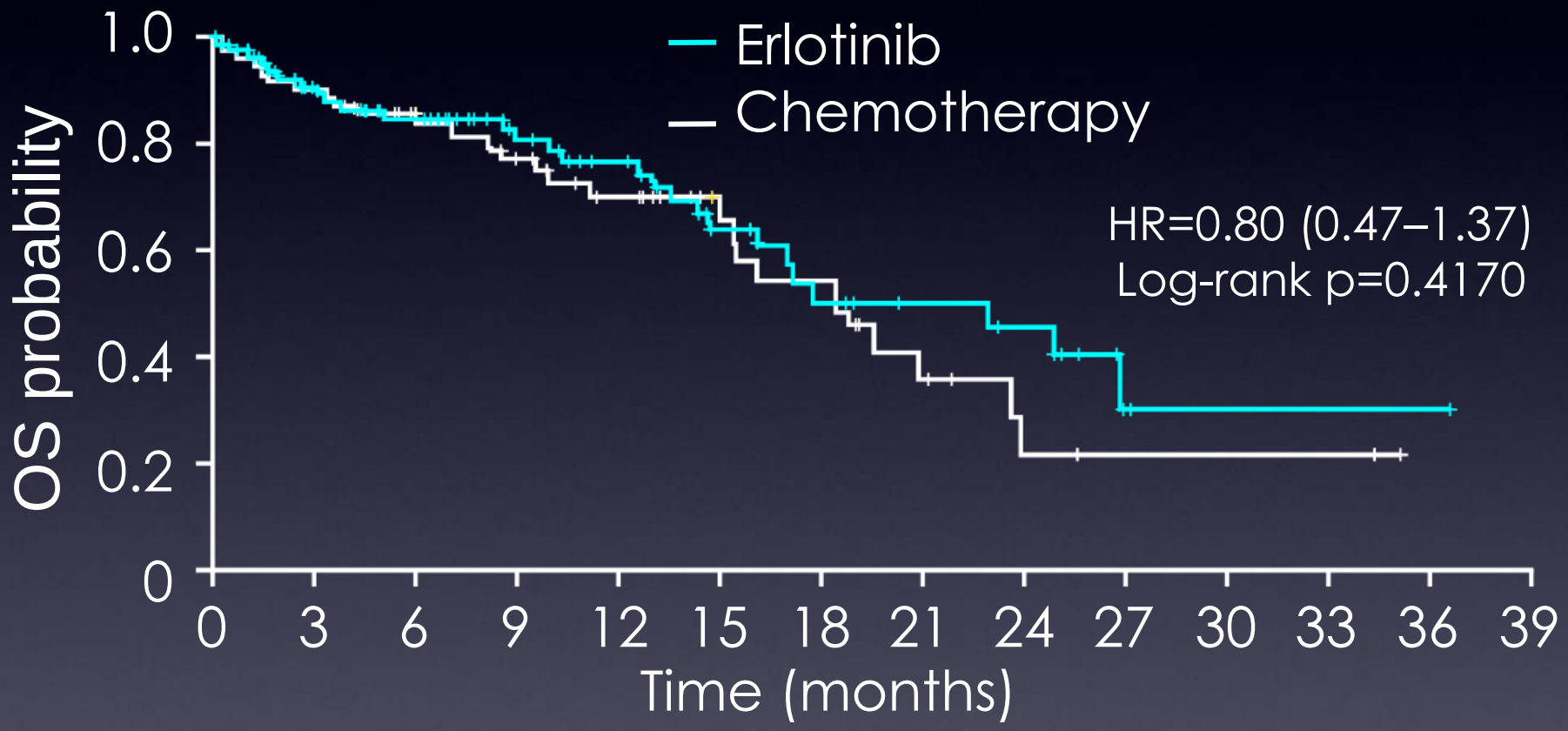
# Progression Free Survival



# Response Rate

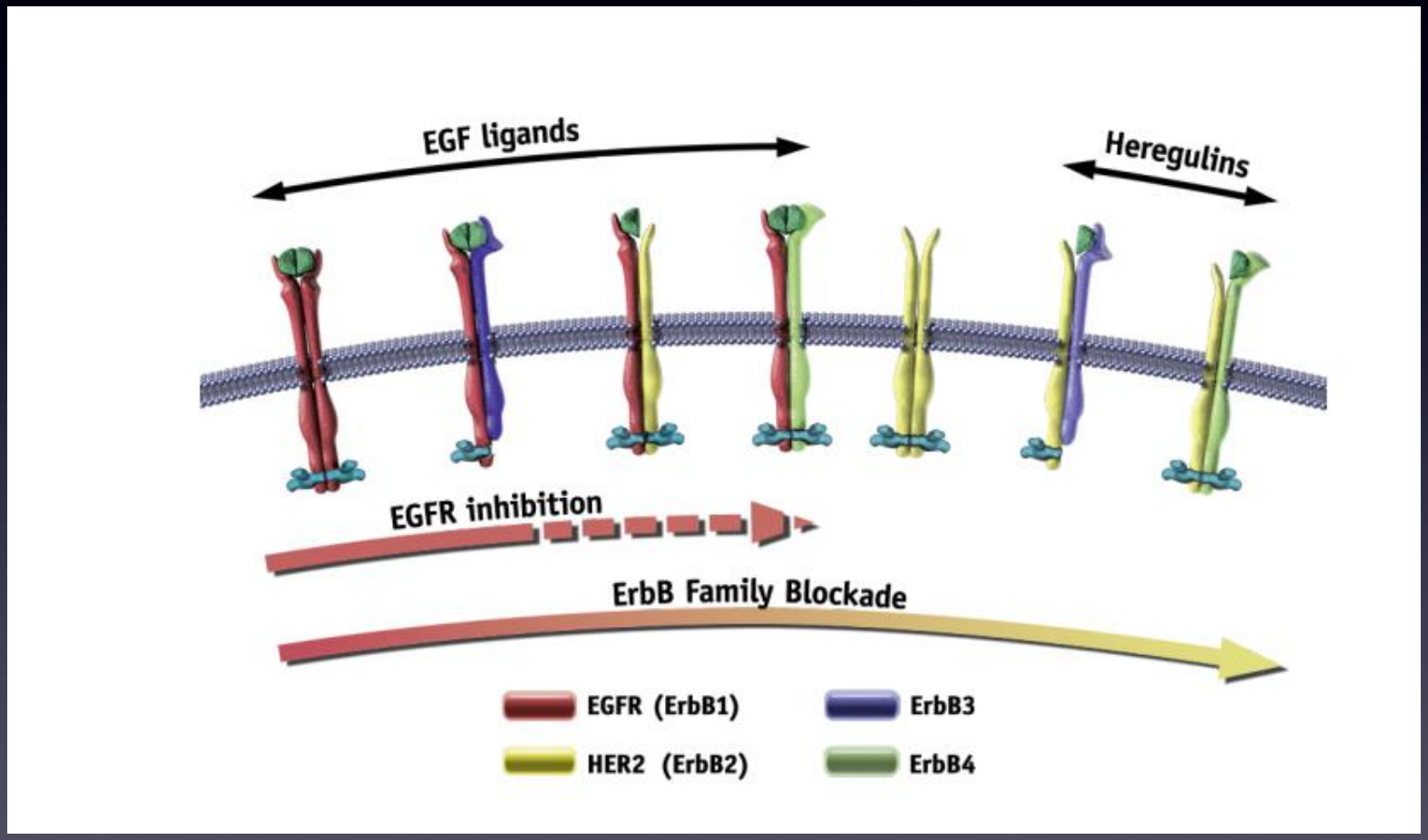
| | Erlotinib (n=86) n (%) | Chemotherapy (n=87) n (%) |
|---|---|---|
| Complete response | 2 (2) | 0 (0) |
| Partial response | 48 (56) | 13 (15) |
| Objective response rate | 50 (58) | 13 (15) |
| Stable disease | 18 (21) | 44 (51) |
| Disease control rate | 68 (79) | 57 (66) |

