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ESMO Clinical Practice Guidelines

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ADVANCED NON SMALL CELL LUNG CANCER

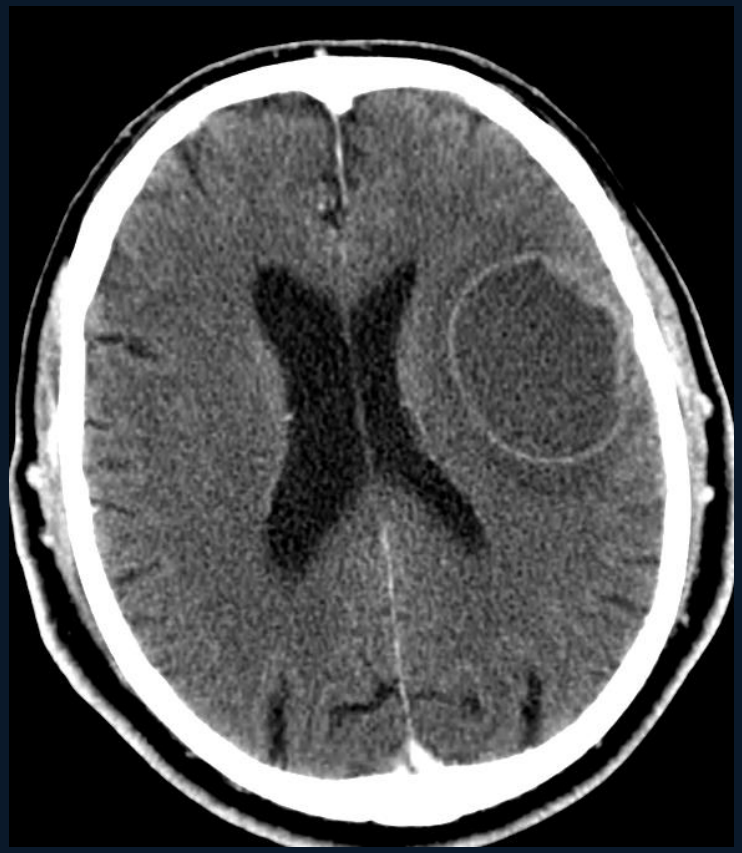
Disclosures

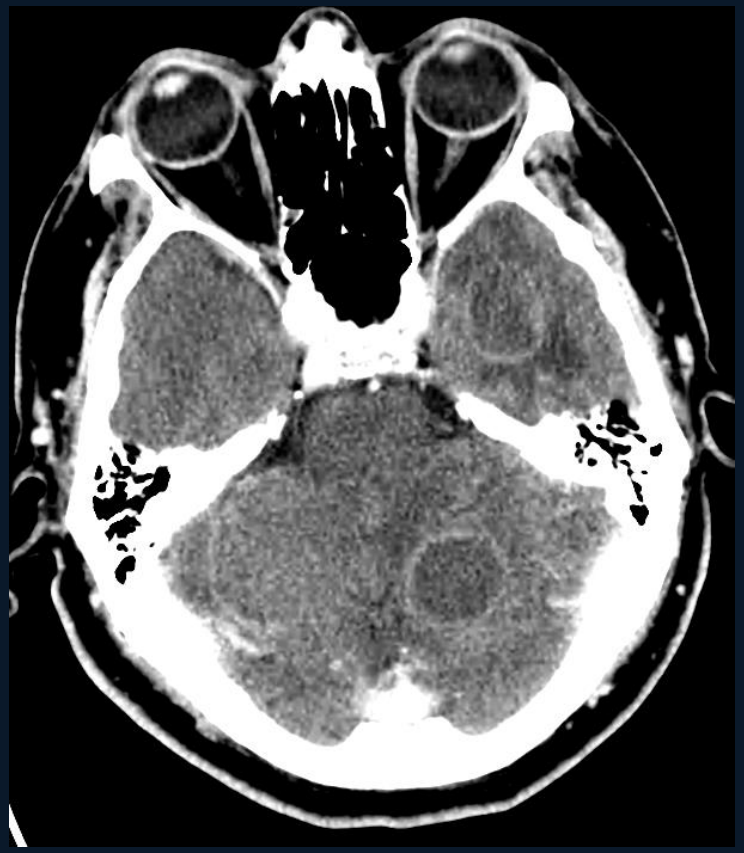
I have provided consultation, attended advisory boards and/or provided lectures for:

F. Hoffmann–La Roche, Ltd; Eli Lilly and Company Oncology, AstraZeneca, Pfizer, Boehringer-Ingelheim, BMS, Daiichi-Sankyo, Morphotek, Merrimack, Merck Serono, MSD, Amgen, Clovis, Astellas and Tesaro, for which I received honoraria.

