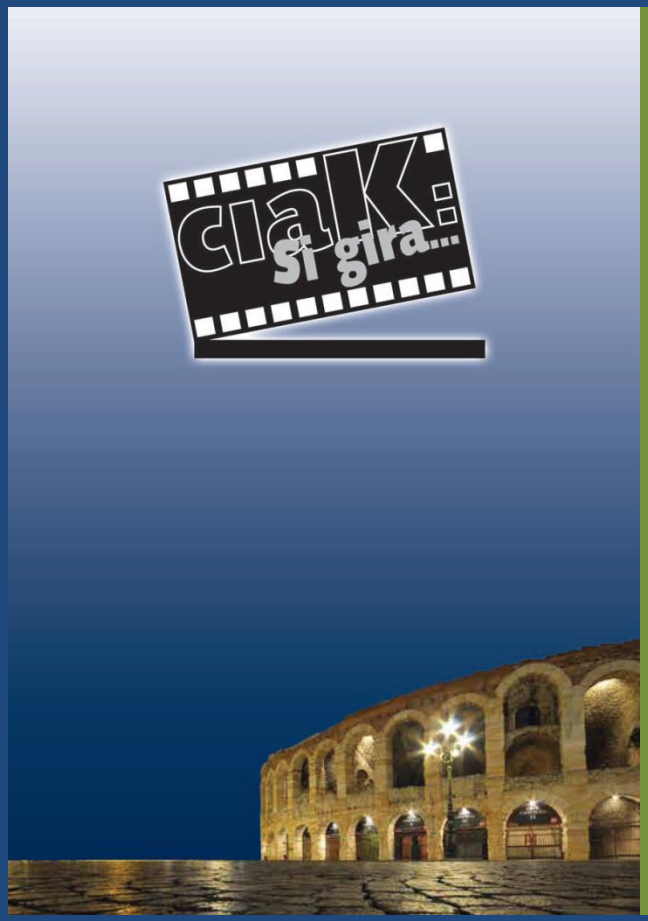
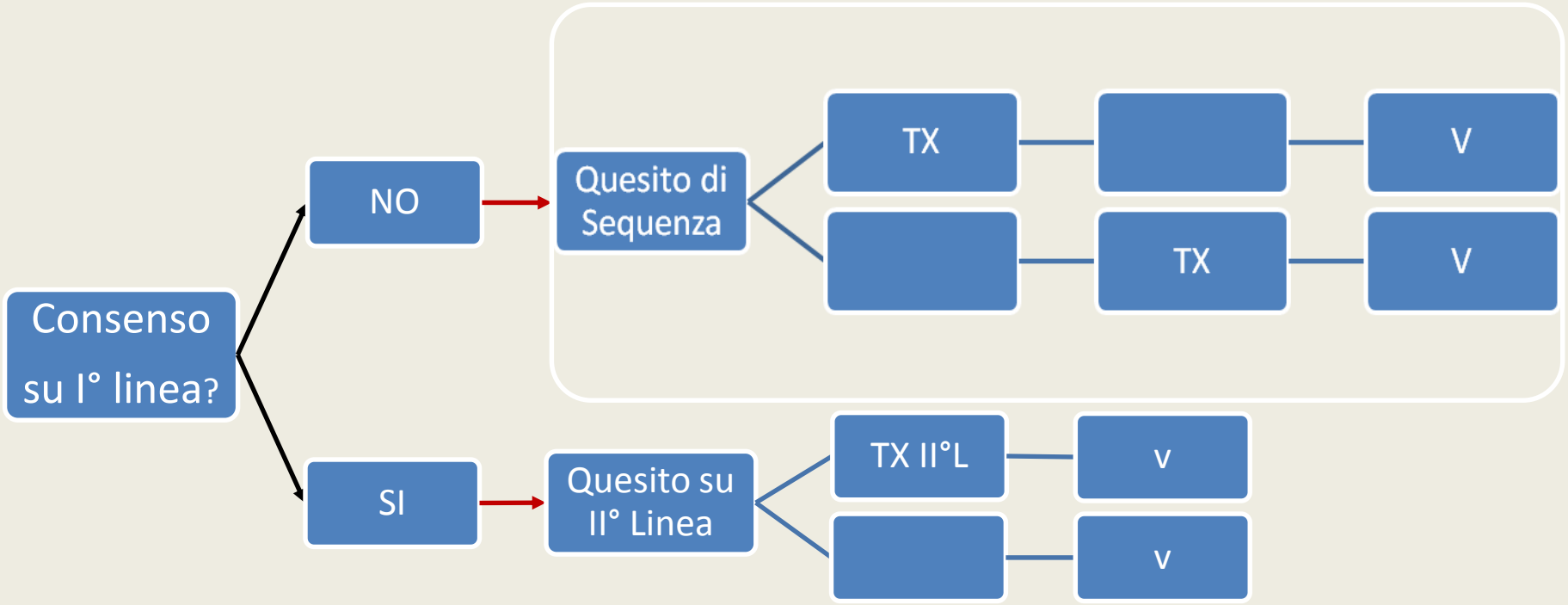


