Best of ASCO 2012
Lung Cancer

P. Fulden Yumuk, MD
Marmara University Medical School
Division of Medical Oncology

- Abst. 6004: Greer JA, et al. Effect of Early Palliative Care on Health Care Costs in Patients with Metastatic NSCLC
- Abst. 7000: Yamamoto S, et al. Is consolidation chemotherapy after concurrent chemo-radiotherapy beneficial for patients with locally advanced NSCLC? A pooled analysis of the literature
- Abst. 7004: Park K, et al. Phase III Trial of Concurrent Thoracic Radiotherapy (TRT) with Either the 1st Cycle or the 3rd Cycle of Cisplatin and Etoposide Chemotherapy to Determine the Optimal Timing of TRT for Limited-Disease SCLC (NCT01125995)
- Abst. 7008: Grogan EL, et al. Accuracy of FDG-PET to diagnose lung cancer in the ACOSOG Z4031 trial
- Abst. 7506: Lilenbaum R, et al. A Phase III Randomized Trial of Single Agent Pemetrexed vs. Carboplatin and Pemetrexed in Patients with Advanced NSCLC and a PS 2
- Abst. 7006: Govindan R, et al. Comprehensive Characterization of Squamous Cell NSCLC
- Abst. 7500: Yang JCH, et al. LUX-Lung 3: a randomized, open-label, Phase III study of afatinib vs cisplatin/pemetrexed as 1st-line treatment for patients with advanced adenocarcinoma of the lung harboring EGFR-activating mutations
- Abst. 7501: Garassino MC, et al. A phase III trial comparing erlotinib versus docetaxel as second-line treatment of NSCLC patients with wild-type EGFR - TAILOR
- Abst. 7508: Shaw AT, et al. Clinical Activity of Crizotinib in Advanced NSCLC Harboring ROS1 Rearrangement
- Abst. 7509: Brahmer JR, et al. Clinical Activity and Safety of Anti-PD-1 (BMS-936558, MDX-1106) in Patients with Advanced NSCLC

Accuracy of FDG-PET to diagnose lung cancer in the ACOSOG Z4031 trial

Abst. 7008

E. L. Grogan, S.A. Deppen, K.V. Ballman, G. Andrade, F. Verdail, M.C. Aldrich, H. Chen, P. Decker, D. Harpole, R. Cerfolio, R. Keenan, D. R. Jones, T. A. D'Amico, J. Shrager, B. Meyers, J.B. Putnam

Summary slide

- FDG-PET performed poorly for diagnosing NSCLC in a national sample of c-Stage I patients
  - Sensitivity - 82%
  - Specificity - 31%
- Majority of false positives were granulomas
- Sensitivity varies by enrolling city
- FDG-PET accuracy improved with lesion size
  - Accuracy < 50% for < 2cm lesions

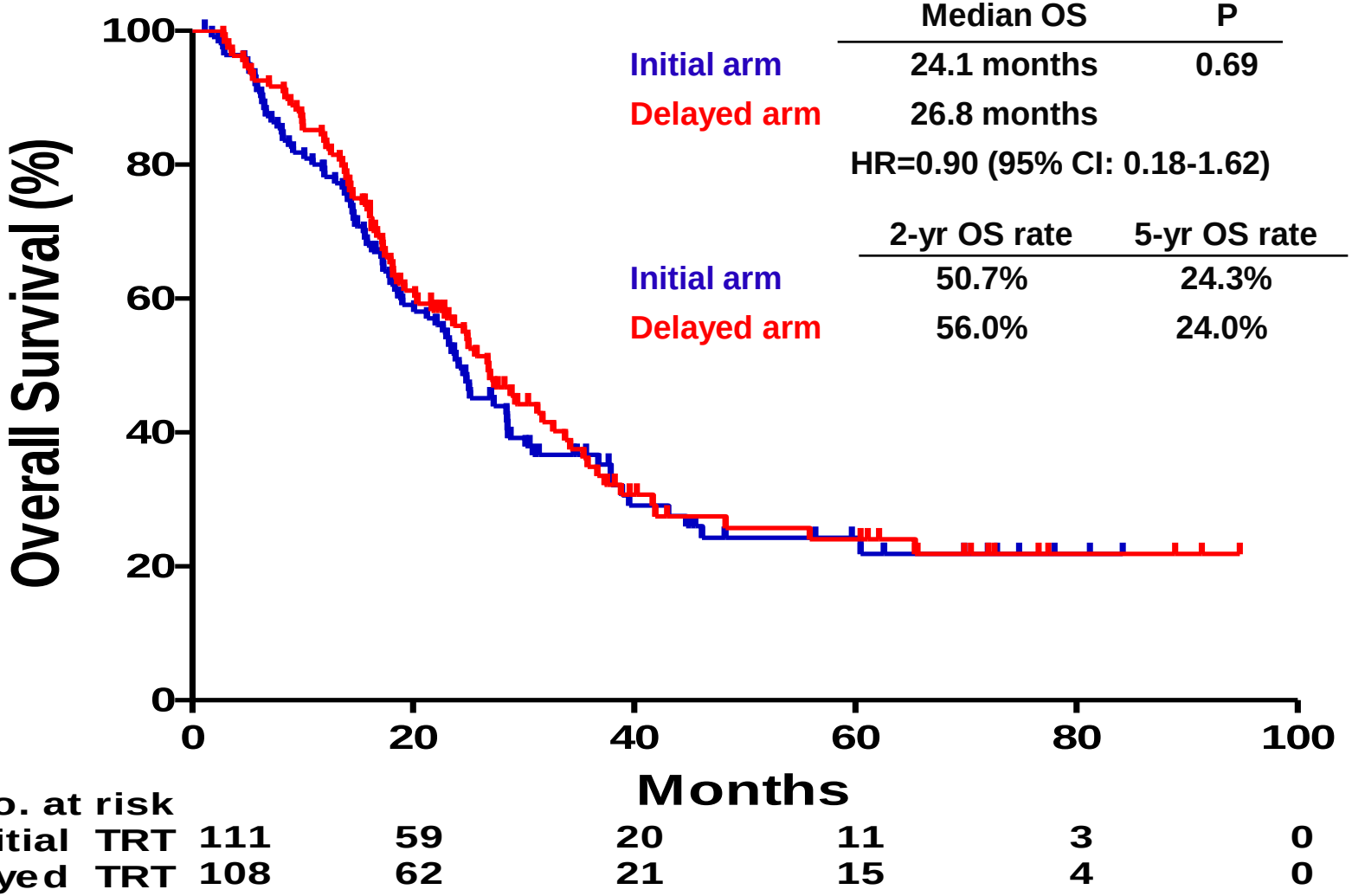
Phase III Trial of Concurrent Thoracic Radiotherapy (TRT) with Either the 1st Cycle or the 3rd Cycle of Cisplatin and Etoposide Chemotherapy to Determine the Optimal Timing of TRT for Limited-Disease Small Cell Lung Cancer (NCT01125995)

Abst. 7004

Keunchil Park,[1] Jong-Mu Sun,[1] Sang-We Kim,[2] Yong Chan Ahn,[1] Eun Kyung Choi,[2] Myung-Ju Ahn,[1] Jin Seok Ahn,[1] Se-Hoon Lee,[1] Sin-Ho Jung,[3] Dae Ho Lee,[2] Hongryull Pyo,[1] Si Yeol Song,[2] Jungmin Jo,[2] Hee Jung Sohn [2] Cheolwon Suh,[2] Jung Shin Lee[2]

[1]Samsung Medical Center, Seoul, Republic of Korea; [2]Asan Medical Center, Seoul, Republic of Korea; [3]Duke University, Durham, NC, USA

Overall Survival



	Median OS	P
Initial arm	24.1 months	0.69
Delayed arm	26.8 months	
	HR=0.90 (95% CI: 0.18-1.62)	

	2-yr OS rate	5-yr OS rate
Initial arm	50.7%	24.3%
Delayed arm	56.0%	24.0%

Is consolidation chemotherapy after concurrent chemo-radiotherapy beneficial for patients with locally advanced non-small cell lung cancer?