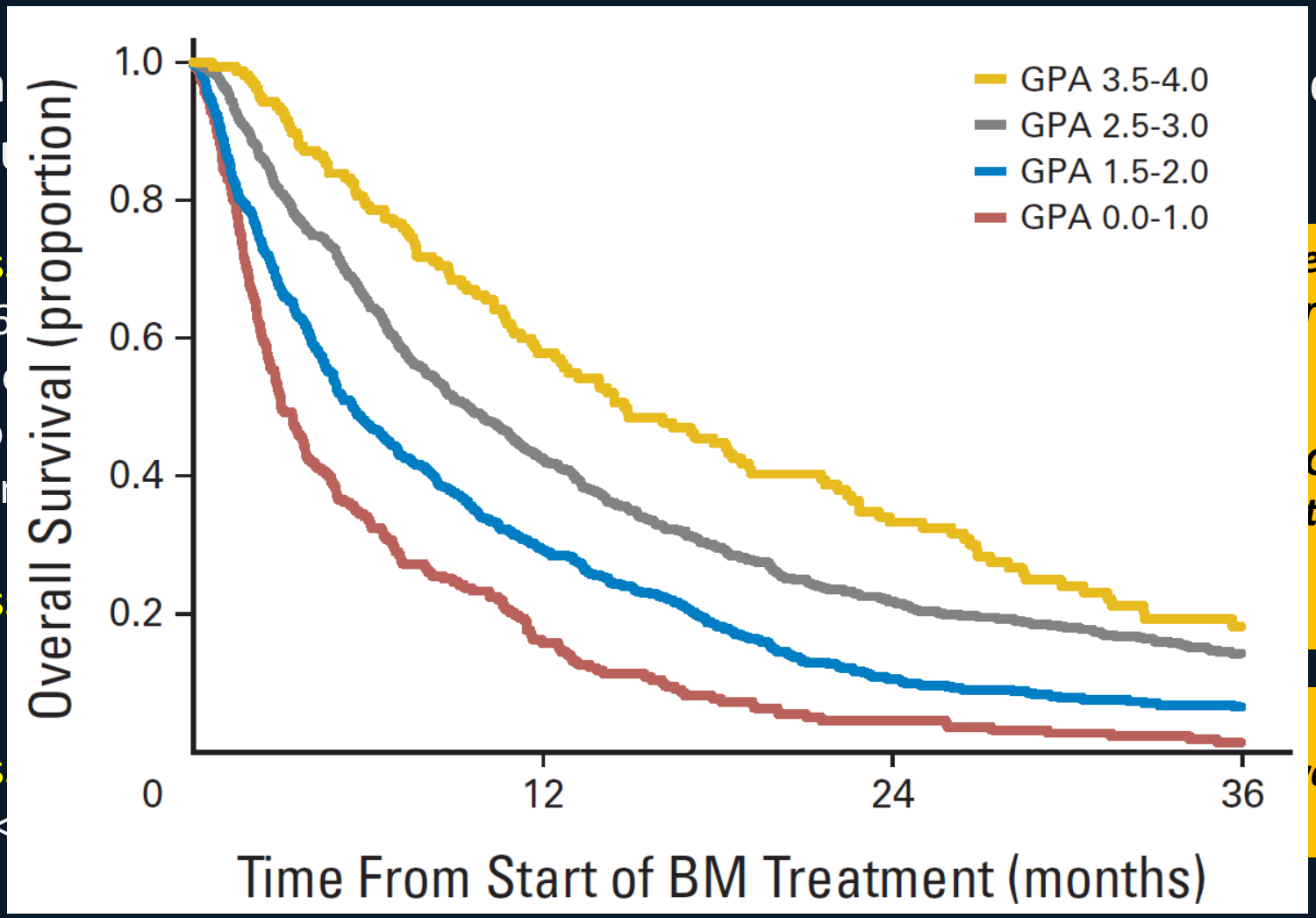
I declare no conflict of interest.