La sequenza terapeutica nel paziente con NSCLC avanzato in base all'istologia e alla caratterizzazione molecolare: Criticità

Valter Torri - Milano



Possibili disegni per la valutazione della miglior sequenza

Due scenari

1. EGFR mutati
2. ALK traslocati

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Critical Reviews in Oncology/Hematology 94 (2015) 213–227

Oncology Hematology
Incorporating Geriatric Oncology

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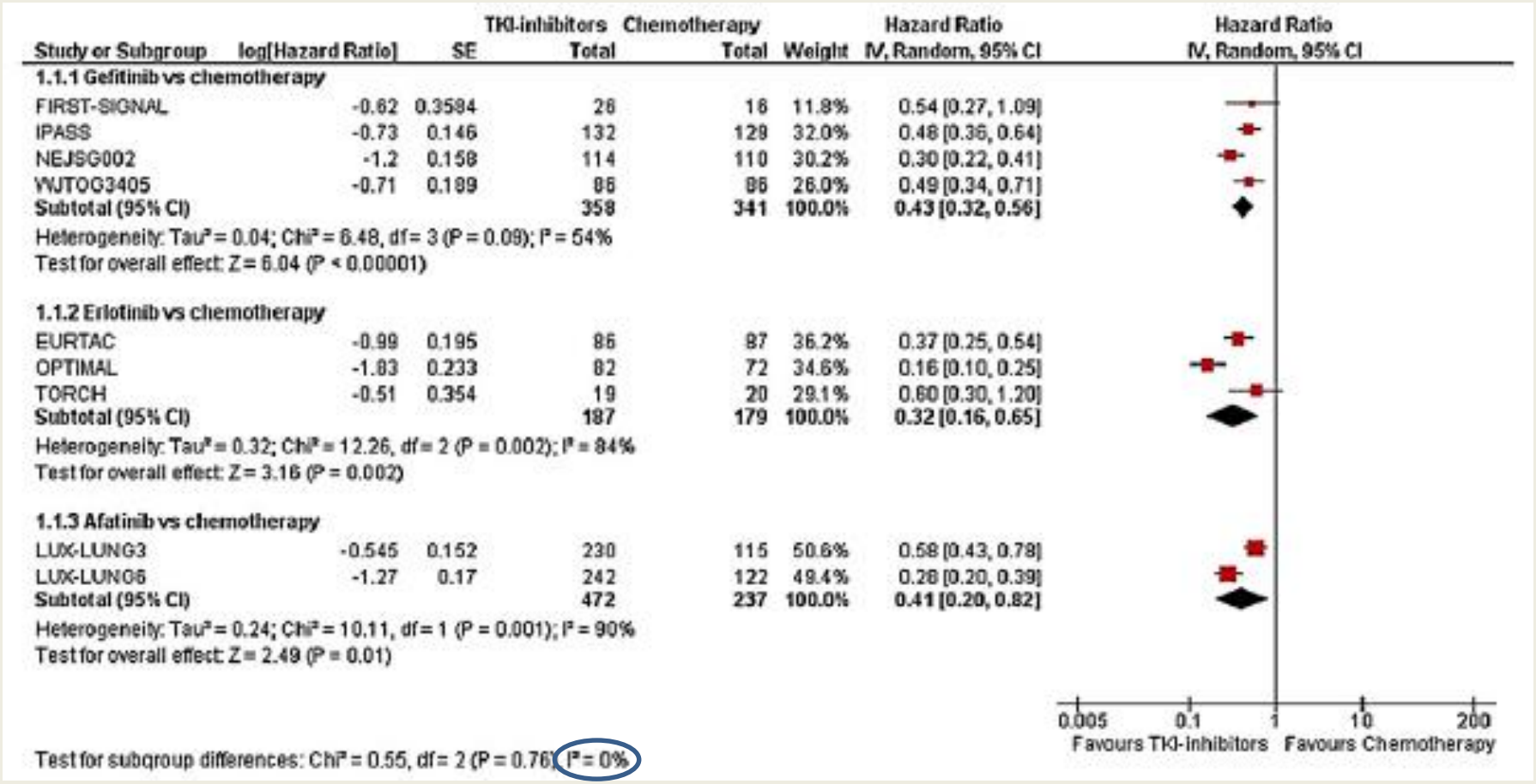
Is there evidence for different effects among EGFR-TKIs? Systematic review and meta-analysis of EGFR tyrosine kinase inhibitors (TKIs) *versus* chemotherapy as first-line treatment for patients harboring EGFR mutations