# Overall Survival

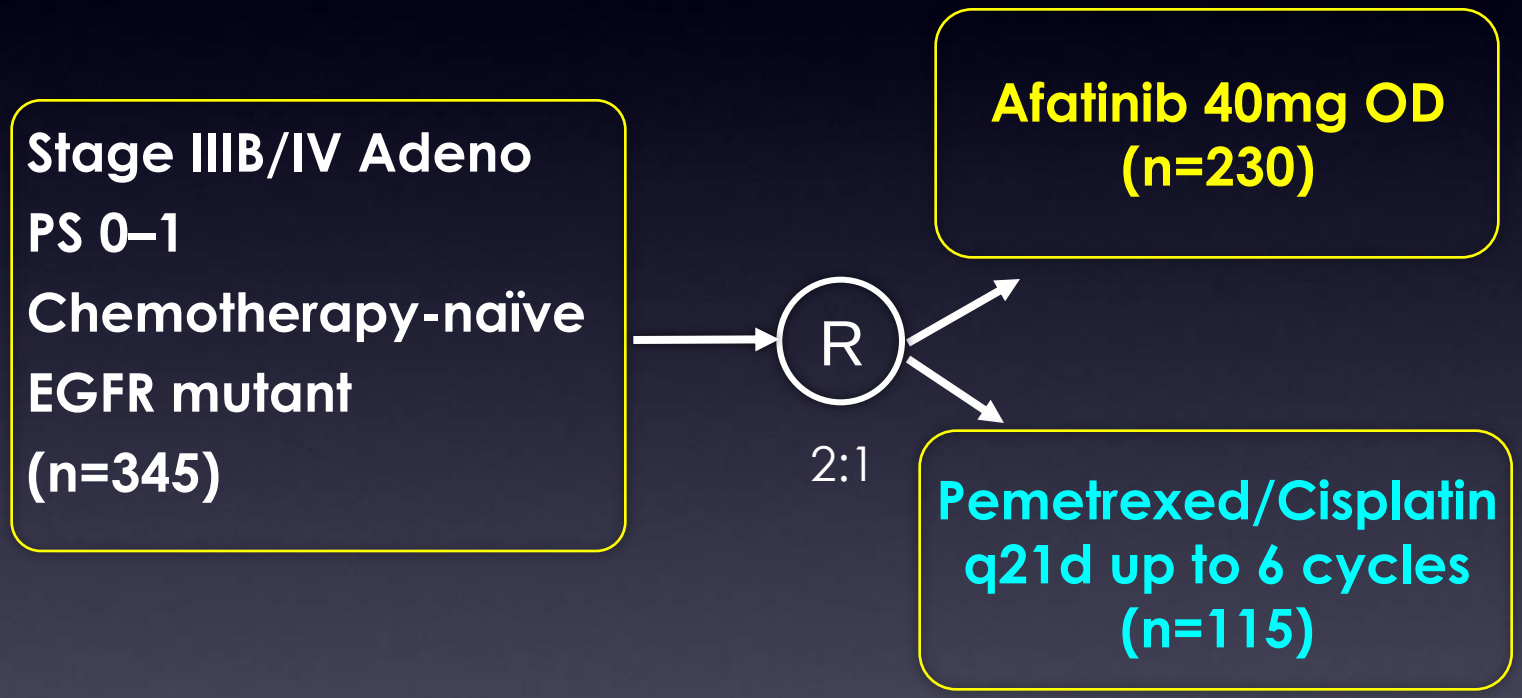


# Afatinib

# Afatinib
# Irreversible ErbB blockade



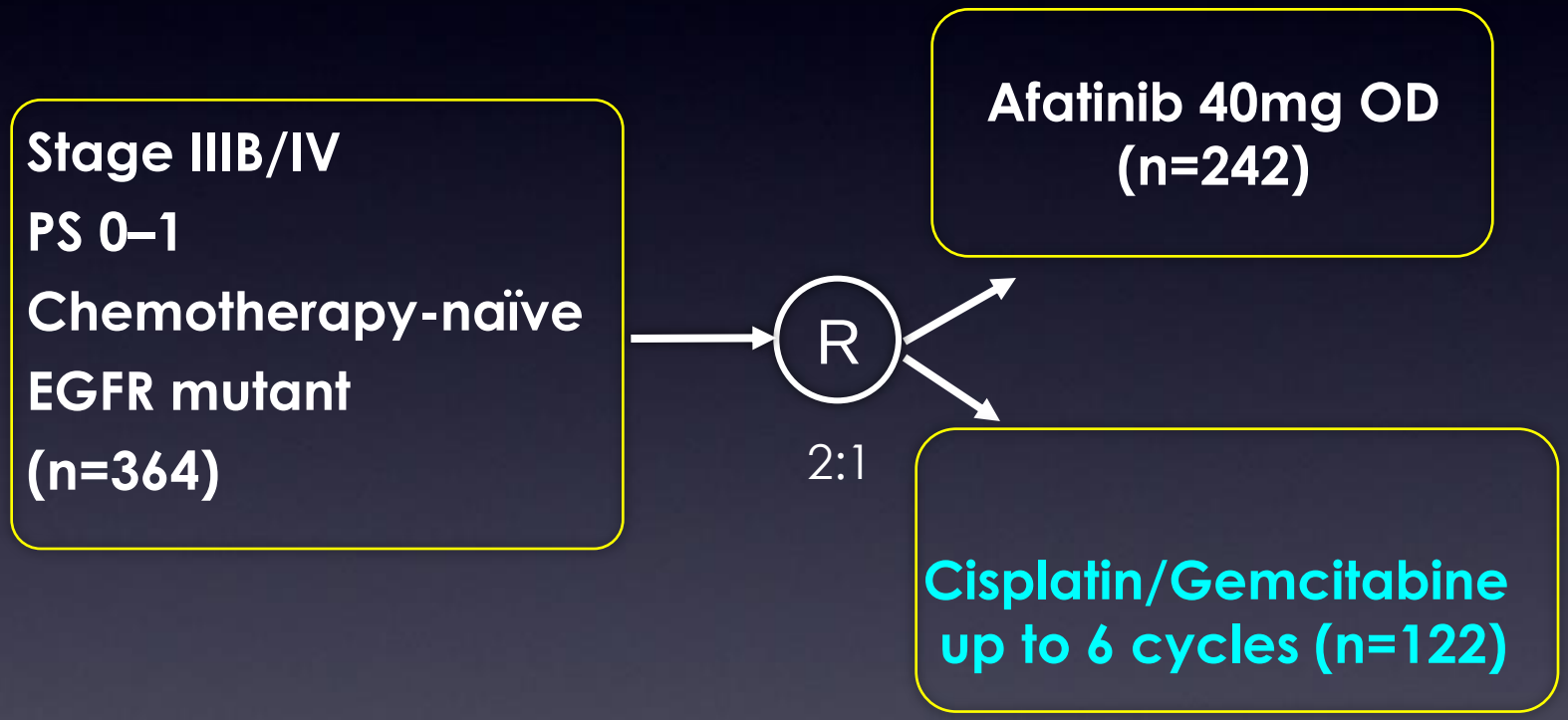
# LUX-LUNG 3




Primary endpoint: PFS (IRR)

*Sequist LV, et al, JCO 2013*

# LUX-LUNG 6




Primary endpoint: PFS (IRR)

Only East Asia

*Wu Y-L, et al, Lancet Oncol 2014*

# LUX-Lung 3 and 6 Efficacy

| | LUX-LUNG 3 | | LUX-LUNG 6 | |
|---|---|---|---|---|
| | Afatinib n=230 | Cis/pem n=115 | Afatinib n=242 | Cis/gem n=122 |
| ORR (%) | 56.1 | 22.5 | 66.9 | 23 |
| Median PFS (mos) | 11.1 | 6.9 | 11.0 | 5.6 |
| HR (95% CII) | 0.58 (0.43–0.78) p=0.0004 | | 0.28 (0.20-0.39) P<0.0001 | |

# Adverse Events

| | Afatinib (n=229) | | | Cis/Pem (n=111) | | |
|---|---|---|---|---|---|---|
| | All Gr (%) | Gr 3 (%) | Gr 4 (%) | All Gr† (%) | Gr 3 (%) | Gr 4 (%) |
| Diarrhea | **218 (95.2)** | 33 (14.4) | 0 | **17 (15.3)** | 0 | 0 |
| Rash/acne | **204 (89.1)** | 37 (16.2) | 0 | **7 (6.3)** | 0 | 0 |
| Stomatitis/mucositis | **165 (72.1)** | 19 (8.3) | 1 (0.4) | **17 (15.3)** | 1 (0.9) | 0 |
| Paronychia | **130 (56.8)** | 26 (11.4) | 0 | **0** | 0 | 0 |
| Dry skin | **67 (29.3)** | 1 (0.4) | 0 | **2 (1.8)** | 0 | 0 |
| | | | | | | |
| Nausea | **41 (17.9)** | 2 (0.9) | 0 | **73 (65.8)** | 4 (3.6) | 0 |
| Decreased appetite | **47 (20.5)** | 7 (3.1) | 0 | **59 (53.2)** | 3 (2.7) | 0 |
| Fatigue | **40 (17.5)** | 3 (1.3) | 0 | **52 (46.8)** | 14 (12.6) | 0 |
| Vomiting | **39 (17.0)** | 7 (3.1) | 0 | **47 (42.3)** | 3 (2.7) | 0 |
| Neutropenia | **2 (0.9)** | 1 (0.4) | 0 | **35 (31.5)** | 17 (15.3) | 3 (2.7) |
| Anemia | **7 (3.1)** | 1 (0.4) | 0 | **31 (27.9)** | 5 (4.5) | 2 (1.8) |

# Other Endpoints

Better tolerated

↑Symptom control

↑Global health status/QoL

Afatinib arm

# LUX-Lung 3 and 6: Updated OS

| | LUX-Lung 3 (n=345) | LUX-Lung 6 (n=364) |
|---|---|---|
| Recruitment period | Aug 09 – Feb 11 | Apr 10 – Nov 11 |
| Primary PFS analysis | Feb 12 (221 events) | Oct 12 (221 events) |
| Required maturity of OS | At least 209 events | At least 237 events |
| OS analysis | Dec 13 (213 events; 61.7%) | Jan 14 (246 events; 67.6%) |
| Median OS follow-up | 41 months | 33 months |
| OS result, overall population | 28.2 vs 28.2 months HR=0.88, p=0.3850 | 23.1 vs 23.5 months HR=0.93, p=0.6137 |

*Yang, et al, Lancet Oncol 2015*

# Trials of EGFR-TKIs vs CT in M+

| Study | N | Median PFS (mos) | | | Median OS (mos) | |
|---|---|---|---|---|---|---|
| | | TKI | Chemo | HR (95 % CI) | TKI | Chemo |
| **IPASS** | **261** | **9.5** | **6.3** | **0.48 (0.36-0.64)** | **21.6** | **21.9** |
| First Signal | 42 | 8.0 | 6.3 | 0.54 (0.26-1.10) | 27.2 | 25.6 |
| NEJ002 | 194 | 10.4 | 5.5 | 0.35 (0.25-0.50) | 27.7 | 26.6 |
| WJTOG | 172 | 9.2 | 6.3 | 0.48 (0.33-0.71) | 36 | 39 |
| OPTIMAL | 154 | 13.7 | 4.6 | 0.16 (0.10-0.26) | 22.6 | 28.8 |
| **EURTAC** | **174** | **10.4** | **5.1** | **0.34 (0.25–0.54)** | **19.3** | **19.5** |
| **LUX-LUNG 3** | **345** | **11.1** | **6.9** | **0.58 (0.43-0.78)** | **28.2** | **28.2** |
| LUX-LUNG 6 | 364 | 11.1 | 5.6 | 0.28 (0.20-0.39 | 23.1 | 23.5 |

# Lux-Lung 7

Stage IIIB/IV adenocarcinoma

*EGFR* mutation (Del19 and/or L858R)

No prior treatment for advanced/ metastatic disease

ECOG PS 0/1
N= 319

**1:1**

**Afatinib 40 mg OD**

Stratified by
Mutation type (Del19/L858R)
Brain metastases (present/absent)