Lung adenocarcinoma, mild aphasia





Radiotherapy for multiple lung carcinoma brain metastases



Sperduto, JCO 2012,
ESMO guidelines, Reck M. et al., Ann Oncol 2014

Timing for radiotherapy for multiple brain metastases in lung carcinoma

- *In patients with asymptomatic brain metastases who have not received prior systemic therapy (e.g. chemotherapy, TKIs), systemic treatment and deferred WBRT should be considered [II, B]*

Treatment	Brain RR (%)	MST (months)
Cisplatin/paclitaxel/vinorelbine or gemcitabine	38	5
Cisplatin/ifosfamide/irinotecan	50	12.7
Cisplatin/fotemustine	23	4
Cisplatin/teniposide	35	5
Carboplatin/vinorelbine/gemcitabine	45	7
Cisplatin/etoposide	37	8
Cisplatin/vinorelbine	27	NA
Cisplatin/pemetrexed	41.9	7.4
Carboplatin/pemetrexed	30	9.1

Robinet, Ann Oncol 2001, Zimmermann, Cancer Treat Rev 2014
ESMO guidelines, Reck M. et al., Ann Oncol 2014

Radiotherapy for brain metastases in EGFR M+ lung carcinoma

- Efficacy of EGFR TKI therapy in brain metastases is accurately paralleled by its efficacy in the lung primary lesions and other metastatic sites
- Whether WBRT can be postponed even in neurologically symptomatic patients is a matter of debate with no prospective data available

N	Selection	Prior treatment	Treatment	Brain RR (%)
17 (subset)	*EGFR* mutated	No	Erlotinib	82
28	*EGFR* mutated	No	Gefitinib or erlotinib	83
9	*EGFR* mutated	No	Gefitinib	89
23	Asian never-smokers	No	Gefitinib or erlotinib	74
40	Unselected	Yes	Erlotinib	86
41	*EGFR* mutated	No	Gefitinib	87.8

Zimmermann, Cancer Treat Rev 2014
ESMO guidelines, Reck M. et al., Ann Oncol 2014

Molecular testing in NSCLC

- *Genetic alterations which are key oncogenic events have been identified in numerous small subsets of NSCLC. Two of these alterations have been validated as reliable targets for selective pathway directed systemic therapy*

- *EGFR mutation testing is recommended in all patients with advanced NSCLC of a non-squamous subtype [I, A]. Testing is not recommended in patients with a confident diagnosis of squamous cell carcinoma, except in never/former light smokers (<15 packs per year) [IV, A]*

ESMO guidelines, Reck M. et al., Ann Oncol 2014

Molecular testing in NSCLC

Tissue should be prioritized for EGFR and ALK testing
EGFR and ALK results should be available within 2 weeks (10 working days)

HER2, and RET) is currently under evaluation

Lindenman, JTO 2013,
ESMO guidelines, Reck M. et al., Ann Oncol 2014

First-line therapy for EGFR M+NSCLC

- *Activating (sensitising) EGFR mutations are predictive for response to EGFR TKIs resulting in an improved RR, PFS, and QoL as well as a better tolerability when compared with first-line chemotherapy*
- *EGFR TKI therapy statistically significantly delays disease progression and should be considered as front-line therapy [I, A]*