Eva Regina Haspinger[a], Francesco Agustoni[a], Valter Torri[b], Francesco Gelsomino[a], Marco Platania[a], Nicoletta Zilembo[a], Rosaria Gallucci[a], Marina Chiara Garassino[a,*], Michela Cinquini[b]

[a] Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
[b] Fondazione IRCCS Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy

Accepted 11 November 2014



EGFR mutati - I° linea

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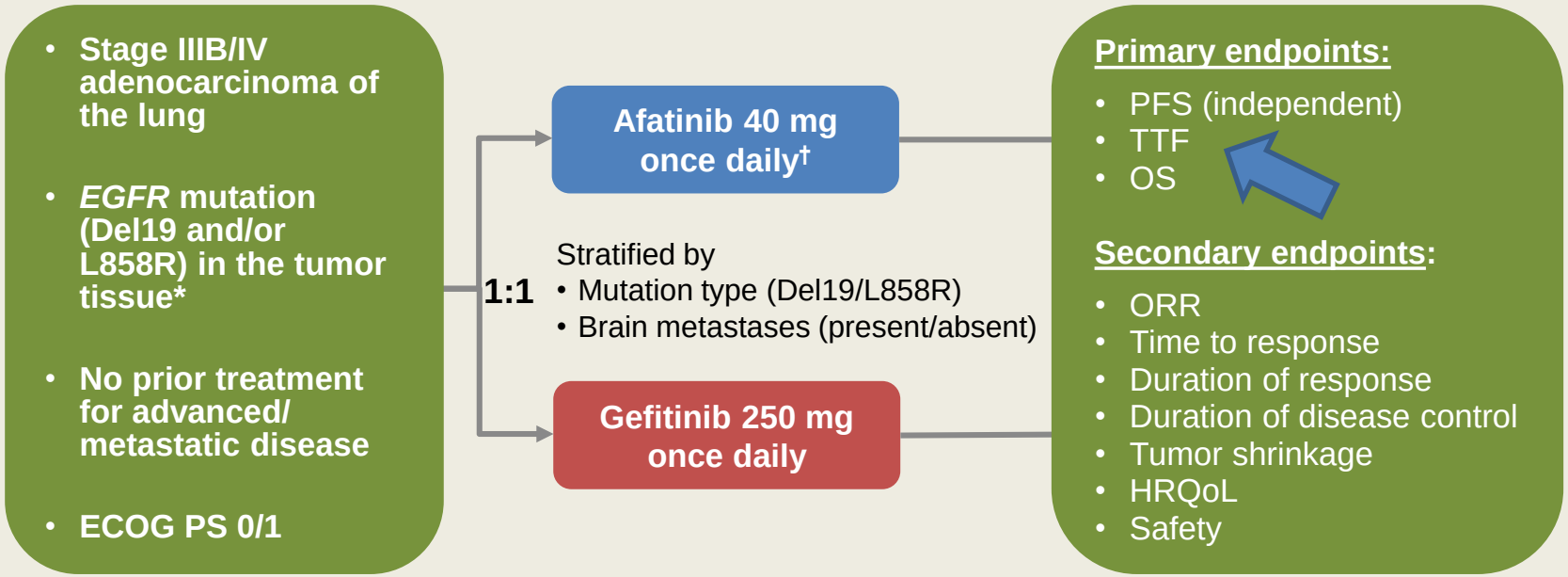
Overall results of comparisons between TKIs and chemotherapy (CT) and overall results of indirect comparisons among TKIs.

Outcome	Gefitinib *versus* Afatinib (ind. comp.)	Conclusion	Erlotinib *versus* Afatinib (ind. comp.)	Conclusion	Gefitinib *versus* Erlotinib (ind. comp.)	Conclusion
Progression-free survival						
Hazard ratio (HR) (95% CI)	HR = 1.05 (0.61, 1.81)	No difference	HR = 0.78 (0.39, 1.55)	No difference	HR = 1.34 (0.63, 2.86)	No difference
Progression-free survival (exon 19 deletion)						
Hazard ratio (HR) (95% CI)	HR = 1.67 (1.05, 2.64)	Afatinib better	HR = 0.83 (0.35, 2.01)	No difference	HR = 2.00 (0.83, 4.80)	No difference
Progression-free survival (L858R mutation)						
Hazard ratio (HR) (95% CI)	HR = 1.08 (0.45, 2.60)	No difference	HR = 0.78 (0.26, 2.32)	No difference	HR = 1.39 (0.62, 3.16)	No difference
Overall survival						
Hazard ratio (HR) (95% CI)	HR = 0.91 (0.65, 1.26)	No difference	HR = 1.10 (0.74, 1.64)	No difference	HR = 0.90 (0.68, 1.19)	No difference
Objective response rate						
Risk ratio (RR) (95% CI)	RR = 0.91 (0.67, 1.23)	No difference	RR = 0.94 (0.65, 1.35)	No difference	RR = 0.96 (0.69, 1.34)	No difference
Diarrhea						
Risk ratio (RR) (95% CI)	RR = 0.29 (0.20, 0.41)	Gefitinib better	RR = 0.36 (0.25, 0.54)	Erlotinib better	RR = 0.80 (0.63, 1.01)	No difference
Rash						
Risk ratio (RR) (95% CI)	RR = 0.41 (0.25, 0.65)	Gefitinib better	RR = 0.41 (0.25, 0.66)	Erlotinib better	RR = 1.00 (0.82, 1.22)	No difference