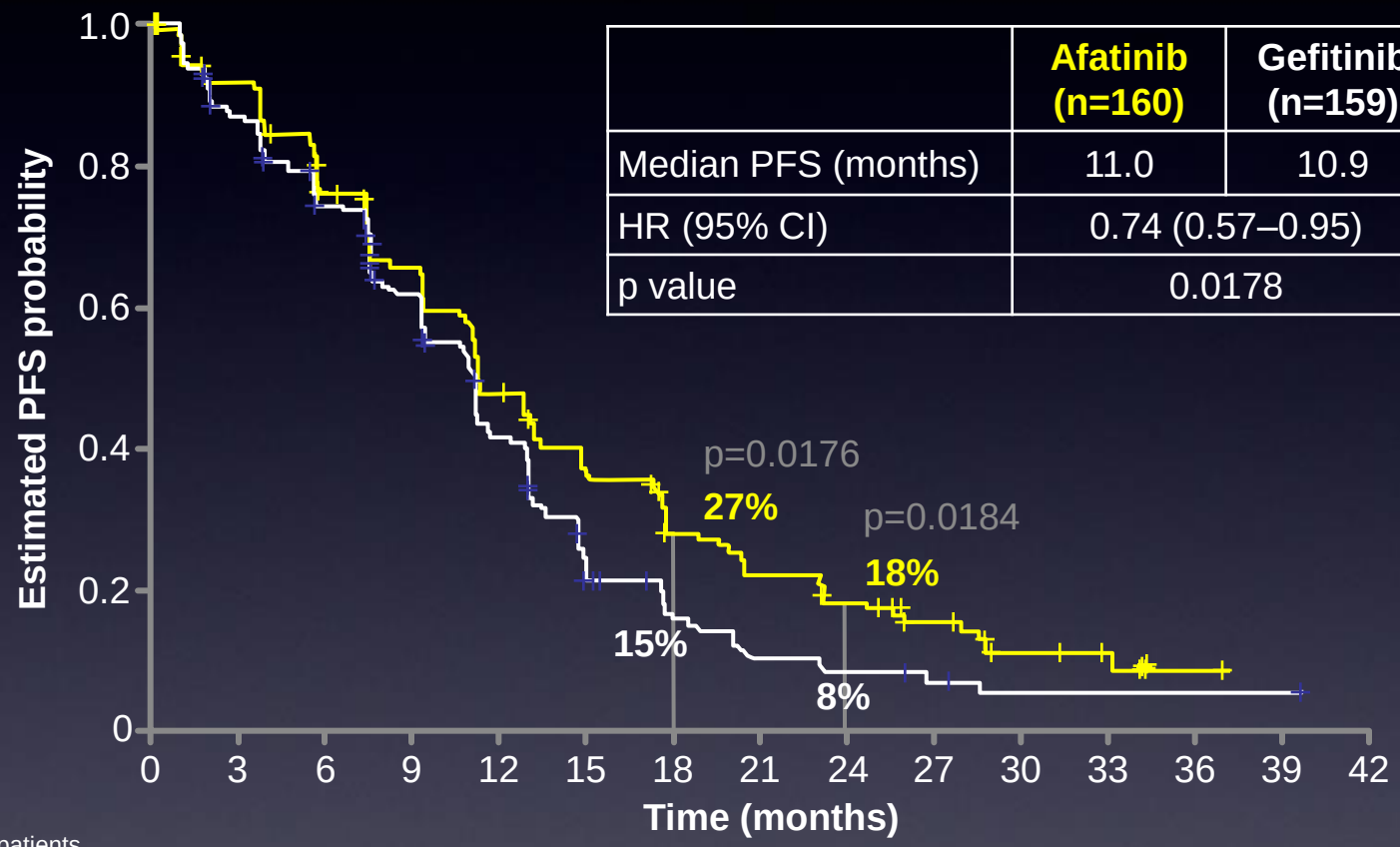
**Gefitinib 250 mg OD**

Treatment beyond progression allowed

Primary endpoints: PFS (IRR), TTF, OS

***Paz-Ares et al, Ann Oncol 2017***

# Progression-free Survival

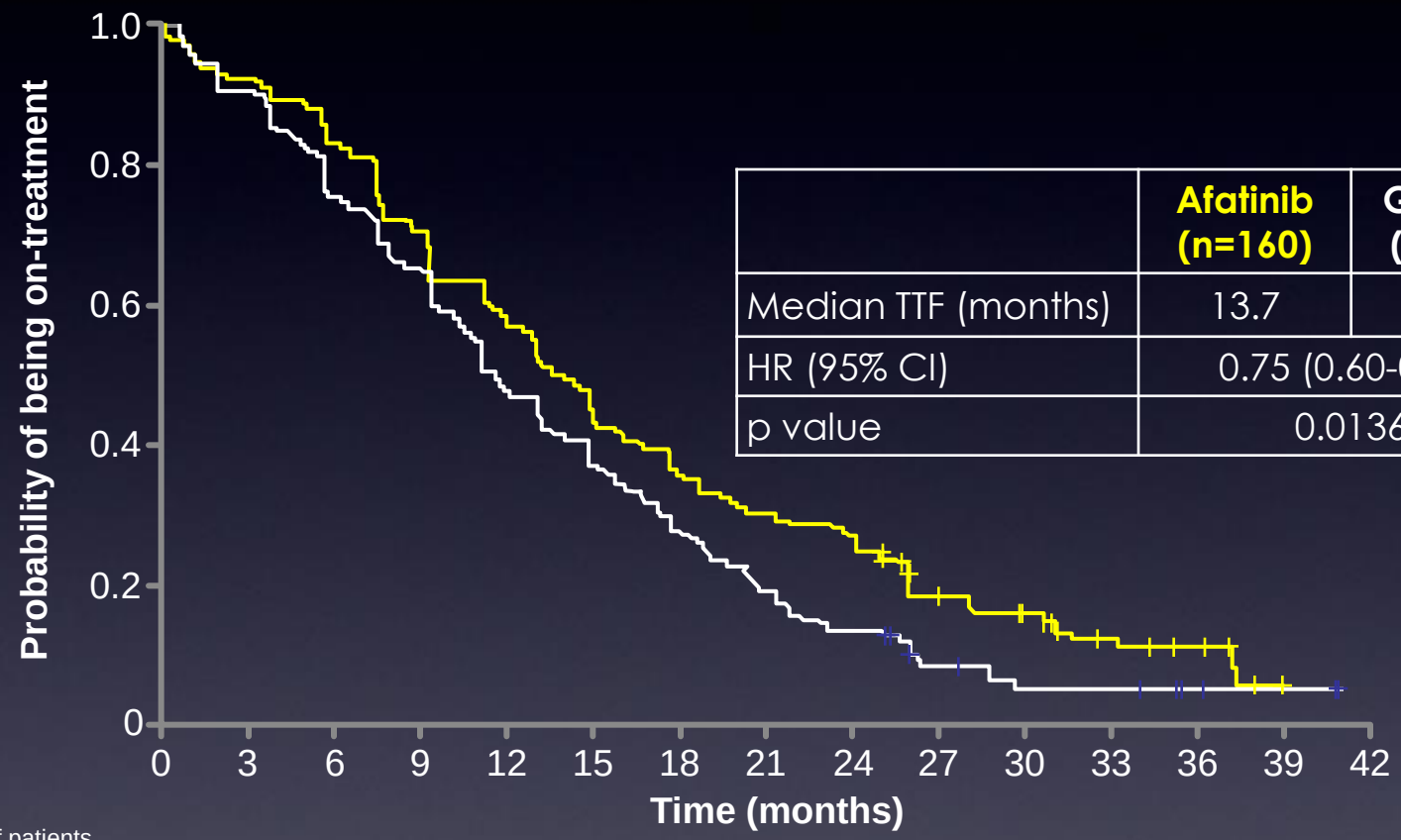



| | Afatinib (n=160) | Gefitinib (n=159) |
|---|---|---|
| Median PFS (months) | 11.0 | 10.9 |
| HR (95% CI) | 0.74 (0.57–0.95) | |
| p value | 0.0178 | |

No. of patients

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Afatinib** | 160 | 142 | 112 | 94 | 67 | 47 | 34 | 27 | 21 | 13 | 6 | 3 | 1 | 0 | 0 |
| **Gefitinib** | 159 | 132 | 106 | 83 | 52 | 22 | 14 | 9 | 7 | 5 | 3 | 3 | 1 | 1 | 0 |

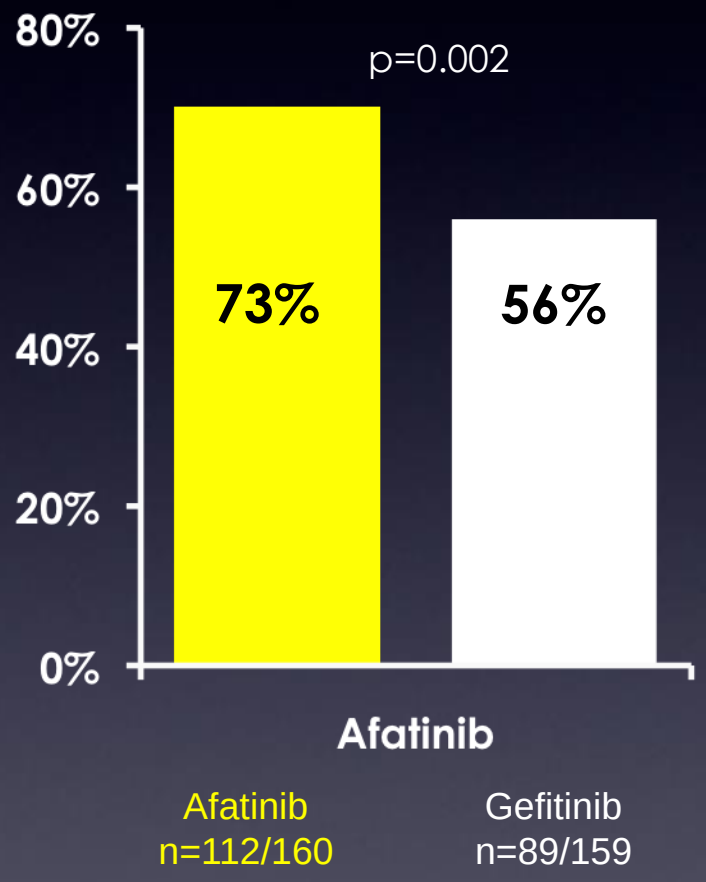
# Time to treatment failure




| | Afatinib (n=160) | Gefitinib (n=159) |
|---|---|---|
| Median TTF (months) | 13.7 | 11.5 |
| HR (95% CI) | 0.75 (0.60-0.94) | |
| p value | 0.0136 | |

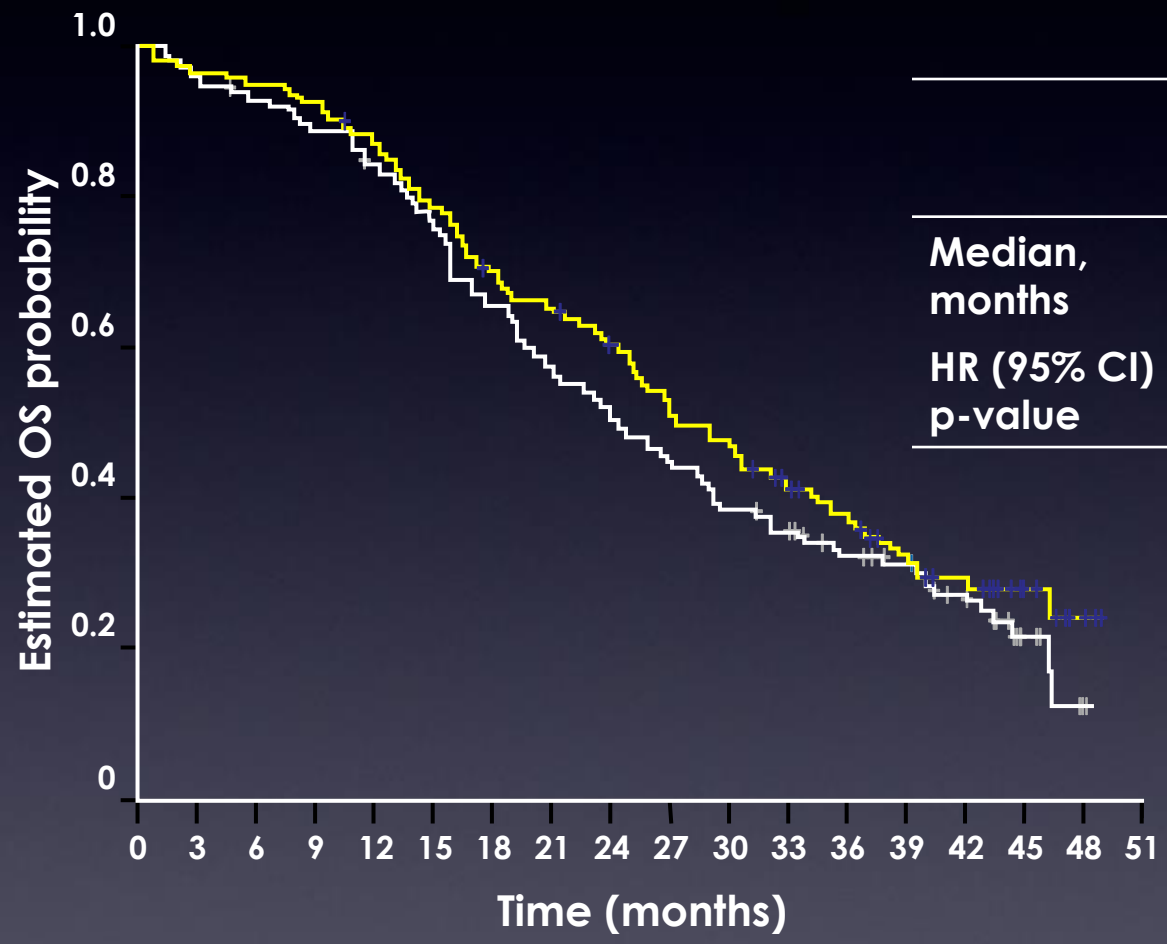
| No. of patients | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Afatinib** | 160 | 148 | 133 | 113 | 91 | 68 | 56 | 48 | 40 | 25 | 18 | 9 | 5 | 0 | 0 |
| **Gefitinib** | 159 | 144 | 120 | 103 | 74 | 59 | 43 | 30 | 21 | 11 | 6 | 6 | 2 | 2 | 0 |