ESMO guidelines, Reck M. et al., Ann Oncol 2014

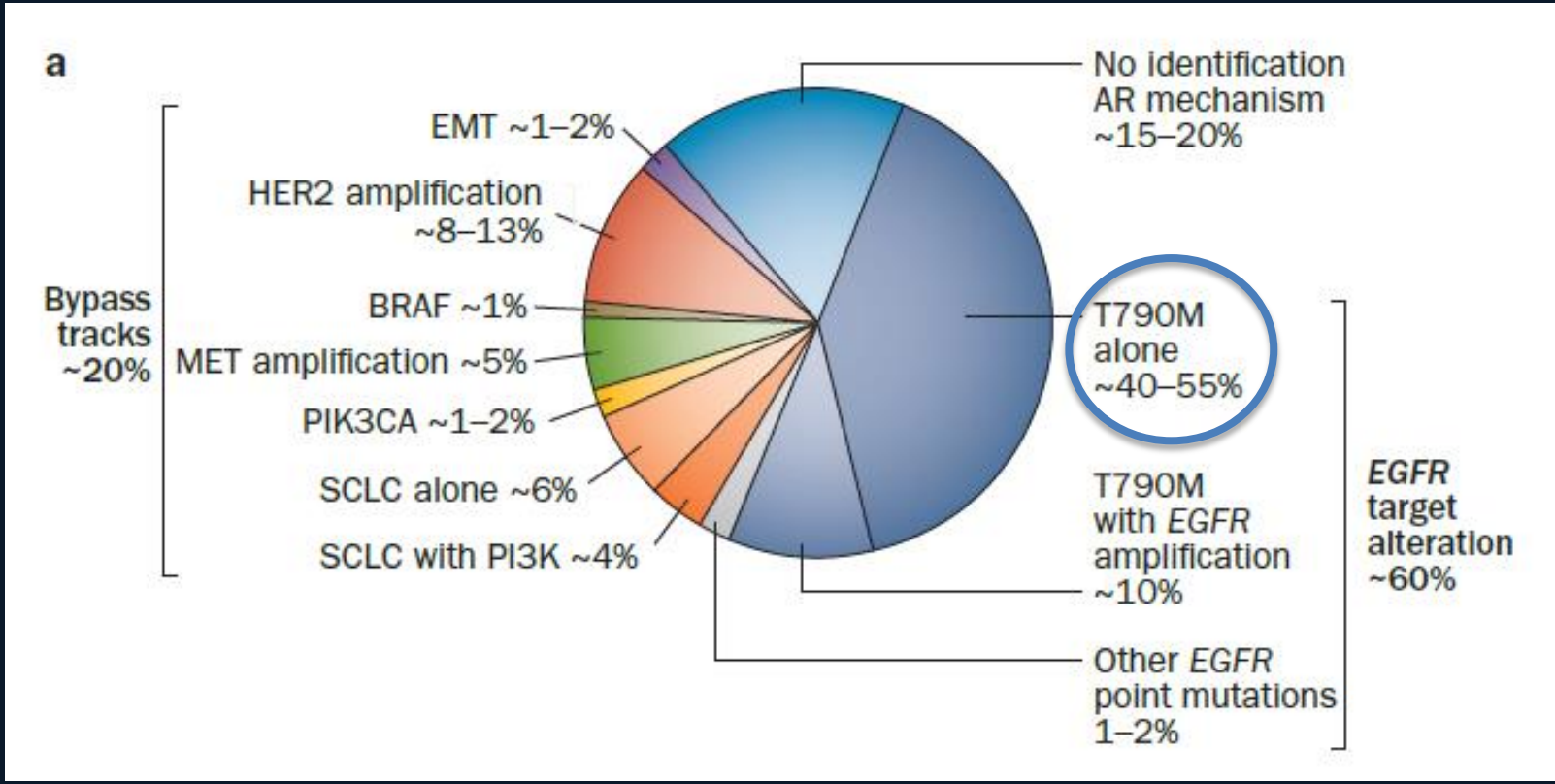
PFS: EGFR TKIs versus Chemotherapy

Study	EGFR TKI	n	Median PFS in TKI arm (months)	P value	HR
OPTIMAL	Erlotinib	154	13.1	<0.0001	0.16
First Signal	Gefitinib	42	8.4	<0.084	0.61
IPASS	Gefitinib	261	9.5	<0.0001	0.48
WJTOG 3405	Gefitinib	177	9.2	<0.001	0.48
NEJSG 002	Gefitinib	200	10.8	<0.001	0.36
Ensure	Erlotinib	217	11	<0.0001	0.34
EURTAC	Erlotinib	174	9.4	<0.0001	0.42
LUX-3	Afatinib	308	13.6	<0.0001	0.47
LUX-6	Afatinib	364	11.0	<0.0001	0.28