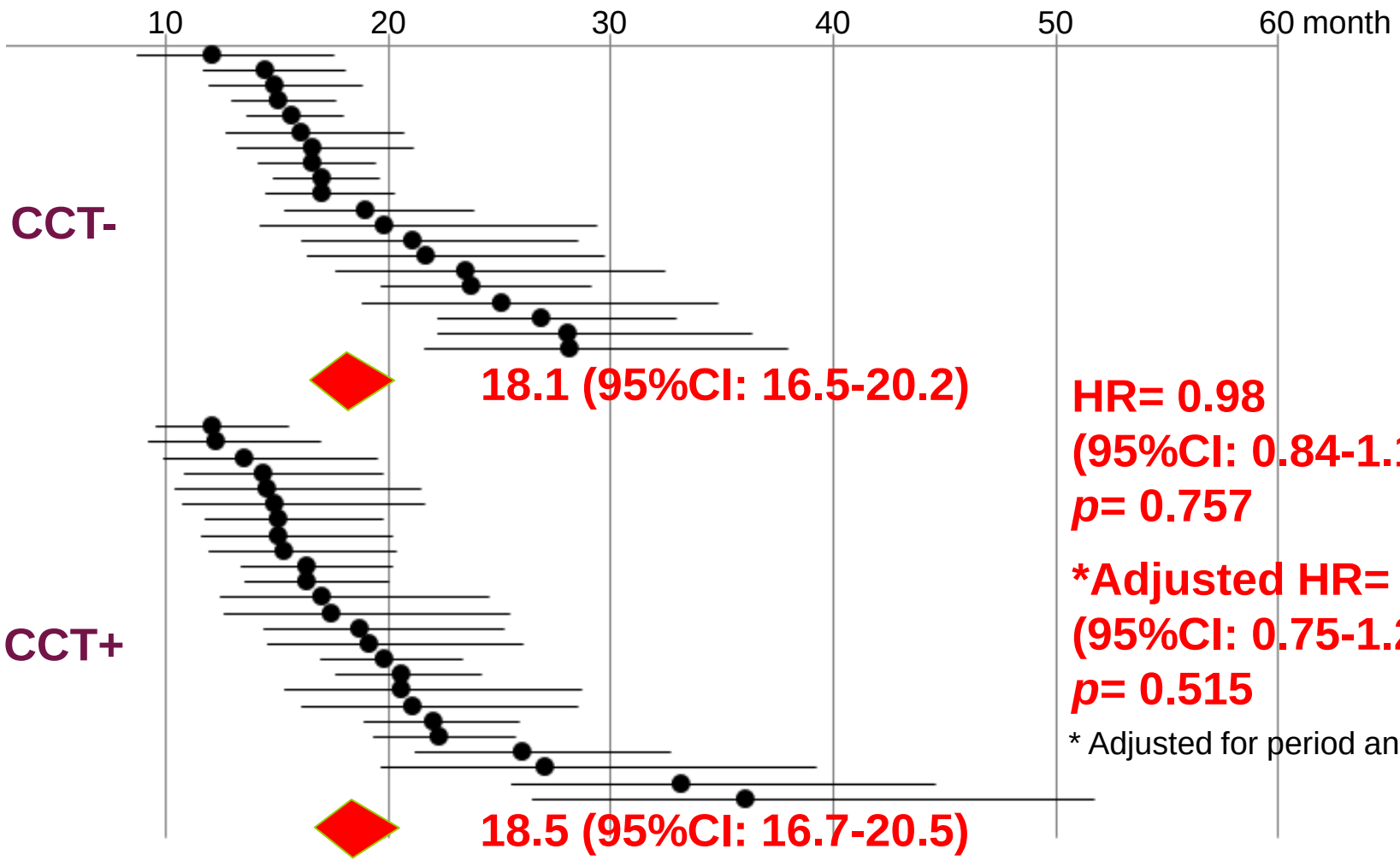
～A pooled analysis of the literature～

Abst. 7000

Satomi Yamamoto[1], Kazuyuki Tsujino[2], Masahiko Ando[3], Tomoya Kawaguchi[1], Akihito Kubo[4], Shunichi Isa[1], Yoshikazu Hasegawa[5], Sai-Hong Ignatius Ou[6], Minoru Takada[7], Takayasu Kurata[8]

1 National Hospital Organization Kinki-Chuo Chest Medical Center,
2 Osaka University Graduate School of Medicine, 3 Nagoya University Hospital,
4 Aichi Medical University School of Medicine, 5 Kishiwada City Hospital,
6 Chao Family Comprehensive Cancer Center, University of California Irvine,
7 Sakai Hospital Kinki University Faculty of Medicine,
8 Kinki University School of Medicine

Individual and pooled median OS



I^2 values for assessing heterogeneity were 15.3% in all studies.

A Phase III Randomized Trial of Single Agent Pemetrexed vs. Carboplatin and Pemetrexed in Patients with Advanced NSCLC and a PS of 2

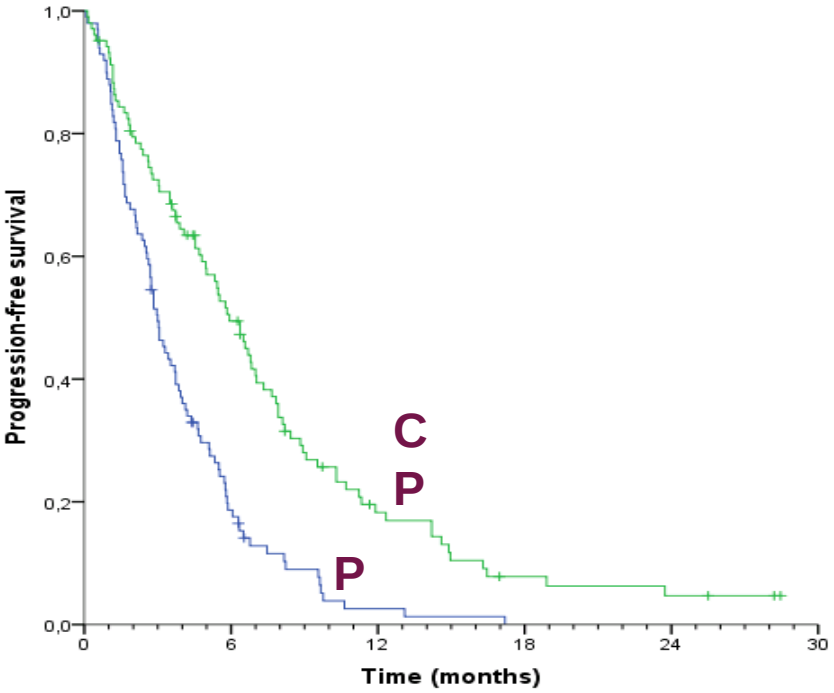
Abst. 7506

Rogerio Lilenbaum, Mauro Zukin, Jose Rodrigues Pereira, Carlos H. Barrios, Ronaldo De Albuquerque Ribeiro, Carlos Augusto de Mendonça Beato, Yeni Neron do Nascimento, Andre Murad, Fabio A. Franke, Maristela Precivale, Luiz Henrique de Lima Araujo, Clarissa Serodio Da Rocha Baldotto, Fernando Meton Vieira, Isabele Avila Small, Carlos G. M. Ferreira