# ORR and DOR




| | Afatinib (n=112) | Gefitinib (n=89) |
|---|---|---|
| Median DoR (mos) | 10 .1 | 8.3 |
| 95% CI | (8.2–11.1) | (7.3–10.2) |

# Overall Survival




| | Afatinib (n=160) | Gefitinib (n=159) |
|---|---|---|
| Median, months | 27.9 | 24.5 |
| HR (95% CI) | 0.86 (0.66–1.12) | |
| p-value | 0.2580 | |

# Efficacy in De1 19 and L858R

| Del 19 | | |
|---|---|---|
| | Afatinib | Gefitinib |
| **Median PFS (months)** | **12.7** | **11.0** |
| HR (95% CI)<br>p value | 0.76 (0.55–1.06)<br>**0.1071** | |
| **Median OS, (months)** | **30.7** | **26.4** |
| HR (95% CI)<br>p-value | 0.83 (0.58–1.17)<br>0.2841 | |

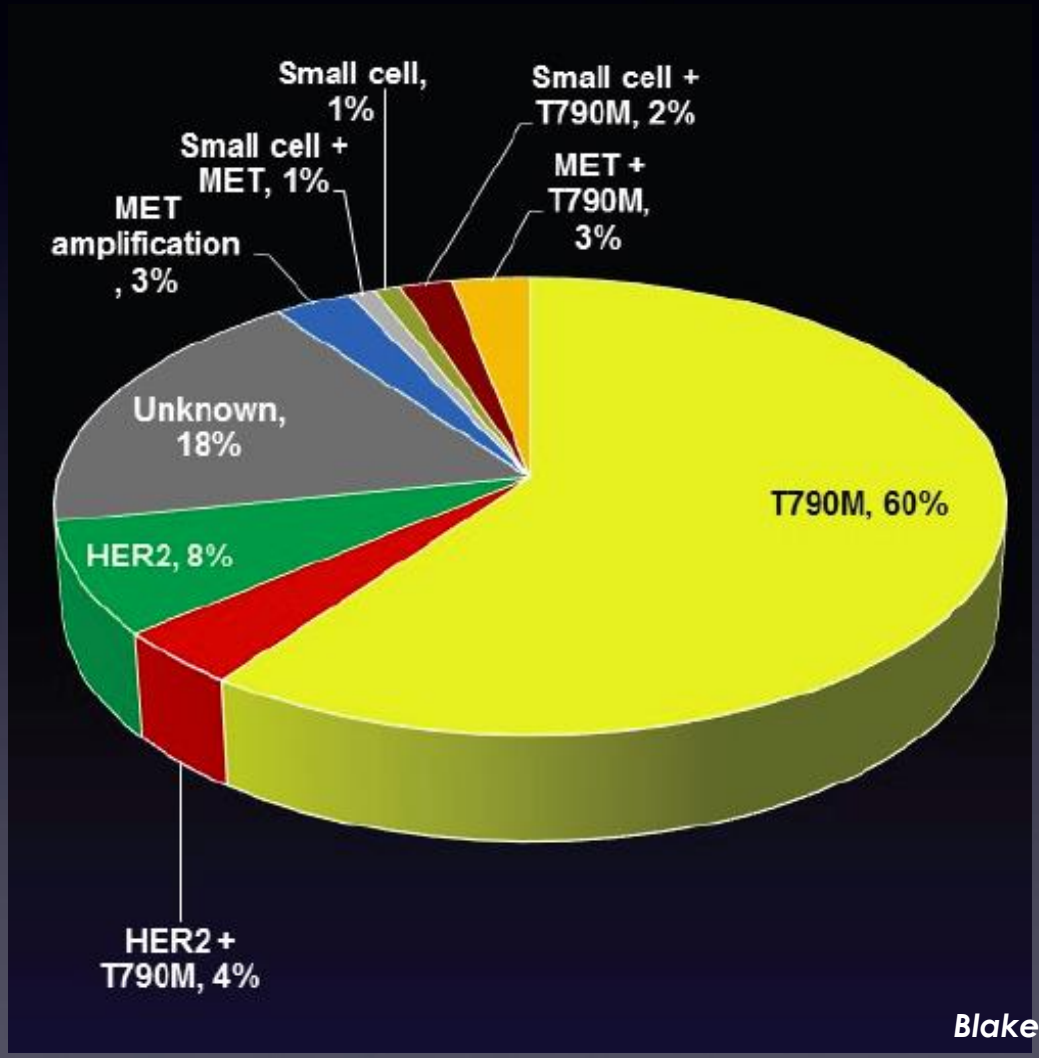
| L858R | | |
|---|---|---|
| | Afatinib | Gefitinib |
| **Median PFS (months)** | **10.9** | **10.8** |
| HR (95% CI)<br>p value | 0.71 (0.47–1.06)<br>0.0856 | |
| **Median OS, (months)** | **25.0** | **21.2** |
| HR (95% CI)<br>p-value | 0.91 (0.62–1.36)<br>0.6585 | |

# Adverse Events

| Events, % | Afatinib (n=160) | Gefitinib (n=159) |
|---|---|---|
| Any AE | 98.8 | 100.0 |
| Drug-related AEs | 97.5 | 96.2 |
| AEs leading to dose reduction* | 41.9 | 1.9* |
| Drug-related AEs leading to discontinuation | 6.3 | 6.3 |
| Serious AEs | 44.4 | 37.1 |
| Drug-related serious AEs | 10.6 | 4.4† |
| Drug-related fatal AE | - | 0.6‡ |

*No dose reductions foreseen for gefitinib according to prescribing information
†Including four patients with drug-related ILD (no drug-related ILD on afatinib)
‡One patient died of hepatic failure