EGFR mutati - I° linea



- Treatment beyond progression allowed if deemed beneficial by investigator
- RECIST assessment performed at Weeks 4, 8 and every 8 weeks thereafter until Week 64, and every 12 weeks thereafter

*Central or local test
†Dose modification to 50, 30, 20 mg permitted in line with prescribing information

Park K, et al. ESMO Asia, Oral Presentation (Abstract N° LBA2 PR)

Lux-lung 7: Study Design

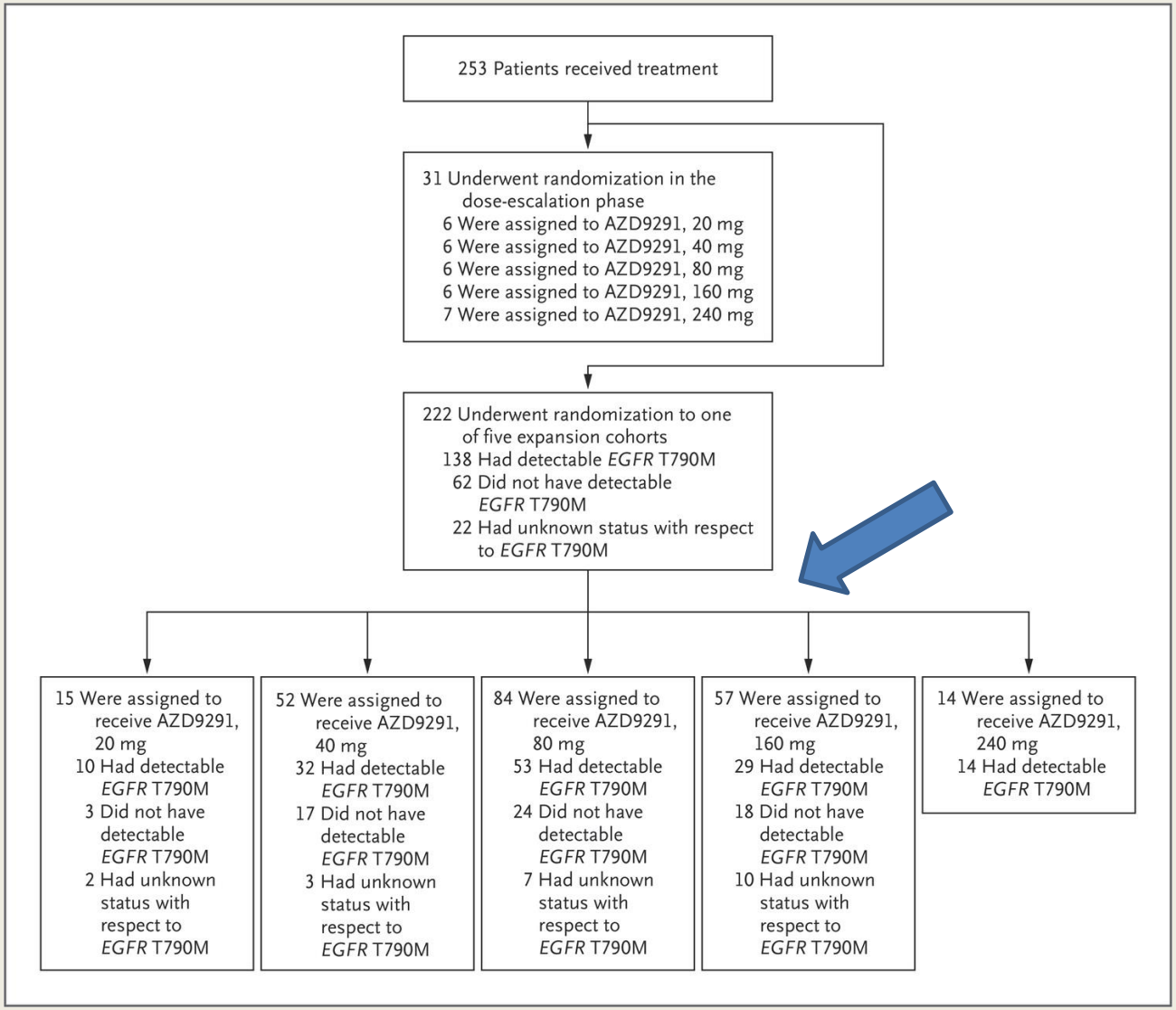
- Afatinib significantly improved PFS of patients with *EGFR*m+ NSCLC relative to gefitinib. Results are consistent across subgroups
- Afatinib treatment was associated with a significant improvement in response rate and TTF
- The improvement in efficacy was observed in both Del19 and L858R populations
- OS data immature (current HR: 0.87, 95%CI: 0.66–1.15)
- AEs in both groups were consistent with previous experience, and were manageable leading to equally low rates of treatment discontinuation
- LUX-Lung 7 confirms the benefit of irreversible ErbB blockade with afatinib over reversible EGFR inhibition with gefitinib in treatment of *EGFR*m+ NSCLC