ASCO Annual '12 Meeting

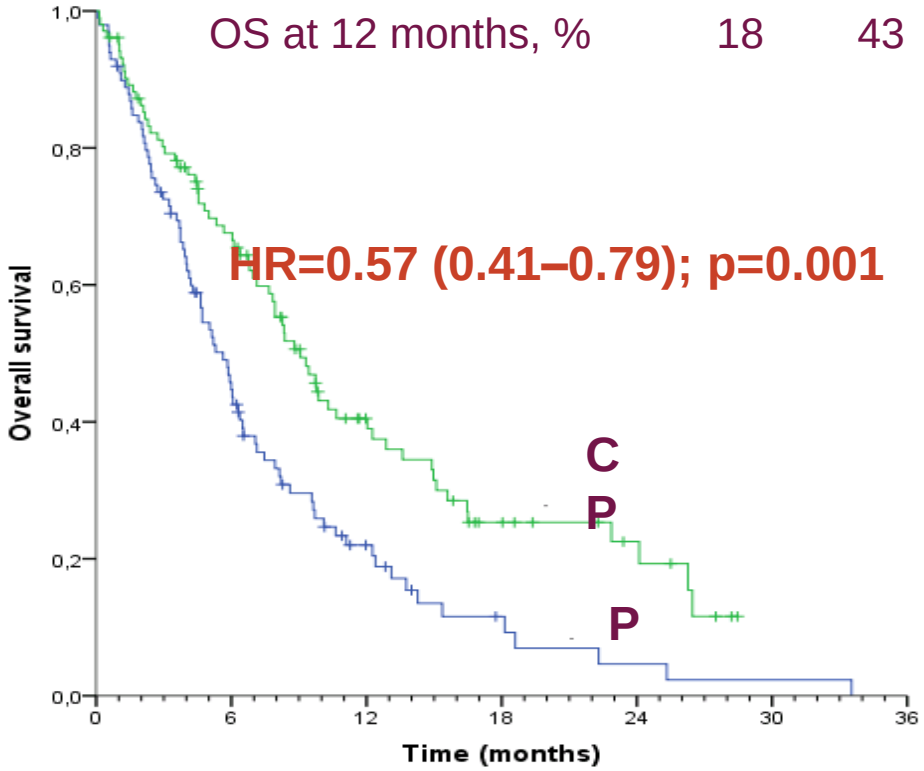
PROGRESSION-FREE SURVIVAL

	P	CP
Median PFS, months	3.0	5.9
PFS at 6 months, %	17	47
PFS at 12 months, %	4	18



OVERALL SURVIVAL

	P	CP
Median, months	5.6	9.1
OS at 6 months, %	50	65
OS at 12 months, %	18	43



Effect of Early Palliative Care on Health Care Costs in Patients with Metastatic NSCLC
Abst. 6004

Greer JA, McMahon P, Tramontano A, Gallagher E, Pirl WF, Jackson V, Temel JS

Massachusetts General Hospital Cancer Center

Summary

- Health care costs at the end of life vary widely among patients with metastatic NSCLC.
- Patients in the palliative care group had a mean total health care cost that was $2,282 less expensive than the standard care group in the final month of life.
- Any increased expenditures of the intervention for outpatient visits and longer lengths of stay in hospice appear to be offset by lower costs for inpatient visits and chemotherapy administration.

TAILOR

TArceva **I**talian **L**ung **O**ptimization t**R**ial

A phase III trial comparing erlotinib versus docetaxel as second-line treatment of NSCLC patients with wild-type EGFR Abst. 7501

M.C. Garassino, O. Martelli, A. Bettini, I. Floriani, E. Copreni, C. Lauricella, M. Ganzinelli, M. Marabese, M. Broggini, S. Veronese, G. Gherardi, F. Longo, M.A. Fabbri, M. Tomirotti, O. Alabiso, M.G. Sarobba, R. Labianca, S. Marsoni, G. Farina, A. Scanni

Fatebenefratelli e Oftalmico Hospital, Milan, Italy

On behalf of the TAILOR investigators

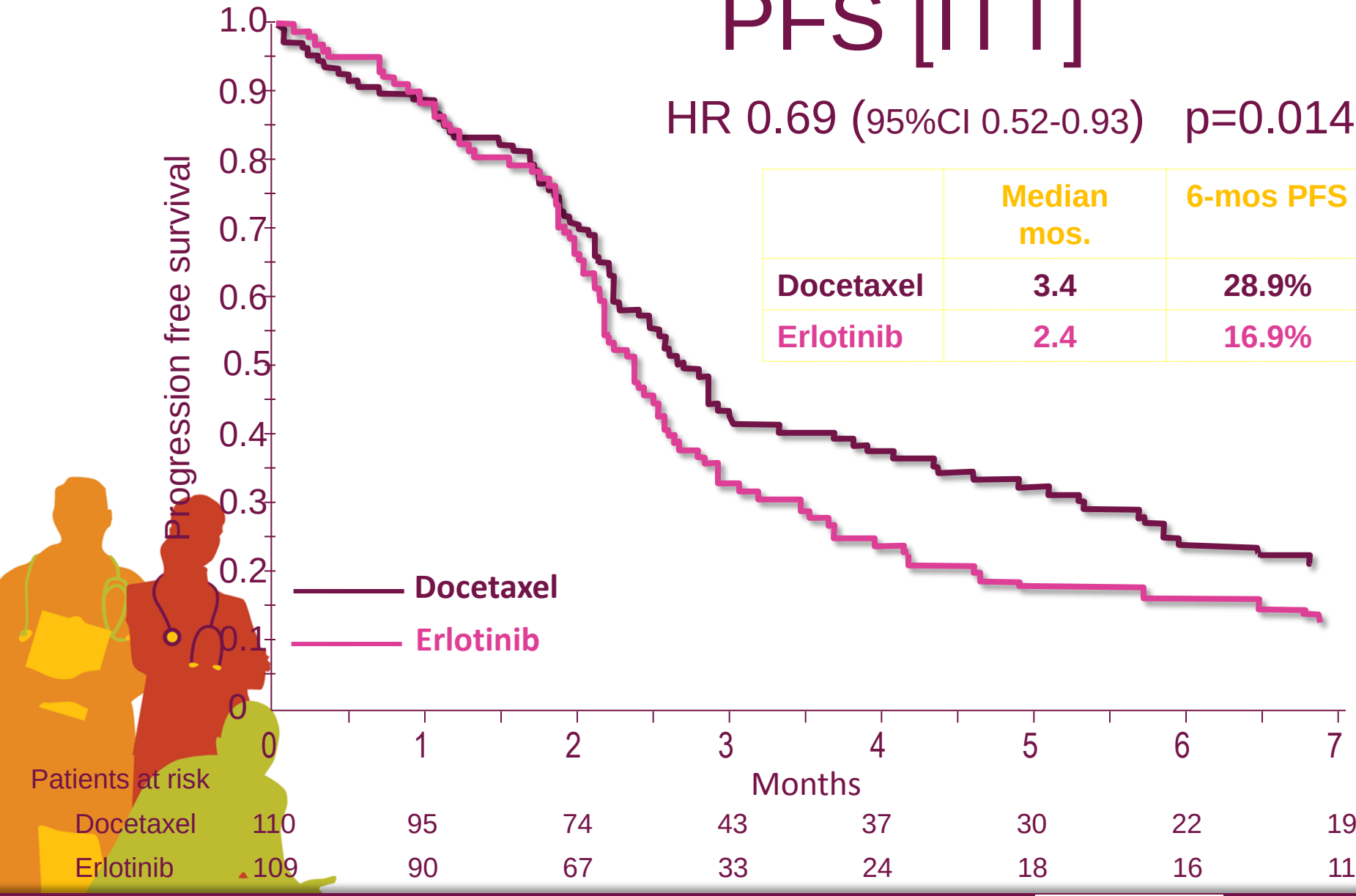
Presented at the 2012 ASCO Annual Meeting. Presented data is the property of the author