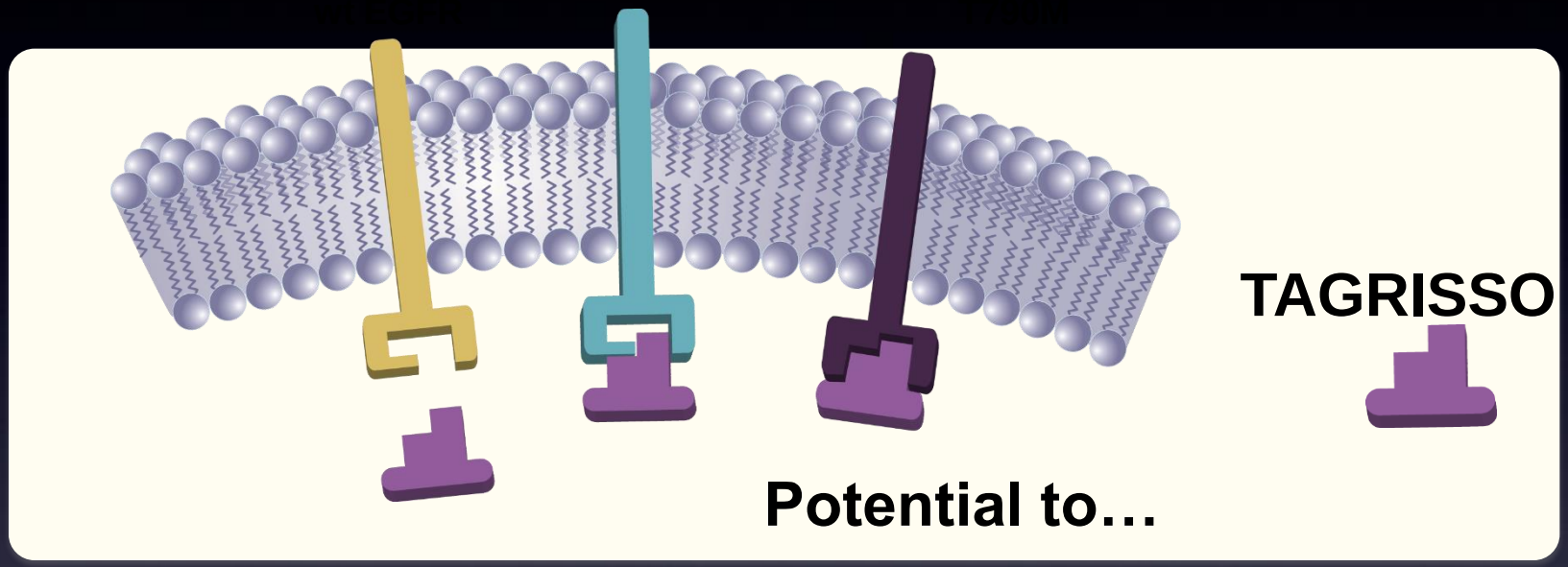
# Mechanisms of resistance




*Blakely et al, Cancer Discovery 2012*

# Tackling T790M resistance mutation

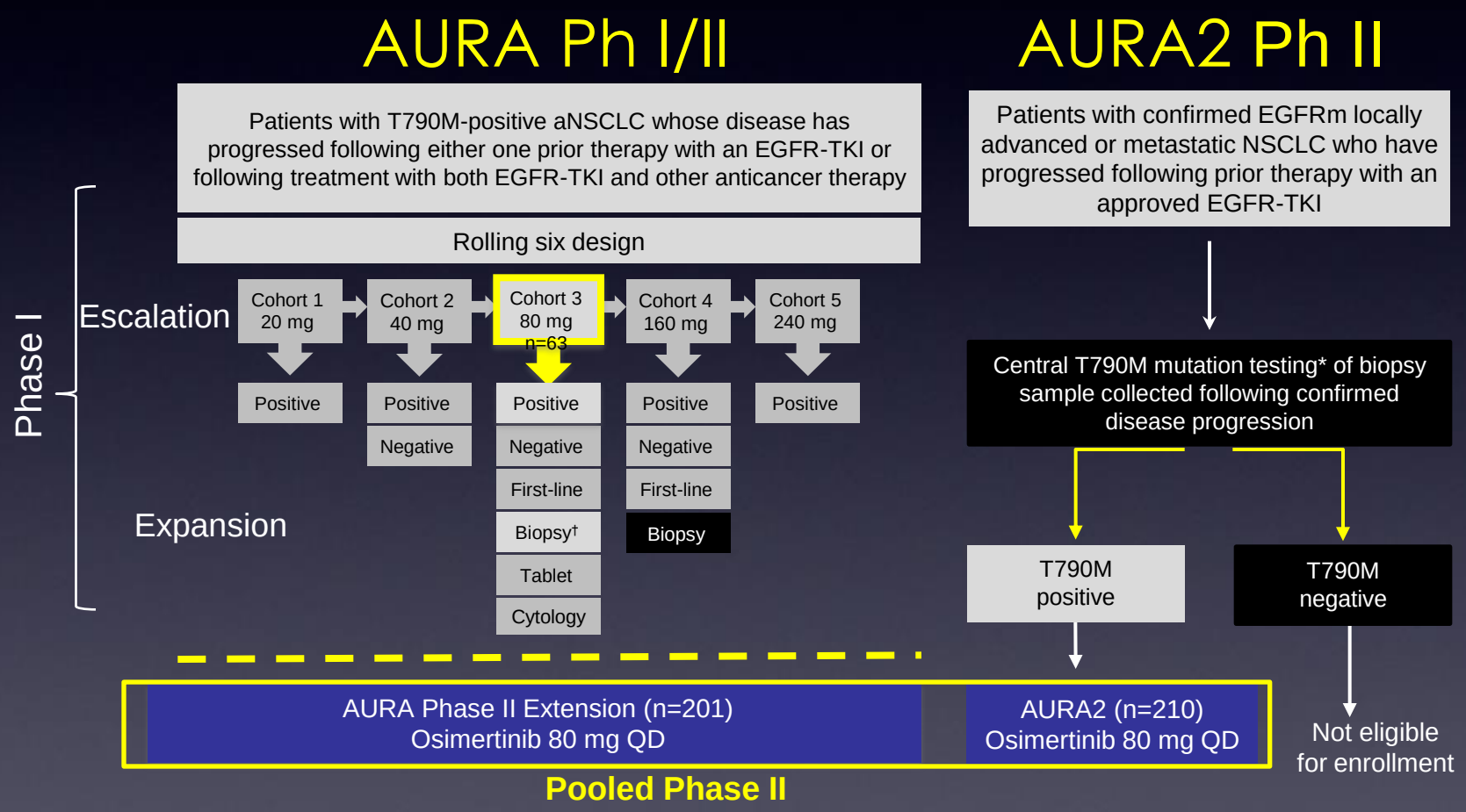
# Osirmetinib




| | | |
|---|---|---|
| Inhibition of T790M | → | Overcome resistance |
| Inhibition of EGFRm | → | Continue targeting sensitizing mutations |
| Low activity on wt EGFR | → | Lower incidence of rash and diarrhoea |

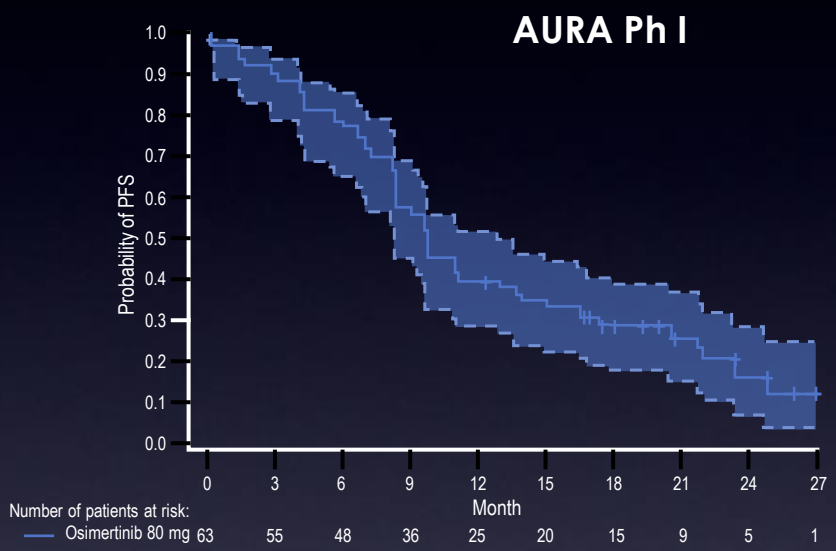
*Cross DAE, et al. Cancer Discovery 2014*

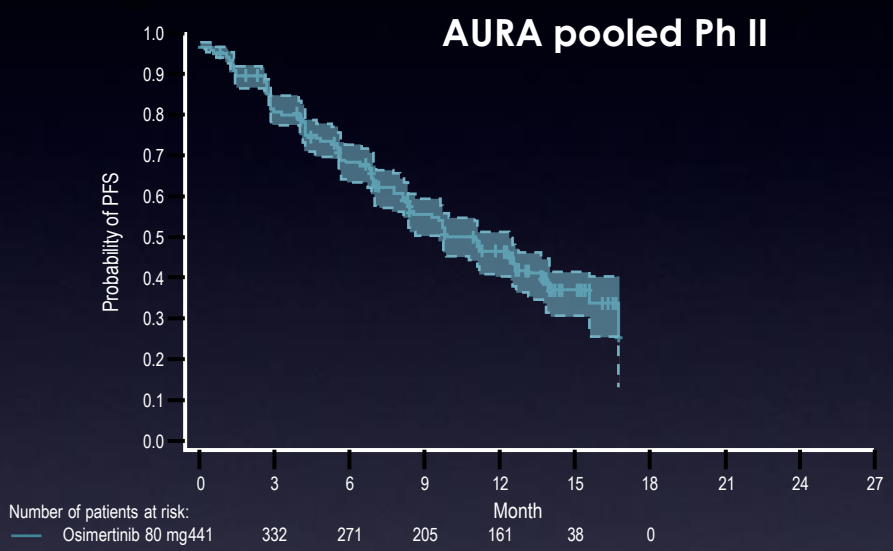
# Osirmetinib Clinical development




*Janne PA et al, NEJM 2015; Goss et al, Lancet Oncol 2016*

# Progression-Free Survival




| | AURA Ph I (80 mg) N=63 | AURA pooled Ph II (80 mg) N=411 |
|---|---|---|
| **Median PFS*, months (95% CI)** | **9.7 (8.3, 13.6)** | **11.0 (9.6, 12.4)** |
| Remaining alive and progression-free,† % (95% CI) | | |
| 12 months | 41 (29, 53) | 48 (42, 53) |
| 18 months | 29 (18, 41) | NC |
| 24 months | 17 (8, 30) | NC |

*Yang JCH, et al. ELCC 2016*

# Adverse Events

| AE category, all causality, n (%) | AURA Ph I (80 mg) N=63* | AURA pooled Ph II (80 mg) N=411† |
|---|---|---|
| Any AE | 62 (98) | 406 (99) |
| Any AE ≥Grade 3 | 29 (46) | 149 (36) |
| Any AE leading to death | 1 (2) | 14 (3) |
| Any AE leading to dose interruption | 16 (25) | 87 (21) |
| Any AE leading to dose reduction | 1 (2) | 16 (4) |
| Any AE leading to discontinuation | 3 (5) | 26 (6) |
| Any serious AE | 18 (29) | 107 (26) |
| **AE category, causally-related‡** | | |
| Any AE | 57 (91) | 364 (89) |
| Any AE ≥Grade 3 | 11 (18) | 56 (14) |
| Any AE leading to discontinuation | 0 | 16 (4) |
| Any serious AE | 3 (5) | 23 (6) |

*Yang JCH, et al. ELCC 2016*

# Drug-related AEs – Ph I exp

| Causally-related AEs occurring in ≥15% of patients overall, n (%) | AURA Ph I (80 mg) N=63* | | | |
|---|---|---|---|---|
| | Grade 1 | Grade 2 | Grade ≥3 | Any grade |
| Rash (grouped terms) | 21 (33) | 2 (3) | 0 | 23 (37) |
| Diarrhoea | 16 (25) | 3 (5) | 1 (2) | 22 (35)† |
| Paronychia (grouped terms) | 11 (18) | 6 (10) | 1 (2) | 18 (29) |
| Dry skin (grouped terms) | 11 (18) | 3 (5) | 0 | 14 (22) |
| Fatigue | 9 (14) | 0 | 0 | 10 (16)‡ |
| Select AEs | | | | |
| ILD (grouped terms) | 0 | 0 | 1 (2) | 1 (2) |
| Hyperglycaemia | 0 | 0 | 0 | 0 |
| QT prolongation | 0 | 0 | 1 (2) | 1 (2) |

*Yang JCH, et al. ELCC 2016*

# Drug-related AEs – pooled Ph2

| Causally-related AEs occurring in ≥15% of patients overall, n (%) | AURA pooled Ph II (80 mg) N=411* | | | |
|---|---|---|---|---|
| | Grade 1 | Grade 2 | Grade ≥3 | Any grade |
| Rash (grouped terms) | 146 (36) | 18 (4) | 3 (<1) | 167 (41) |
| Diarrhoea | 138 (34) | 17 (4) | 2 (<1) | 157 (38) |
| Dry skin (grouped terms) | 116 (28) | 9 (2) | 0 | 125 (30) |
| Paronychia (grouped terms) | 88 (21) | 30 (7) | 0 | 118 (29) |
| Select AEs | | | | |
| ILD (grouped terms) | 4 (1) | 0 | 8 (2) | 12 (3) |
| Hyperglycaemia | 0 | 1 (<1) | 0 | 1 (<1) |
| QT prolongation | 7 (2) | 3 (<1) | 4 (1) | 14 (3) |

*Yang JCH, et al. ELCC 2016*

# AURA3 study

**Key eligibility criteria**

- Locally advanced or metastatic NSCLC
- Evidence of disease progression following first-line EGFR-TKI therapy
- Documented EGFRm and central confirmation of tumour EGFR T790M mutation after first-line EGFR-TKI treatment
- PS 0 or 1
- No more than one prior line of treatment for advanced NSCLC
- Stable asymptomatic CNS metastases allowed

**R 2:1**

**Osimertinib**
80 mg OD
**(n=279)**

**Platinum-pemetrexed**
+/-
maintenance pemetrexed
**(n=140)**

**Endpoints Primary:**

•PFS by investigator assessment (RECISTv1.1)