Park K, et al. ESMO Asia, Oral Presentation (Abstract N° LBA2 PR)

ESTABLISHED IN 1812 APRIL 30, 2015 VOL. 372 NO. 18

AZD9291 in EGFR Inhibitor–Resistant Non–Small-Cell Lung Cancer

Pasi A. Jänne, M.D., Ph.D., James Chih-Hsin Yang, M.D., Ph.D., Dong-Wan Kim, M.D., Ph.D., David Planchard, M.D., Ph.D., Yuichiro Ohe, M.D., Suresh S. Ramalingam, M.D., Myung-Ju Ahn, M.D., Ph.D., Sang-We Kim, M.D., Ph.D., Wu-Chou Su, M.D., Leora Horn, M.D., Daniel Haggstrom, M.D., Enriqueta Felip, M.D., Ph.D., Joo-Hang Kim, M.D., Ph.D., Paul Frewer, M.Sc., Mireille Cantarini, M.D., Kathryn H. Brown, Ph.D., Paul A. Dickinson, Ph.D., Serban Ghiorghiu, M.D., and Malcolm Ranson, M.B., Ch.B., Ph.D.



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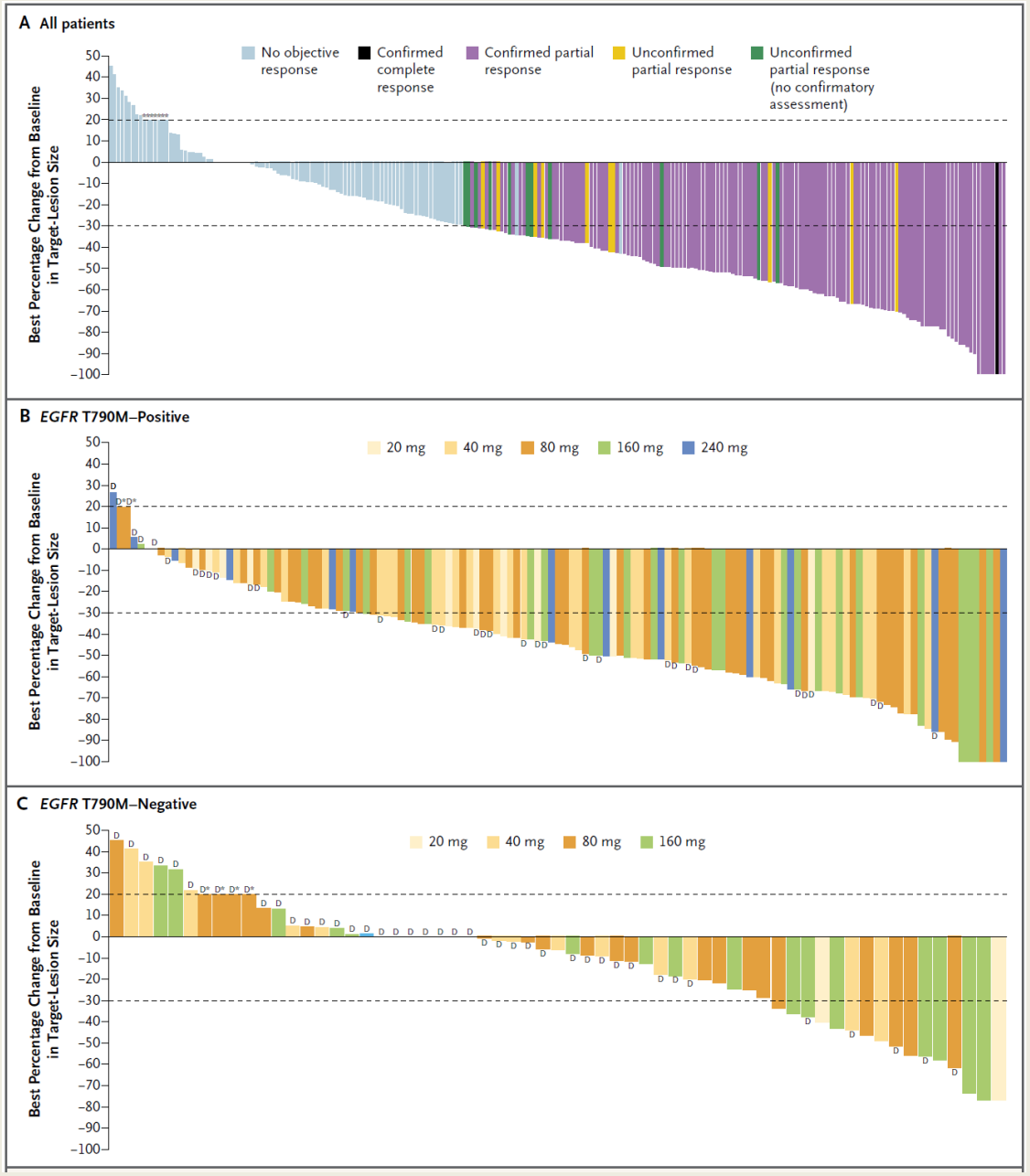