ASCO Annual Meeting

PFS [ITT]

HR 0.69 (95%CI 0.52-0.93) p=0.014

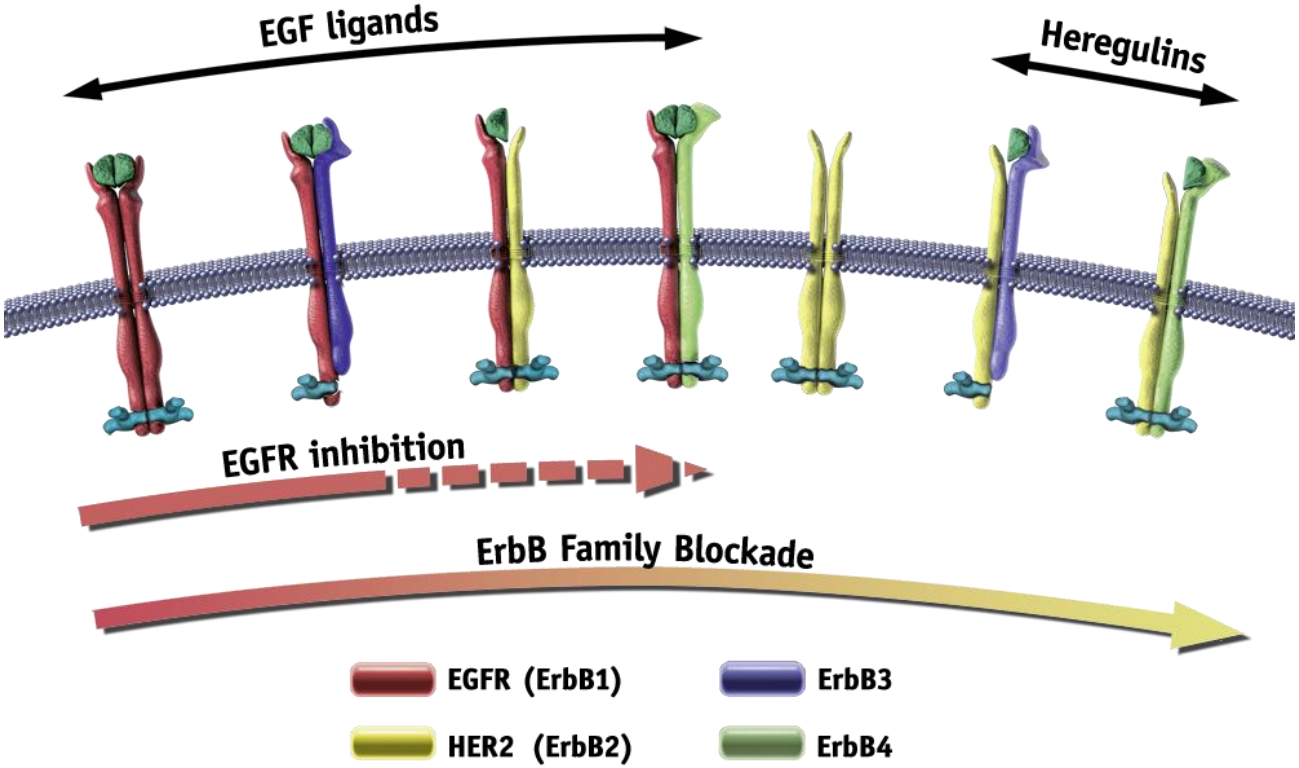
	Median mos.	6-mos PFS
Docetaxel	3.4	28.9%
Erlotinib	2.4	16.9%



LUX-Lung 3: a randomized, open-label, Phase III study of afatinib vs cisplatin/pemetrexed as 1st-line treatment for patients with advanced adenocarcinoma of the lung harboring EGFR-activating mutations
Abst. 7500

J.C.-H. Yang, M. Schuler, N. Yamamoto, K. O'Byrne, V. Hirsh, T. Mok, S.L. Geater, S. Orlov, C.-M. Tsai, M. Boyer, W.-C. Su, J. Bennouna, T. Kato, V. Gorbunova, K.H. Lee, R. Shah, D. Massey, R. Lorence, M. Shahidi, L. Sequist, on behalf of all LUX-Lung 3 investigators