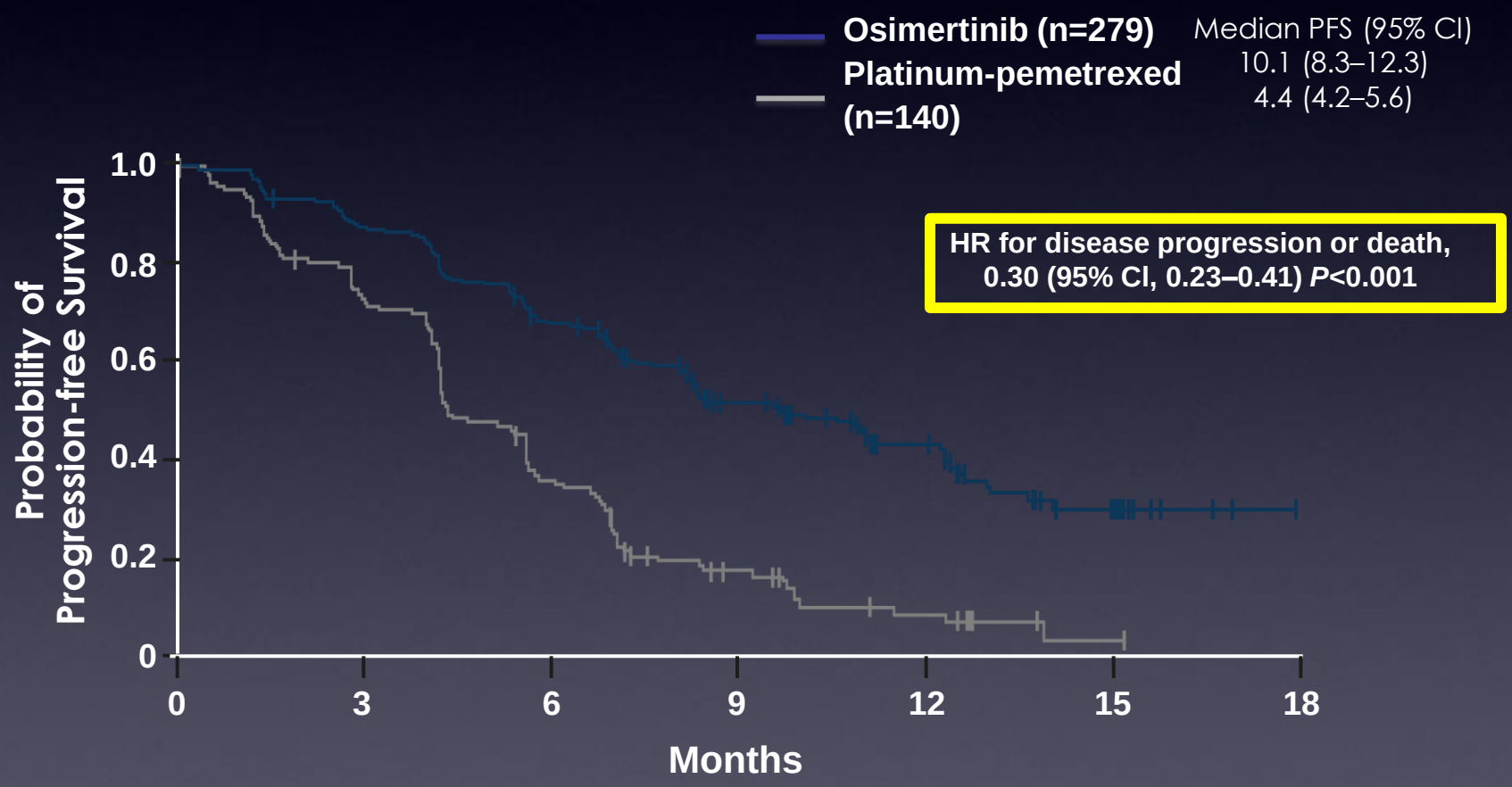
**Secondary and exploratory:**

•OS
•ORR
•DoR
•DCR
•Tumour shrinkage
•BICR-assessed PFS
•PROs
•Safety and tolerability

**Optional crossover:** Protocol amendment allowed patients on chemotherapy to begin post-BICR confirmed progression open-label osimertinib treatment

*Mok TS et al, NEJM 2016*

# Progression-free Survival (investigator)



# Response Rate

| | Osimertinib (n=279) | Platinum-pemetrexed (n=140) |
|---|---|---|
| **ORR, % (95% CI)** | **71% (65, 76)** | **31% (24, 40)** |
| Odds ratio* (95% CI) | 5.39 (3.47, 8.48); P<0.001 | |
| Complete response, n (%)<br>Partial response, n (%)<br>Stable disease ≥6 weeks, n (%)<br>Progression, n (%)<br>RECIST progression, n (%)<br>Death<br>Not evaluable, n (%) | 4 (1)<br>193 (69)<br>63 (23)<br>18 (6)<br>15 (5)<br>3 (1)<br>1 (<1) | 2 (1)<br>42 (30)<br>60 (43)<br>26 (19)<br>22 (16)<br>4 (3)<br>10 (7) |
| **DCR†, % (95% CI)** | **93 (90, 96)** | **74 (66, 81)** |
| Odds ratio* (95% CI) | 4.76 (2.64, 8.84); *P*<0.001 | |
| **Median time to response‡, weeks (95% CI)** | **6.1 (NC, NC)** | **6.4 (6.3, 7.0)** |
| **Median DoR#, months (95% CI)** | **9.7 (8.3, 11.6)** | **4.1 (3.0, 5.6)** |

# Safety

| AE category*, n (%) | Osimertinib (n=279) | Platinum-pemetrexed (n=136) |
|---|---|---|
| Any AE | 273 (98) | 135 (99) |
| Any AE Grade ≥3 | 63 (23) | 64 (47) |
| Any AE leading to death | 4 (1) | 1 (1) |
| Any serious AE | 50 (18) | 35 (26) |
| Any AE leading to discontinuation | 19 (7) | 14 (10) |
| **AE category, possibly causally related†, n (%)** | | |
| Any AE | 231 (83) | 121 (89) |
| Any AE Grade ≥3 | 16 (6) | 46 (34) |
| Any AE leading to death | 1 (<1) | 1 (1) |
| Any serious AE | 8 (3) | 17 (13) |
| Any AE leading to discontinuation | 10 (4) | 12 (9) |

# Adverse Events

| N (%)<br>15% cut-off | Osimertinib (n=279) | | Platinum-pemetrexed (n=136) | |
|---|---|---|---|---|
| | Any grade | Grade ≥3 | Any grade | Grade ≥3 |
| **Any AE** | 273 (98) | 63 (23) | 135 (99) | 64 (47) |
| Diarrhoea | 113 (41) | 3 (1) | 15 (11) | 2 (1) |
| Rash† | 94 (34) | 2 (1) | 8 (6) | 0 |
| Dry skin† | 65 (23) | 0 | 6 (4) | 0 |
| Paronychia† | 61 (22) | 0 | 2 (1) | 0 |
| Decreased appetite | 50 (18) | 3 (1) | 49 (36) | 4 (3) |
| Cough | 46 (16) | 0 | 19 (14) | 0 |
| Nausea | 45 (16) | 2 (1) | 67 (49) | 5 (4) |
| Fatigue | 44 (16) | 3 (1) | 38 (28) | 1 (1) |
| Stomatitis | 41 (15) | 0 | 21 (15) | 2 (1) |
| Constipation | 39 (14) | 0 | 47 (35) | 0 |
| Vomiting | 31 (11) | 1 (<1) | 27 (20) | 3 (2) |
| Thrombocytopaenia† | 28 (10) | 1 (<1) | 27 (20) | 10 (7) |
| Neutropaenia† | 22 (8) | 4 (1) | 31 (23) | 16 (12) |
| Leukopenia† | 22 (8) | 0 | 20 (15) | 5 (4) |
| Anaemia† | 21 (8) | 2 (1) | 41 (30) | 16 (12) |
| Asthenia | 20 (7) | 3 (1) | 20 (15) | 6 (4) |
| **Select adverse events** | | | | |
| Interstitial lung disease† | 10 (4) | 1 (<1) | 1 (1) | 1 (1) |
| QT prolongation | 10 (4) | 1 (<1) | 1 (1) | 0 |

# Take Home Message

Screen for EGFR mutations!

EGFR-TKIs are standard of care in EGFR M+

Look for T790M resistance mutation

# Backup Slides

# Aura 3 – EGFR Plasma ctDNA

Patients with tissue sample available at screening (n=756)

| **Plasma ctDNA test results, n** | **Tissue T790M positive (n=399)** | **Tissue Exon 19 deletion positive (n=427)** | **Tissue L858R positive (n=253)** |
|---|---|---|---|
| Plasma positive | 184 | 273 | 139 |
| Plasma negative | 175 | 60 | 67 |
| No plasma test / invalid | 37 / 3 | 91 / 3 | 47 / 0 |
| **Percent agreement using tissue test as reference, % (95% CI)*** | | | |
| Positive percent agreement (sensitivity) | **51 (46, 57)** | 82 (77, 86) | 68 (61, 74) |
| Negative percent agreement (specificity) | **77 (71, 83)** | 98 (96, 100) | 99 (98, 100) |
| Overall concordance | 61 (57, 65) | 89 (86, 91) | 88 (85, 90) |

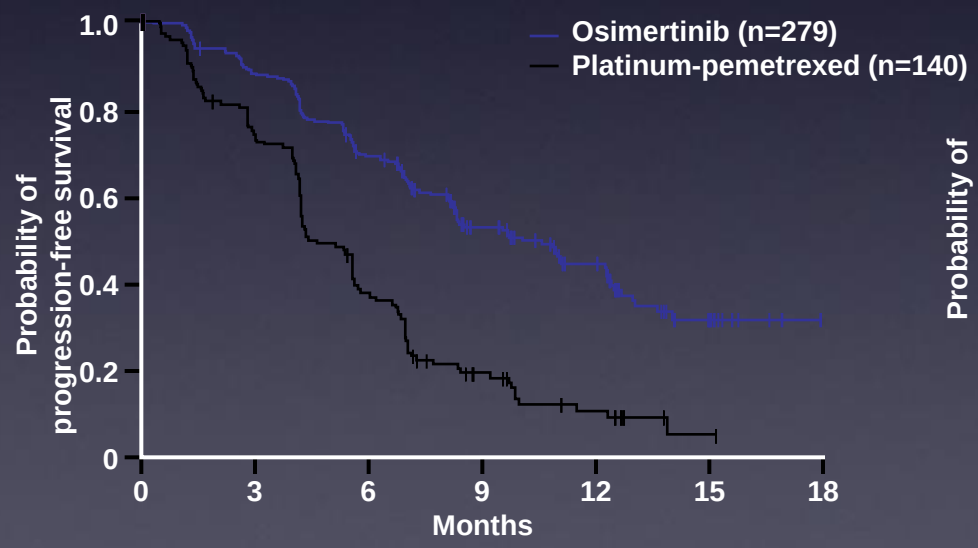
# AURA3: Efficacy in pts with plasma and tumour tissue T790M+ status

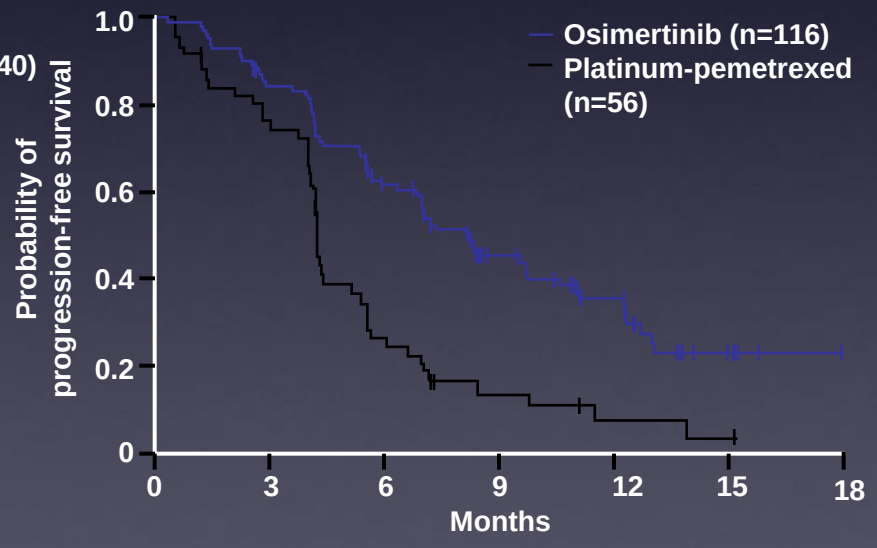
**Tumour T790M-positive (ITT)**

| | Osimertinib | Platinum-pemetrexed |
|---|---|---|
| PFS HR (95% CI) | 0.30 (0.23, 0.41)*, p<0.001 | |
| Median PFS, months (95% CI) | 10.1 (8.3, 12.3) | 4.4 (4.2, 5.6) |
| ORR†, % (95% CI) | 71 (65, 76) | 31 (24, 40) |