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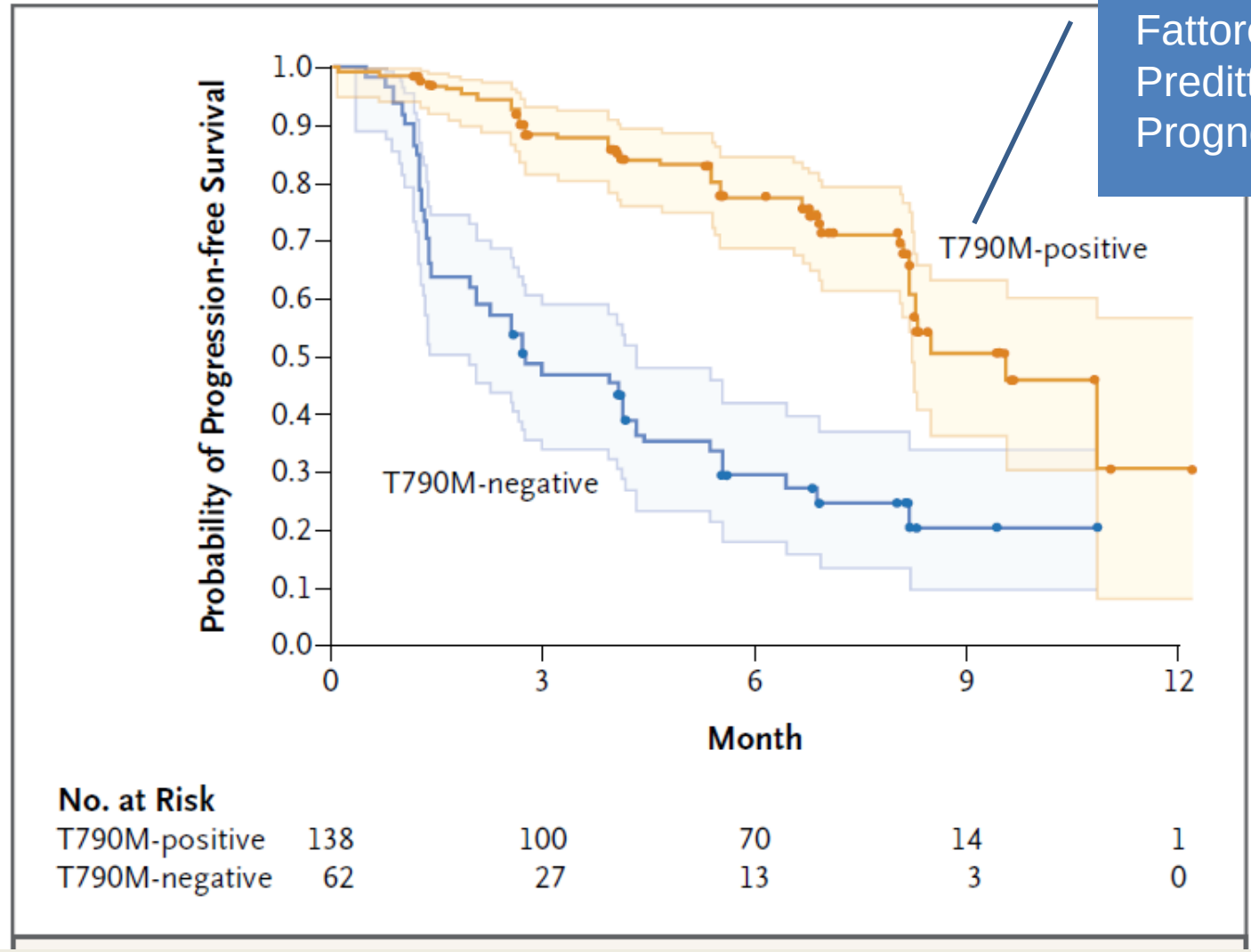


Fattore Predittivo e/o Prognostico?