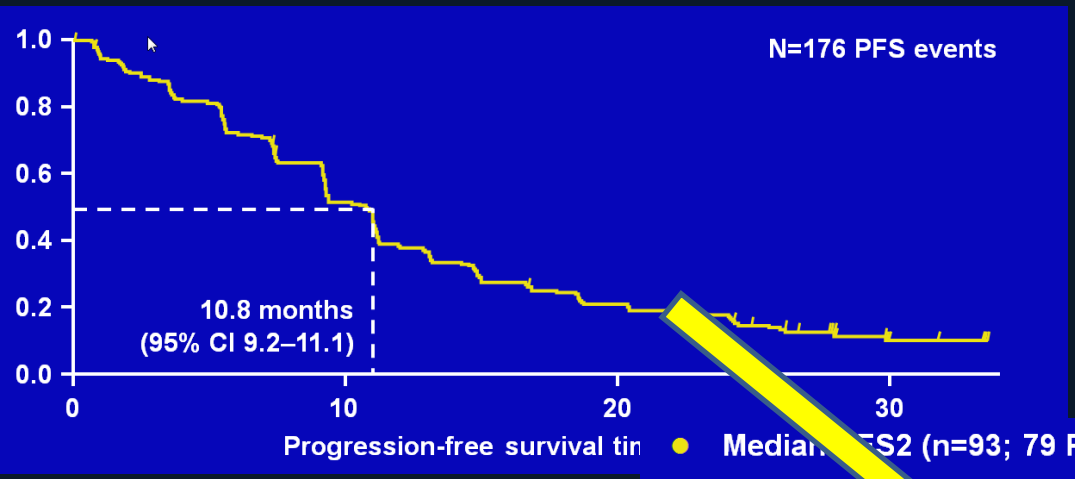
Treatment of EGFR-addicted NSCLC at resistance, harboring T790M

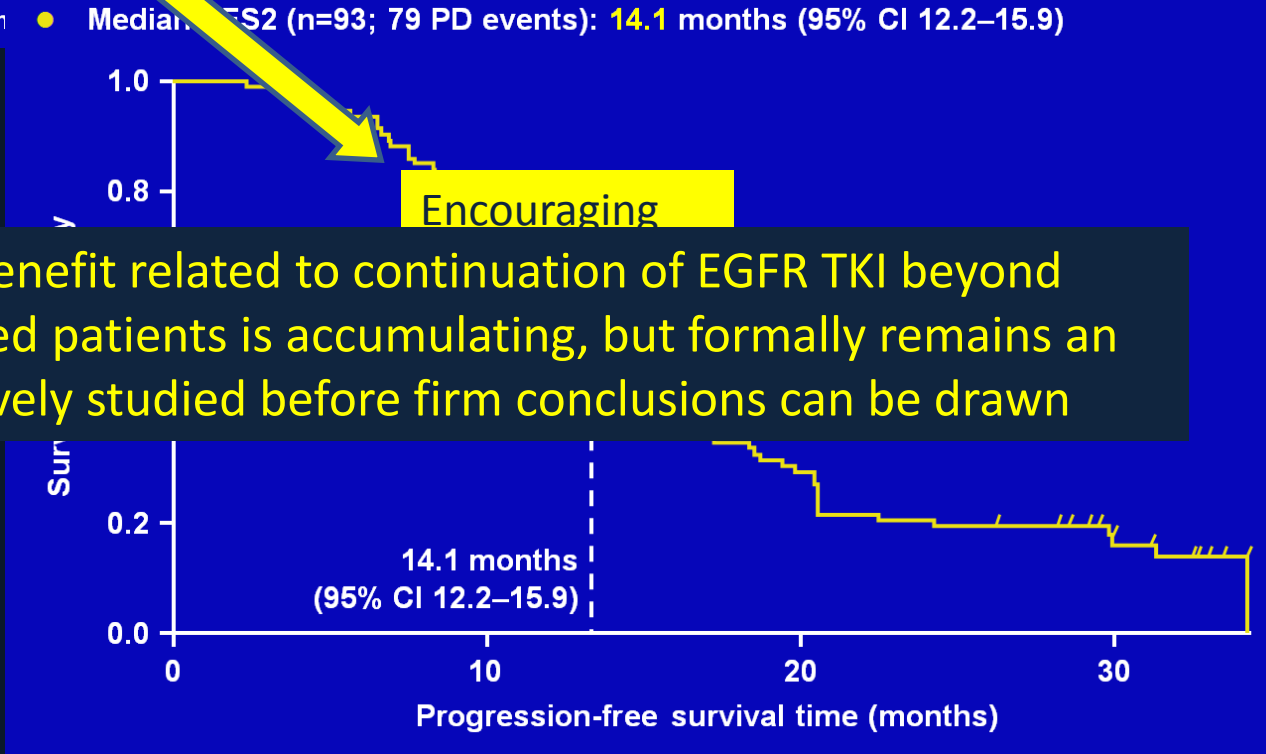
1) Chemotherapy
2) Gefitinib beyond RECIST progression
3) Chemotherapy + EGFR TKI
4) Afatinib
5) Afatinib + cetuximab
6) 3rd generation EGFR TKI (AZD9291, CO-1686, HM61713, through a clinical trial)