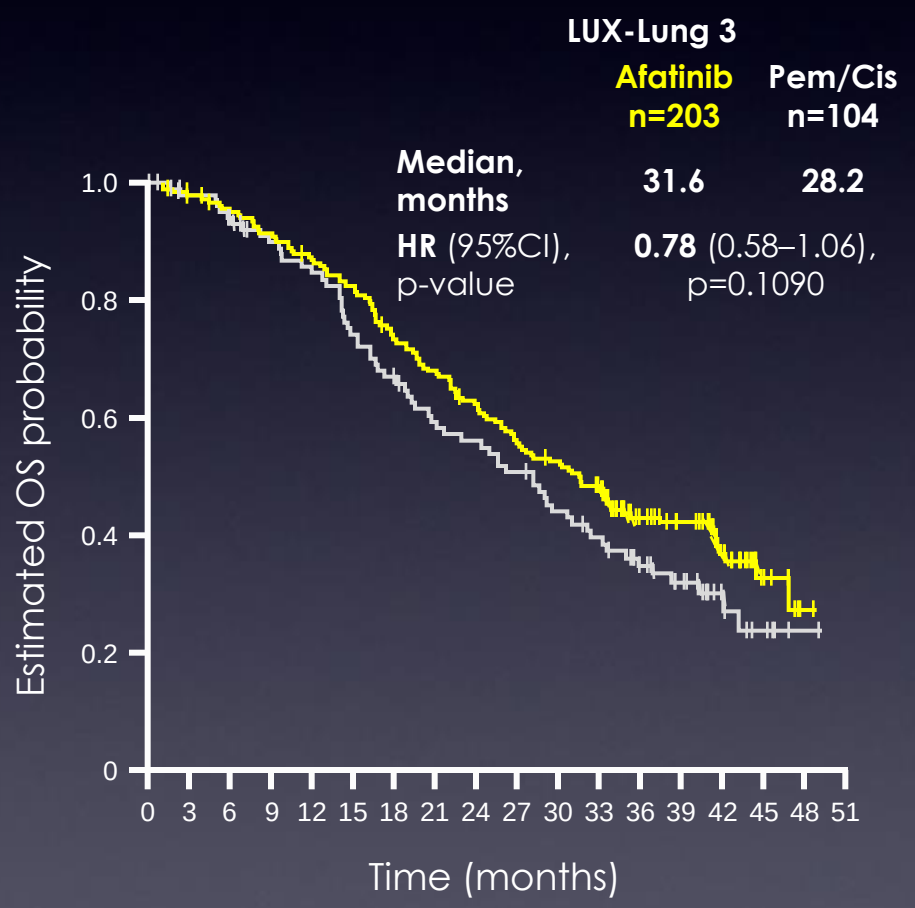
**Plasma T790M-positive status**

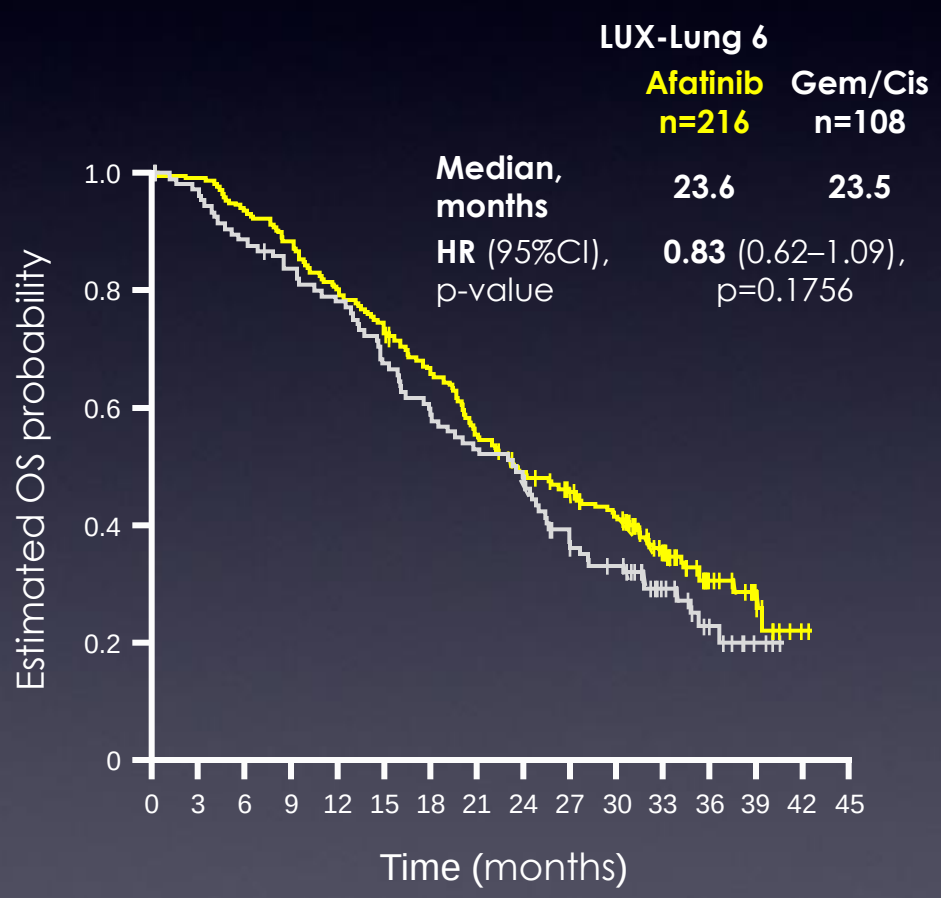
| | Osimertinib | Platinum-pemetrexed |
|---|---|---|
| PFS HR (95% CI) | 0.42 (0.29, 0.61) | |
| Median PFS, months (95% CI) | 8.2 (6.8, 9.7) | 4.2 (4.1, 5.1) |
| ORR†, % (95% CI) | 77 (68, 84) | 39 (27, 53) |



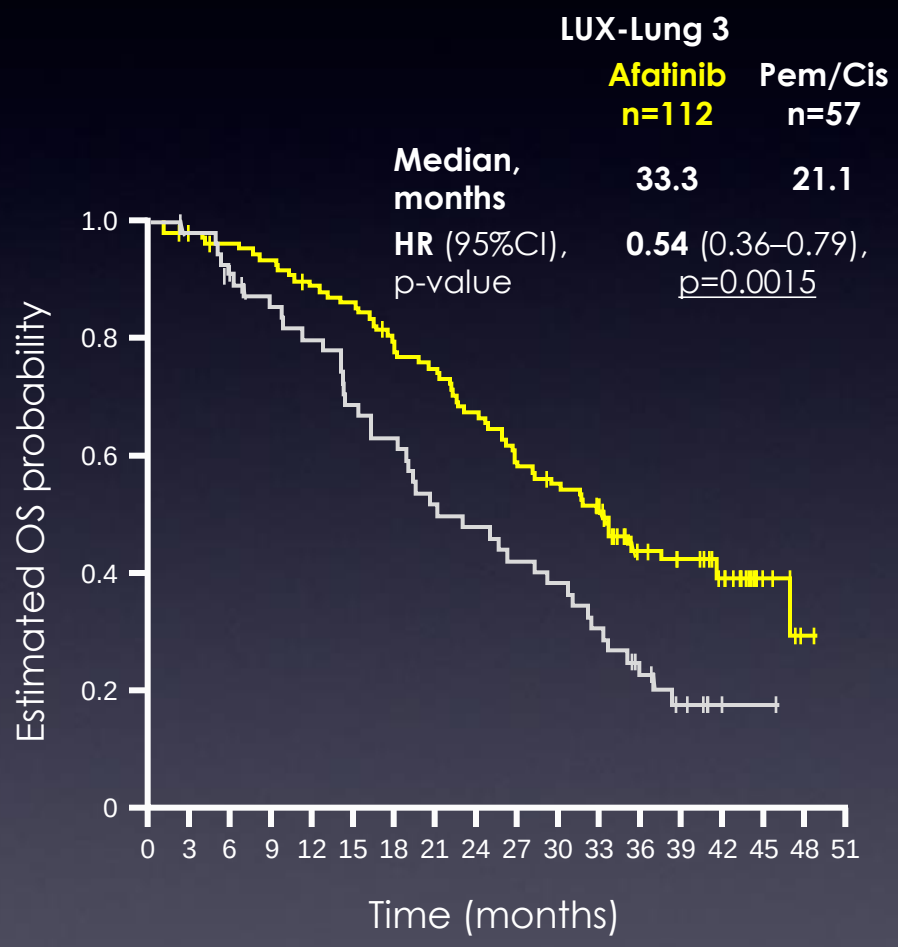



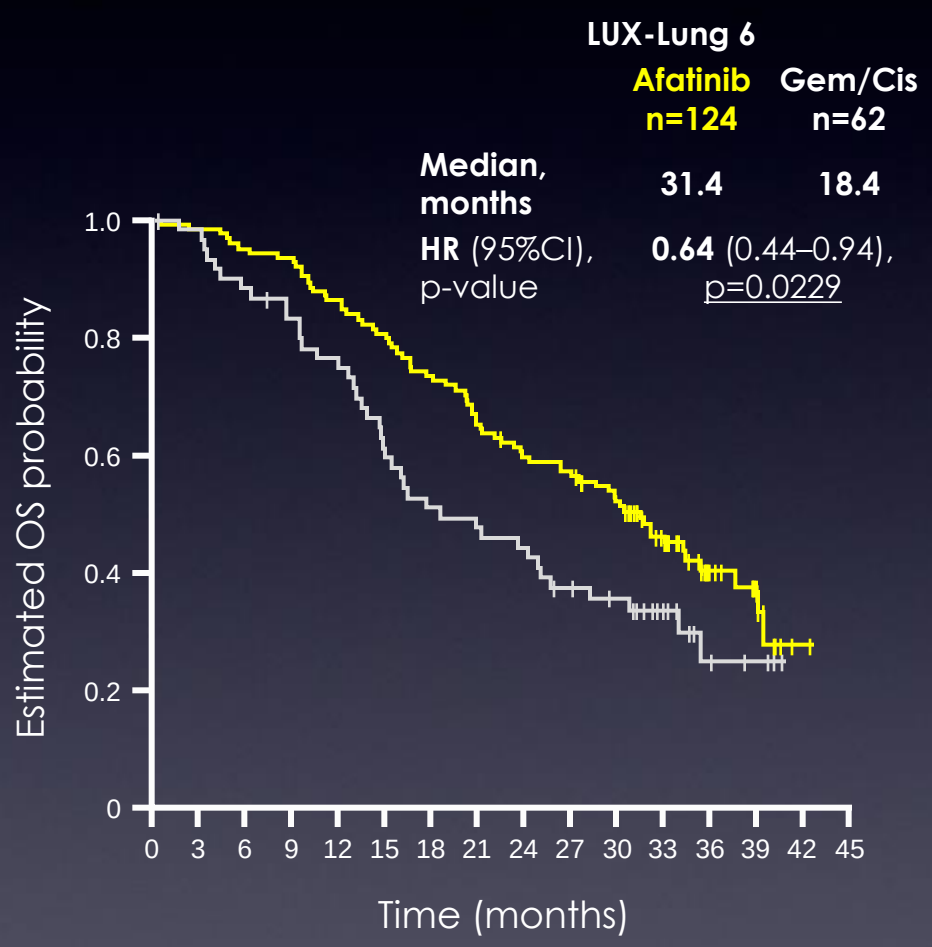
# LUX-Lung 3 and 6: OS in common mutations