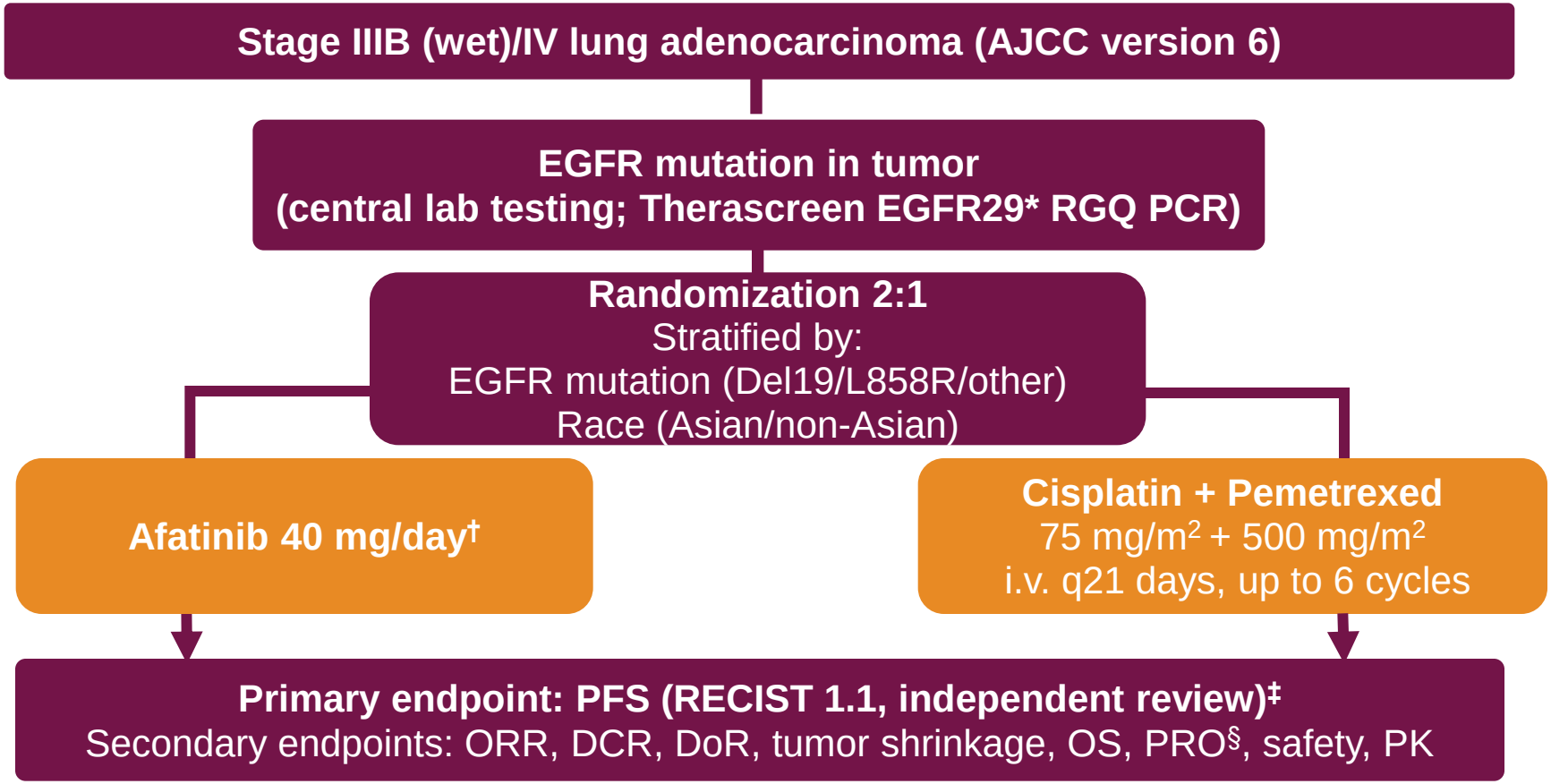
Afatinib: an irreversible ErbB Family Blocker



- Afatinib is an orally available, irreversible ErbB Family Blocker, with high efficacy potential
  - Inhibition of ErbB Family receptor heterodimerization
  - *In vitro* activity against EGFR-resistant T790M mutation

Li D, et al. *Oncogene* 2008;27:4702–11.

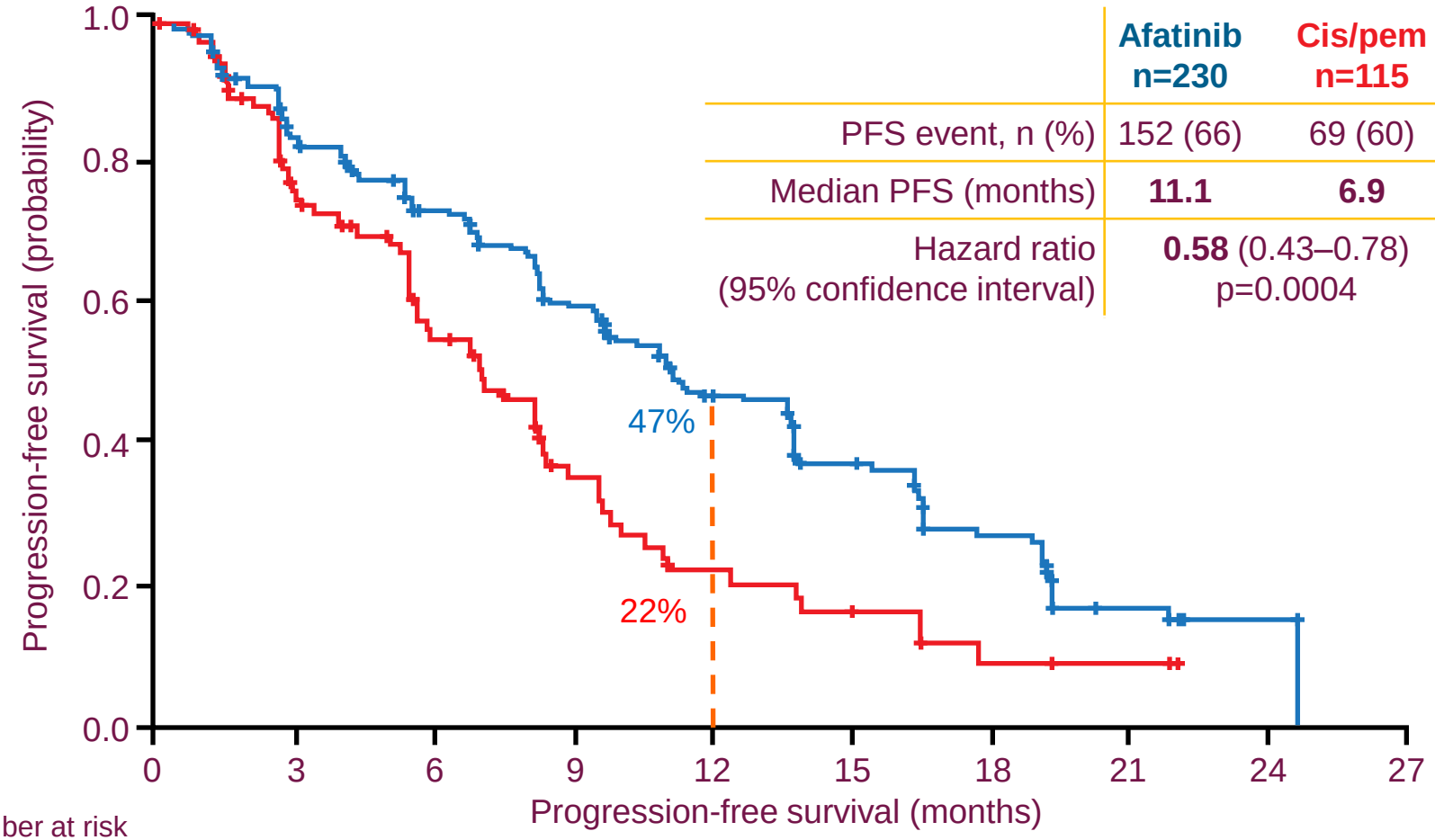
LUX-Lung 3



*EGFR29:19 deletions in exon 19, 3 insertions in exon 20, L858R, L861Q, T790M, G719S, G719A and G719C (or G719X), S768I.
†Dose escalated to 50 mg if limited AE observed in cycle 1. Dose reduced by 10 mg decrements in case of related G3 or prolonged G2 AE.
‡Tumor assessments: q6 weeks until Week 48 and q12 weeks thereafter until progression/start of new therapy.
§Patient-reported outcomes: Q-5D, EORTC QLQ-C30 and QLQ-LC13 at randomization and q3 weeks until progression or new anti-cancer therapy.