II° Linea

- AURA2
  - Open Label Study in NSCLC after Previous EGFR TKI Therapy in EGFR and T790M Mutation Positive Tumors. [I°EP: PFS]
- AURA3
  - Multicenter, phase III, open-label study comparing the efficacy of AZD9291 with platinum-based chemotherapy (CT) as second- line treatment in patients with progressing advanced/ metastatic T790M positive NSCLC, with documented EGFR mutations, who have received prior EGFR-TKI therapy. [I°EP: PFS]

I° Linea

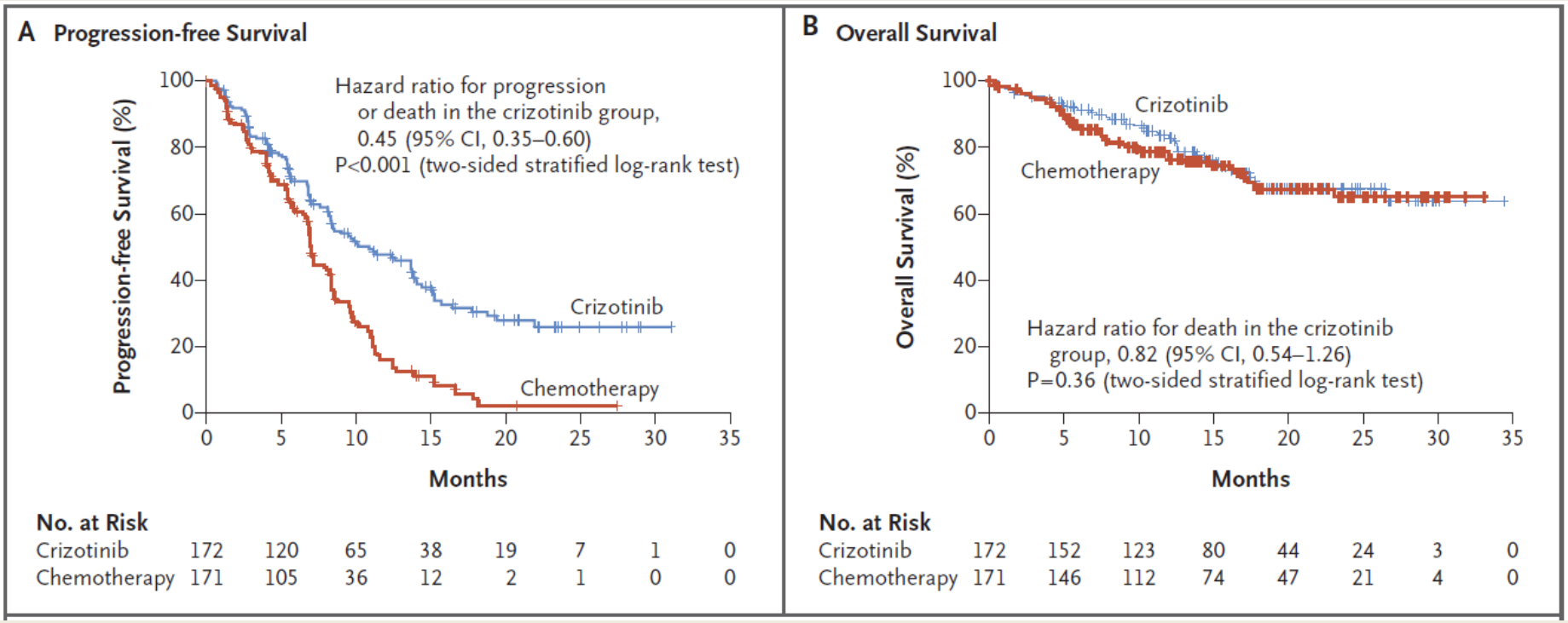
- FLAURA
  - Randomized, phase III study called comparing AZD9291, vs. gefitinib or erlotinib in treatment-naïve patients with advanced NSCLC showing EGFR-TKI sensitizing mutations. [I°EP: PFS]