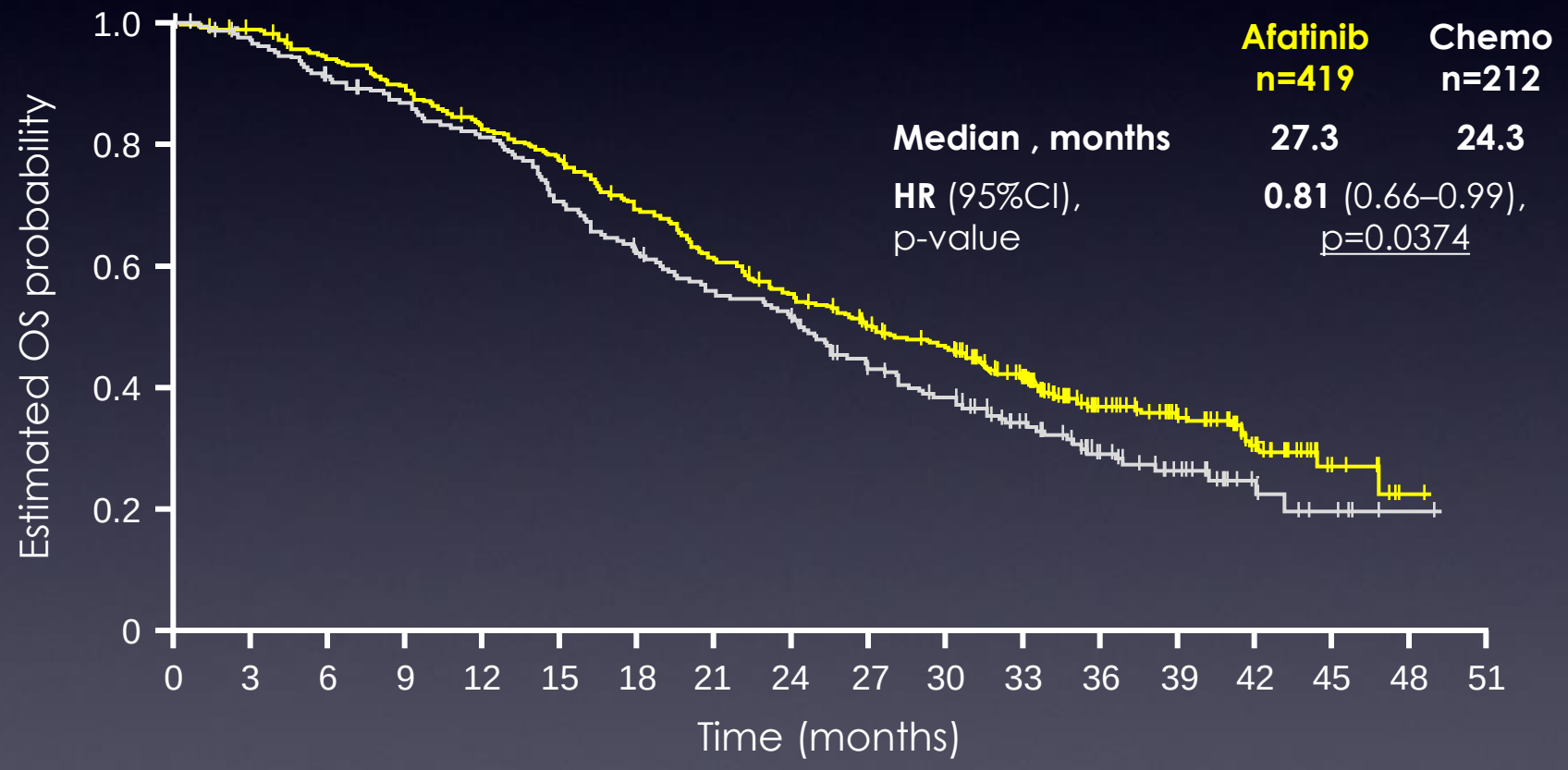



# OS in Del19 subgroup

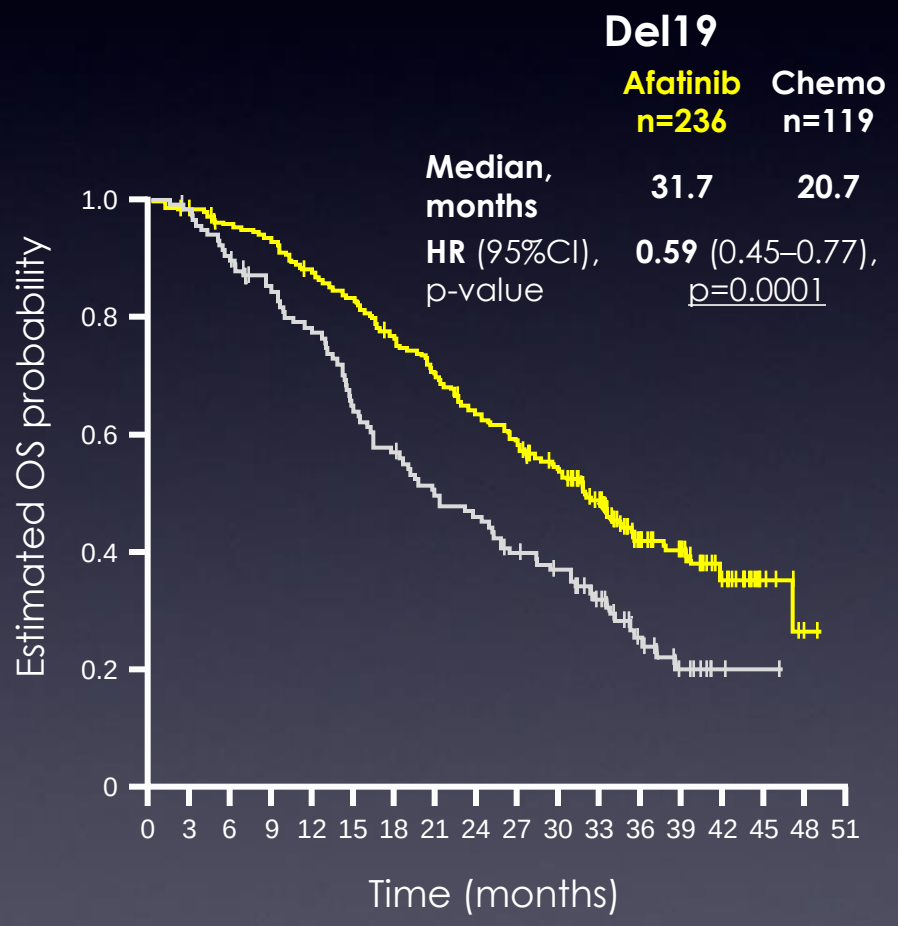


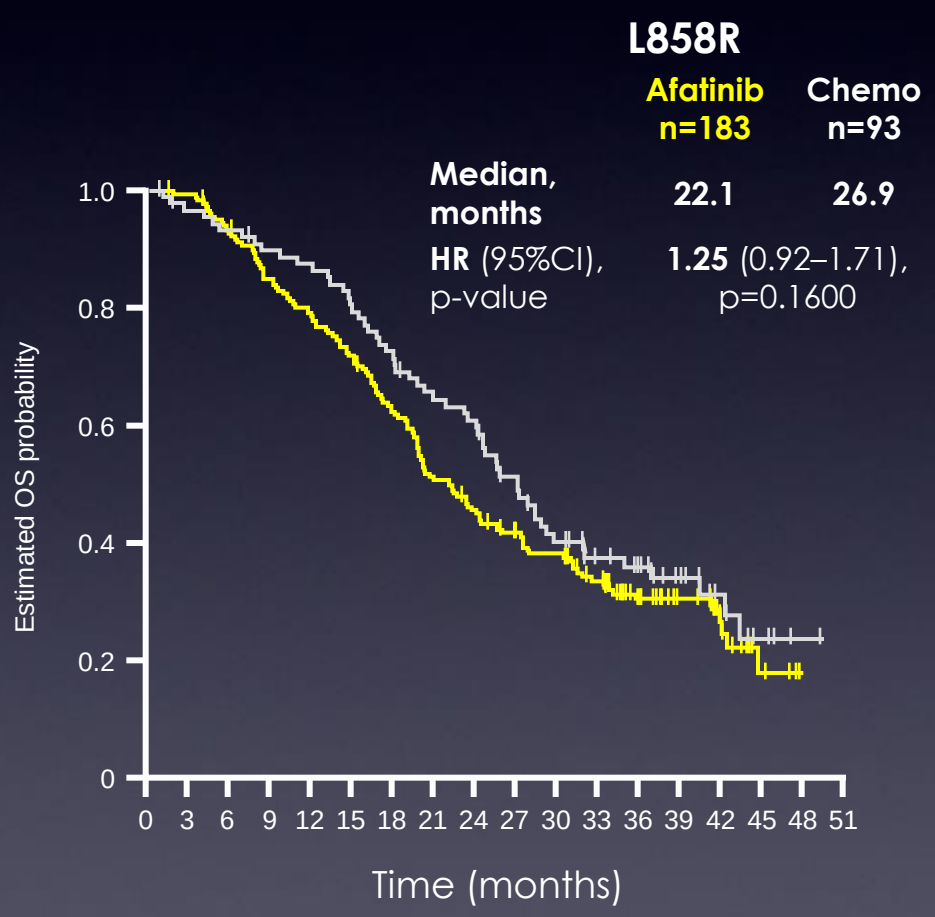



# Combined OS analysis: common mutations (n=631)



# Combined OS analysis: mutation categories



# Treatment at progression

| | LUX-Lung 3 | | LUX-Lung 6 | |
|---|---|---|---|---|
| | **Afatinib (n=203)** | **Pem/Cis (n=104)** | **Afatinib (n=216)** | **Gem/Cis (n=108)** |
| Discontinued treatment, n (%) | 184 (100) | 104 (100) | 194 (100) | 108 (100) |
| Subsequent systemic therapy, n (%) | 144 (78) | 88 (85) | 123 (63) | 70 (65) |
| **Chemotherapy, n (%)** | **131 (71)** | **49 (47)** | **114 (59)** | **29 (27)** |
| **EGFR TKI therapy, n (%)** | **81 (44)** | **78 (75)** | **50 (26)** | **61 (56)** |
| Erlotinib | 61 (33) | 46 (42) | 21 (11) | 22 (20) |
| Gefitinib | 28 (15) | 44 (42) | 19 (10) | 39 (36) |
| Afatinib | 2 (1) | 7 (7) | – | – |
| AZD9291 | 2 (1) | 1 (1) | – | – |
| Dacomitinib | – | 1 (1) | – | – |
| Icotinib | – | – | 11 (6) | 3 (3) |
| EGFR TKI combinations | 5 (3) | 9 (9) | 5 (3) | 3 (3) |
| Other systemic therapy, n (%) | 5 (3) | 2 (2) | 3 (2) | 4 (4) |
| Radiotherapy, n (%) | 32 (17) | 21 (20) | 4 (2) | 0 (0) |