Primary endpoint: PFS

Independent review – all randomized patients



	Afatinib n=230	Cis/pem n=115
PFS event, n (%)	152 (66)	69 (60)
Median PFS (months)	**11.1**	**6.9**
Hazard ratio (95% confidence interval)	**0.58** (0.43–0.78) p=0.0004	

Number at risk

Afatinib	230	180	151	120	77	50	31	10	3	0
Cis/Pem	115	72	41	21	11	7	3	2	0	0

Summary

- LUX-Lung 3 is the largest global prospective trial in EGFR mutation-positive lung cancer and the first using cisplatin and pemetrexed as the comparator
- LUX-Lung 3 met its primary endpoint of PFS (independent review)
  - **Overall study population:**
    - Median PFS of 11.1 months for afatinib; 6.9 months for chemotherapy (HR=0.58 [95% CI: 0.43–0.78]; p=0.0004)
  - **Patients with common mutations (Del19+L858R):**
    - Median PFS of 13.6 months for afatinib; 6.9 months for chemotherapy (HR=0.47 [95% CI: 0.34–0.65]; p<0.0001)
  - Consistent efficacy in all relevant subgroups

Summary (continued)

- Afatinib significantly improved rates of response and disease control versus chemotherapy

- Safety profile consistent with previous afatinib studies
  - Diarrhea and rash were the most frequent AEs; manageable with low treatment discontinuation rate

- First-line afatinib significantly prolonged PFS with associated delay in worsening of lung cancer-related symptoms and improvement in quality of life in EGFR mutation-positive lung adenocarcinoma patients

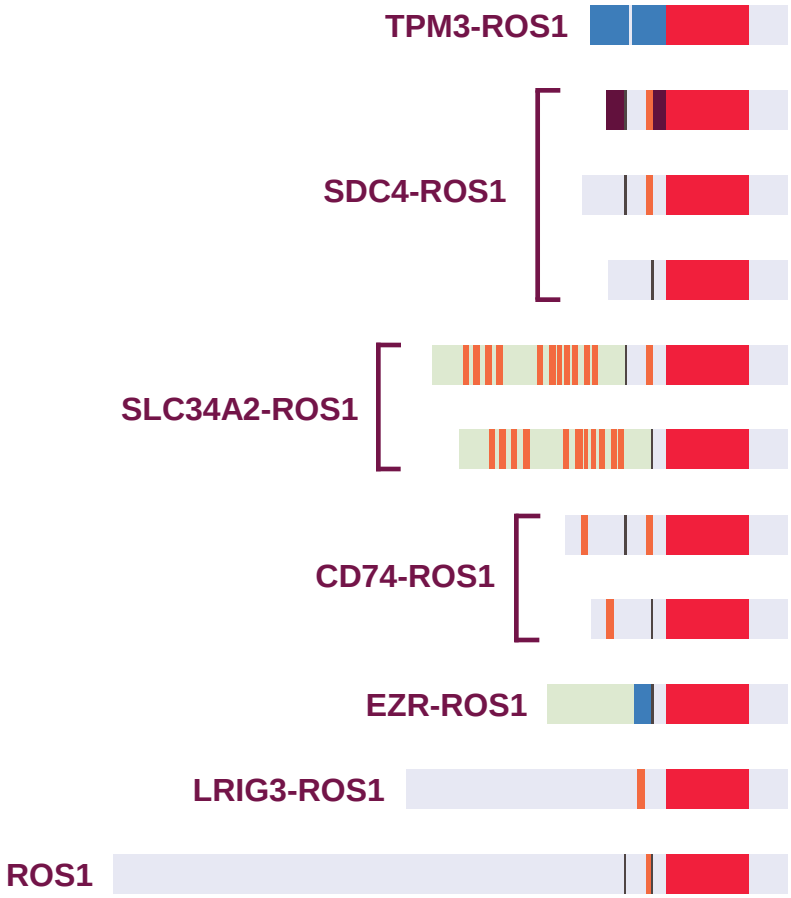
Abstract #7508

Clinical Activity of Crizotinib in Advanced Non-Small Cell Lung Cancer (NSCLC) Harboring ROS1 Rearrangement

Alice T. Shaw[1], D. Ross Camidge[2], Jeffrey A. Engelman[1], Benjamin J. Solomon[3], Eunice L. Kwak[1], Jeffrey W. Clark[1], Ravi Salgia[4], Geoffrey I. Shapiro[5], Yung-Jue Bang[6], Weiwei Tan[7], Lesley Tye[7], Keith D. Wilner[7], Patricia Stephenson[8], Marileila Varella-Garcia[2], Kristen Bergethon[1], A. John Iafrate[1], and Sai-Hong I. Ou[9]

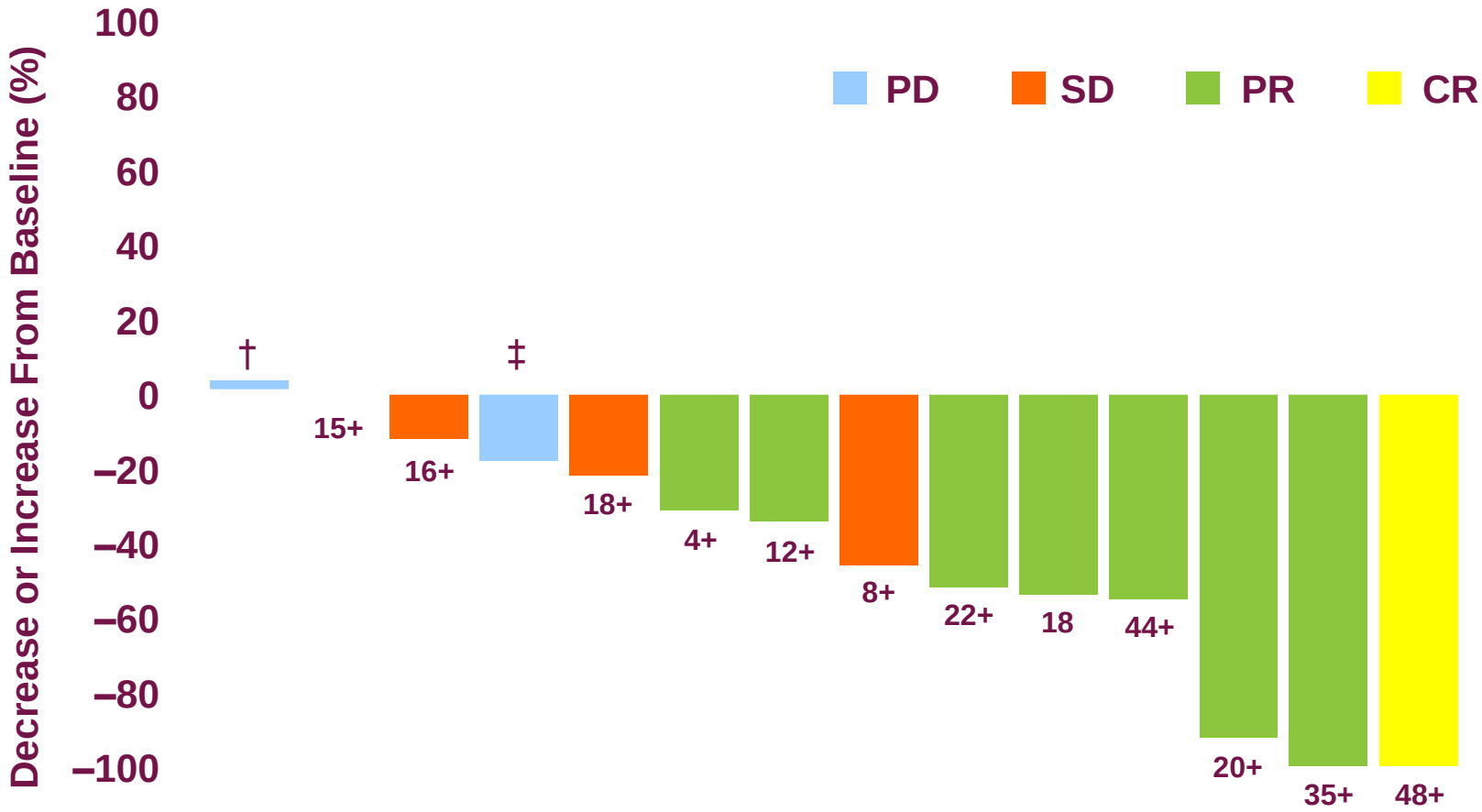
[1]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [2]University of Colorado Cancer Center, Aurora, CO, USA; [3]Peter MacCallum Cancer Centre, East Melbourne, Australia; [4]University of Chicago Cancer Center, Chicago, IL, USA; [5]Dana Farber Cancer Institute, Boston, MA, USA; [6]Seoul National University, Seoul, Korea; [7]Pfizer Inc, La Jolla, CA, USA; [8]Rho, Inc, Chapel Hill, NC; [9]Chao Family Comprehensive Cancer Center, Orange, CA, USA