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

First-Line Crizotinib versus Chemotherapy in *ALK*-Positive Lung Cancer

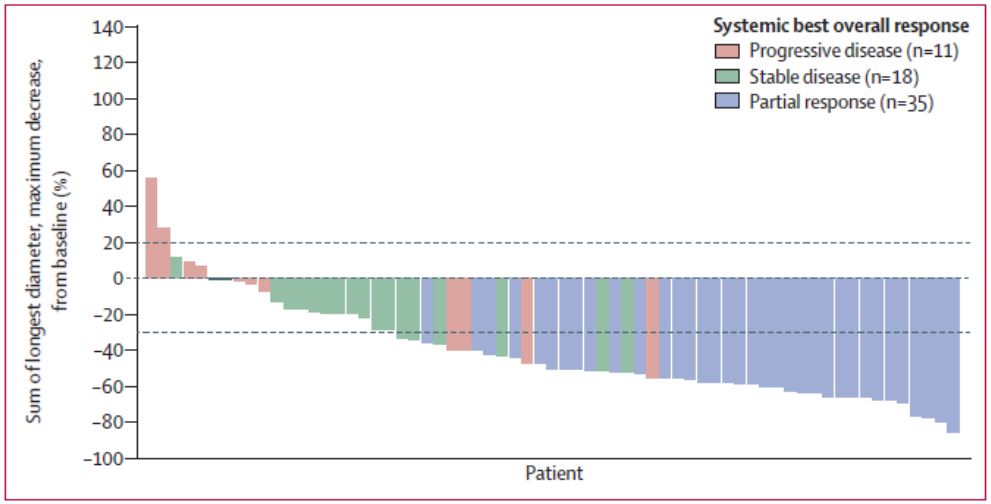
Benjamin J. Solomon, M.B., B.S., Ph.D., Tony Mok, M.D., Dong-Wan Kim, M.D., Ph.D., Yi-Long Wu, M.D., Kazuhiko Nakagawa, M.D., Ph.D., Tarek Mekhail, M.D., Enriqueta Felip, M.D., Ph.D., Federico Cappuzzo, M.D., Jolanda Paolini, B.Sc., Tiziana Usari, B.Sc., Shrividya Iyer, Ph.D., Arlene Reisman, M.P.H., Keith D. Wilner, Ph.D., Jennifer Tursi, M.Sc., and Fiona Blackhall, M.D., Ph.D., for the PROFILE 1014 Investigators*



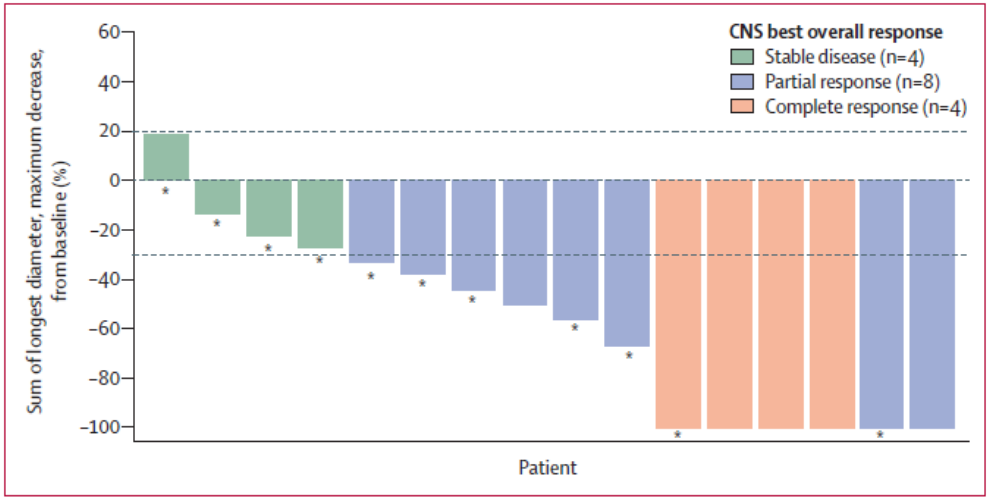
Alectinib in *ALK*-positive, crizotinib-resistant, non-small-cell lung cancer: a single-group, multicentre, phase 2 trial

*Alice T Shaw, Leena Gandhi, Shirish Gadgeel, Gregory J Riely, Jeremy Cetnar, Howard West, D Ross Camidge, Mark A Socinski, Alberto Chiappori, Tarek Mekhail, Bo H Chao, Hossein Borghaei, Kathryn A Gold, Ali Zeaiter, Walter Bordogna, Bogdana Balas, Oscar Puig, Volkmar Henschel, Sai-Hong Ignatius Ou, on behalf of the study investigators**

Lancet Oncol 2016; 17: 234-42



Waterfall plot of best overall systemic response at the updated analysis



Waterfall plot of best overall CNS response at the updated analysis

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