ROS1 Rearrangements in NSCLC



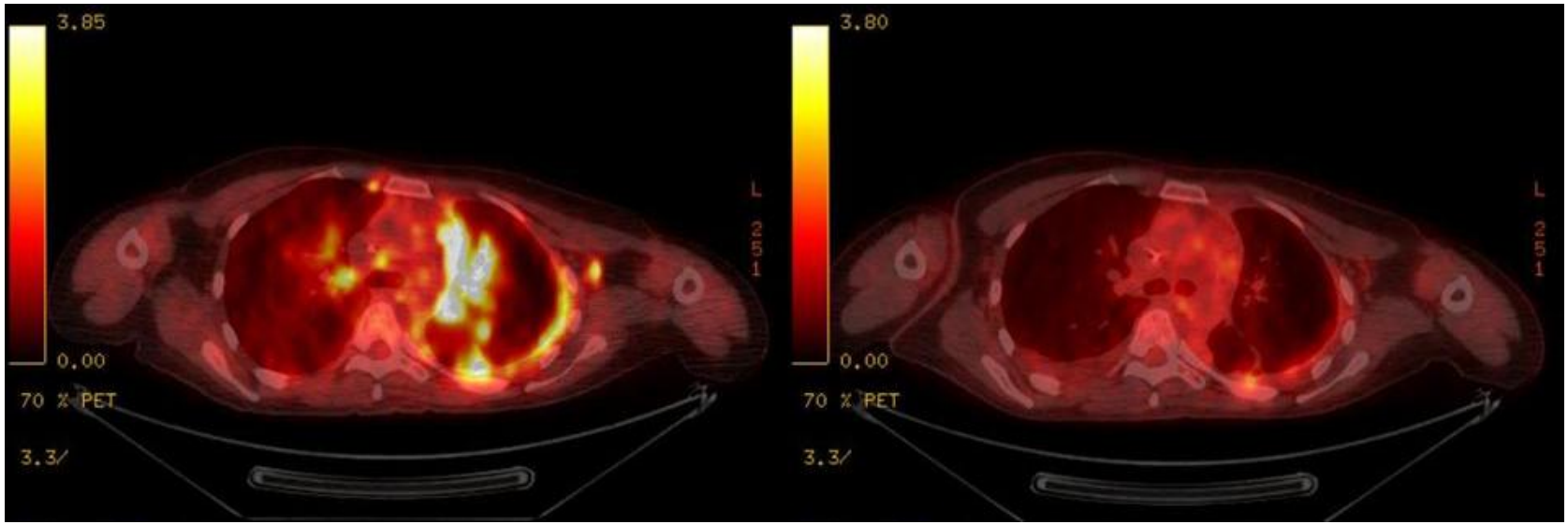
- Present in ~1% of NSCLC cases (also found in some GBMs and cholangiocarcinomas)
- Enriched in younger never or light smokers with adenocarcinoma histology
- No overlap with other oncogenic drivers

Summary of Tumor Responses to Crizotinib in Patients with Advanced ROS1+ NSCLC (N=14*)



Data in the database as of Apr

Rapid Responses to Crizotinib in Patients with ROS1-Positive NSCLC



Baseline **After 4 weeks of crizotinib**

Summary

- ROS1 rearrangement defines a distinct subset of NSCLC
- Crizotinib demonstrates marked antitumor activity in patients with advanced ROS1-positive NSCLC
- These results validate ROS1 as a therapeutic target in lung cancer

Clinical Activity and Safety of Anti-PD-1 (BMS-936558, MDX-1106) in Patients with Advanced NSCLC Abst. 7509

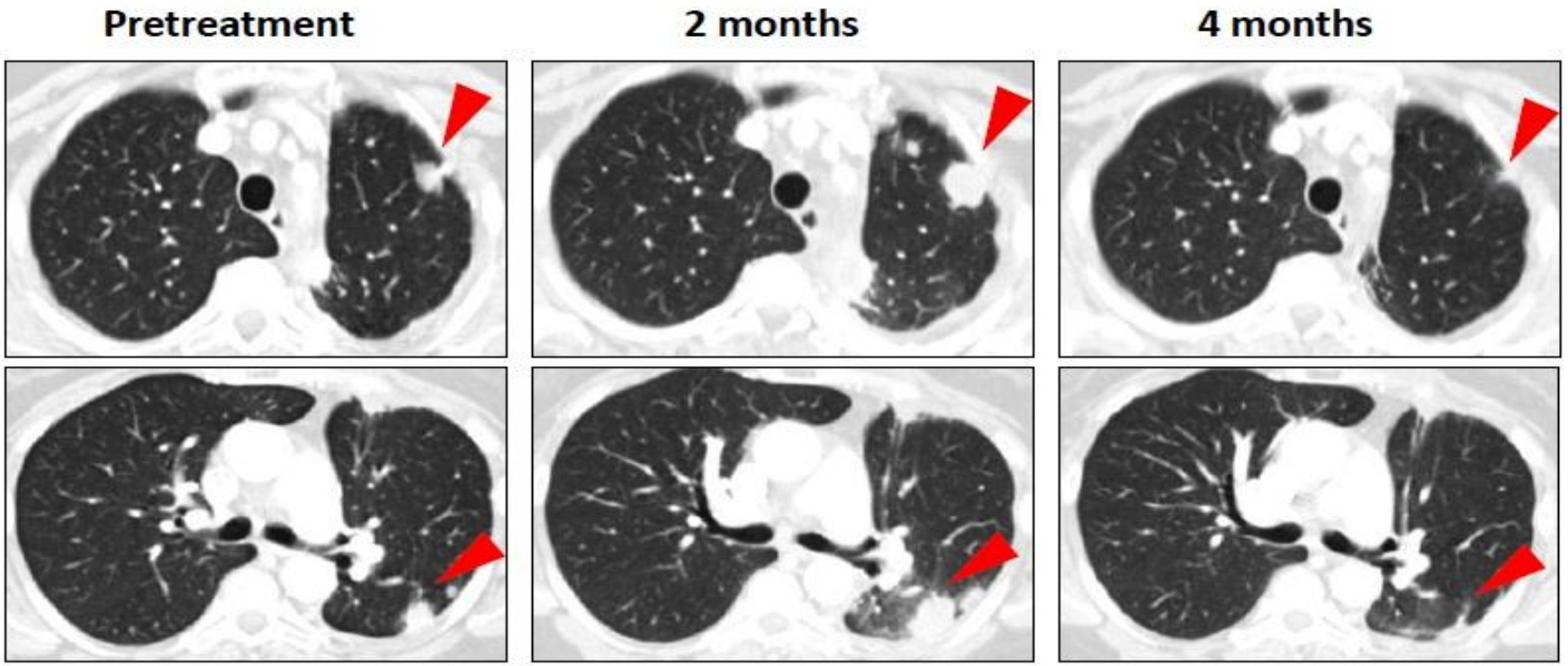
J.R. Brahmer,[1] L. Horn,[2] S.J. Antonia,[3] D. Spigel,[4] L. Gandhi,[5] L.V. Sequist,[6] J.M. Wigginton,[7] D. McDonald,[7] G. Kollia,[7] A. Gupta,[7] S. Gettinger[8]

[1]Sidney Kimmel Cancer Center at Johns Hopkins, Baltimore, MD; [2]Vanderbilt-Ingram Cancer Center, Nashville, TN; [3]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; [4]Sarah Cannon Research Institute/Tennessee Oncology, PLLC, Nashville, TN; [5]Dana-Farber Cancer Institute, Boston, MA; [6]Massachusetts General Hospital Cancer Center, Boston, MA; [7]Bristol-Myers Squibb, Princeton, NJ; [8]Yale University School of Medicine, New Haven, CT

Summary of Key Safety Results

- A maximum tolerated dose was not identified at doses up to 10 mg/kg
- There was no apparent relationship between drug dose and AE frequency in all treated patients or NSCLC patients
- In the total patient population across all tumor types:
  - Grade 3-4 drug-related AEs occurred in 14% of patients
  - Grade 1-2 pneumonitis was noted in 6 (2%) patients
  - Three drug-related deaths occurred in patients with pneumonitis (2 with NSCLC and 1 with CRC)
- In NSCLC patients:
  - Grade 3-4 drug-related AEs occurred in 8% of patients
  - Grade 1-2 pneumonitis was noted in 4 (3%) patients

Response of Metastatic NSCLC (BMS-936558, 10mg/kg)



- Initial progression in pulmonary lesions of a NSCLC patient with non-squamous histology was followed by regression
- Dx ‘04, EGFR mutation +; Rx Gem/carbo, erlotinib, erlotinib +

Conclusions

- BMS-936558 can be administered safely in an outpatient setting to heavily pretreated NSCLC patients
- Durable clinical benefit was seen in both squamous and non-squamous NSCLC
- These findings support the importance of the PD-1 pathway in NSCLC therapy across different histologies
- Preliminary data correlating PD-L1 expression in pretreatment tumor biopsies with clinical outcomes will be further explored
- Clinical registration trials of BMS-936558 in patients with NSCLC are planned

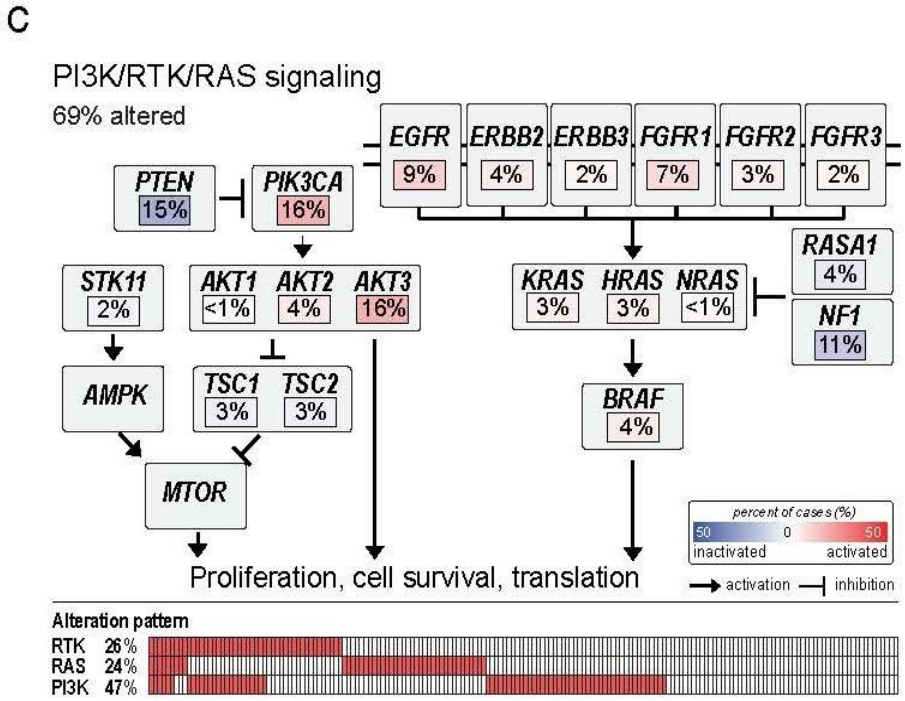
Comprehensive Characterization of Squamous Cell NSCLC
Abst. 7006

Ramaswamy Govindan, Peter Hammerman, Neil Hayes, Matthew Wilkerson, Steve Baylin and Matthew Meyerson

On Behalf of the Lung Cancer Working Group of

The Cancer Genome Atlas (TCGA) Project

Therapeutic targets in squamous cell lung carcinoma



Gene	Event Type	Frequency
CDKN2A	Deletion/Mutation /Methylation	72%
PI3KCA	Mutation	16%
PTEN	Mutation/Deletion	15%
FGFR1	Amplification	15%
EGFR	Amplification	9%
PDGFRA	Amplification/ Mutation	9%
CCND1	Amplification	8%
DDR2	Mutation	4%
BRAF	Mutation	4%
ERBB2	Amplification	4%
FGFR2	Mutation	3%

Summary

- Complex genomes with frequent and unique rearrangements
- A clear and reproducible sub-classification
- Distinct transforming mechanism defined by common *NFE2L2* activation in the classical subtype
- High somatic mutation rates includes near universal *TP53* mutation and frequent loss of *CDKN2A* function
- Multiple mechanisms for *CDKN2A* inactivation
- Therapeutic identified in 127 patients (75%) including FGFRs, PI3 kinase pathway, EGFR/ERBB2 and Cyclin/CDK complexes