Treatment of EGFR M+ NSCLC at resistance



Aspiration trial (Park, ESMO 2014)

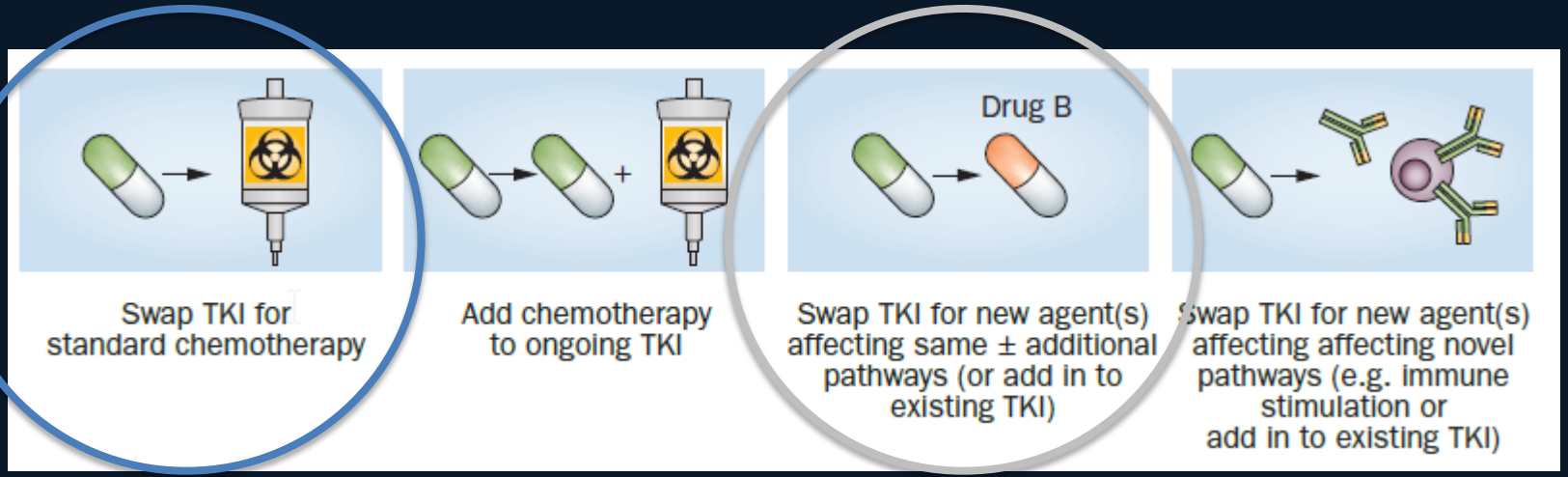




Encouraging

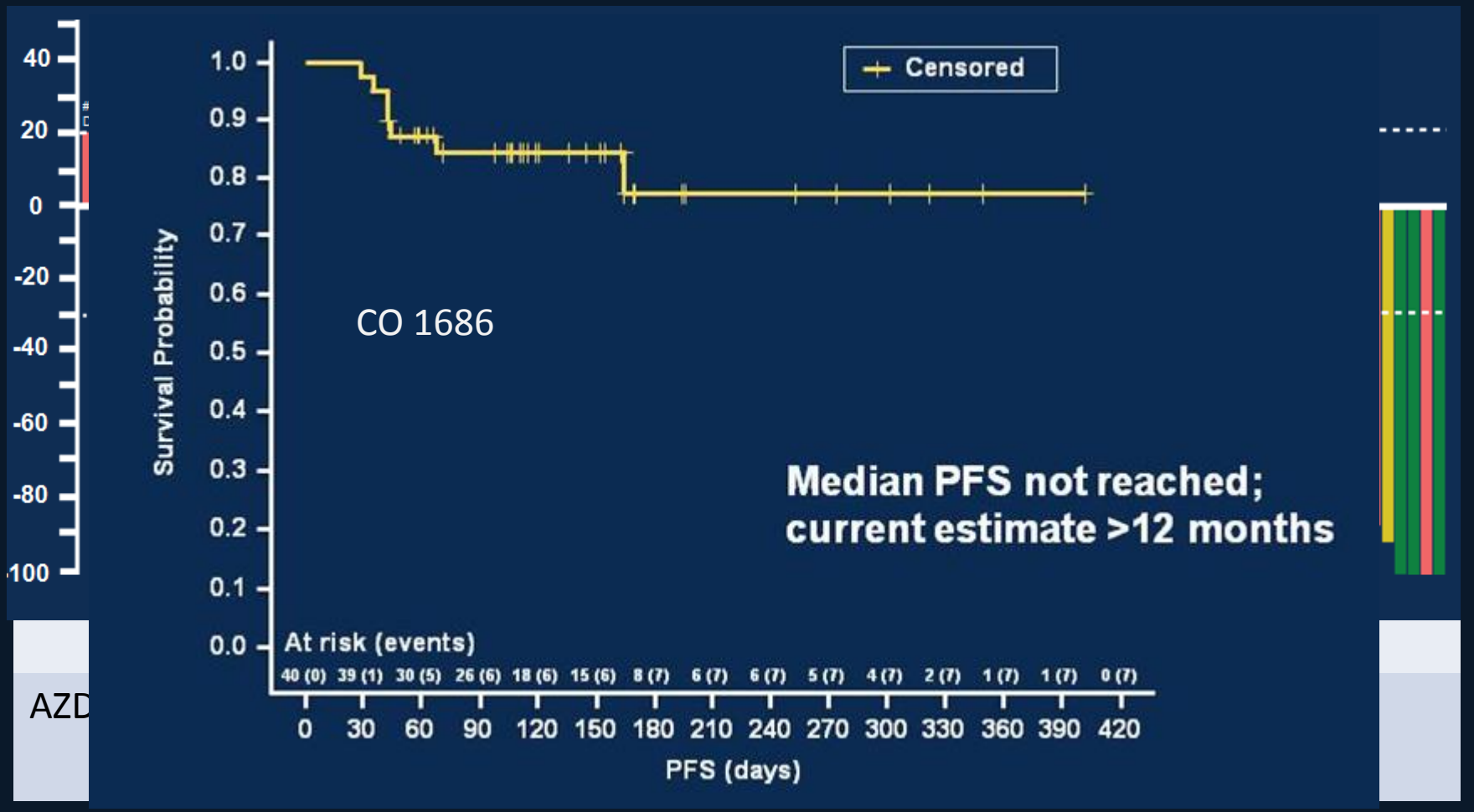
Evidence of clinical benefit related to continuation of EGFR TKI beyond progression in selected patients is accumulating, but formally remains an issue to be prospectively studied before firm conclusions can be drawn

Treatment of EGFR-addicted NSCLC at resistance



Camidge, Nat Rev Clin Oncol 2014
ESMO guidelines, Reck M. et al., Ann Oncol 2014

TKI after progression on TKI



modified from Thomas Lynch, ASCO 2014; Kim, ASCO 2014; Janne ASCO 2014; Sequist ASCO 2014

First line chemotherapy after EGFR TKI failure

1) Cisplatin / pemetrexed
2) Cisplatin / pemetrexed / bevacizumab
3) Carboplatin / pemetrexed
4) Carboplatin / pemetrexed / bevacizumab
5) Docetaxel
6) Pemetrexed
7) Carboplatin / paclitaxel /bevacizumab

Chemo after TKI, any evidence?

Little prospective data on chemo after TKI in mEGFR disease

ESMO Presidential session: IMPRESS TRIAL

Study	Regimen	N	RR	Design
Gridelli, JCO 2012	Cis/gem	13	15%	Prospective
Wu, IJC 2010	Various	41	15%	Retrospective
Goldberg, ASCO 2012	Various	28	18%	Retrospective
Yoshimura, JTO 2012	Pem/TKI	27	26%	Prospective

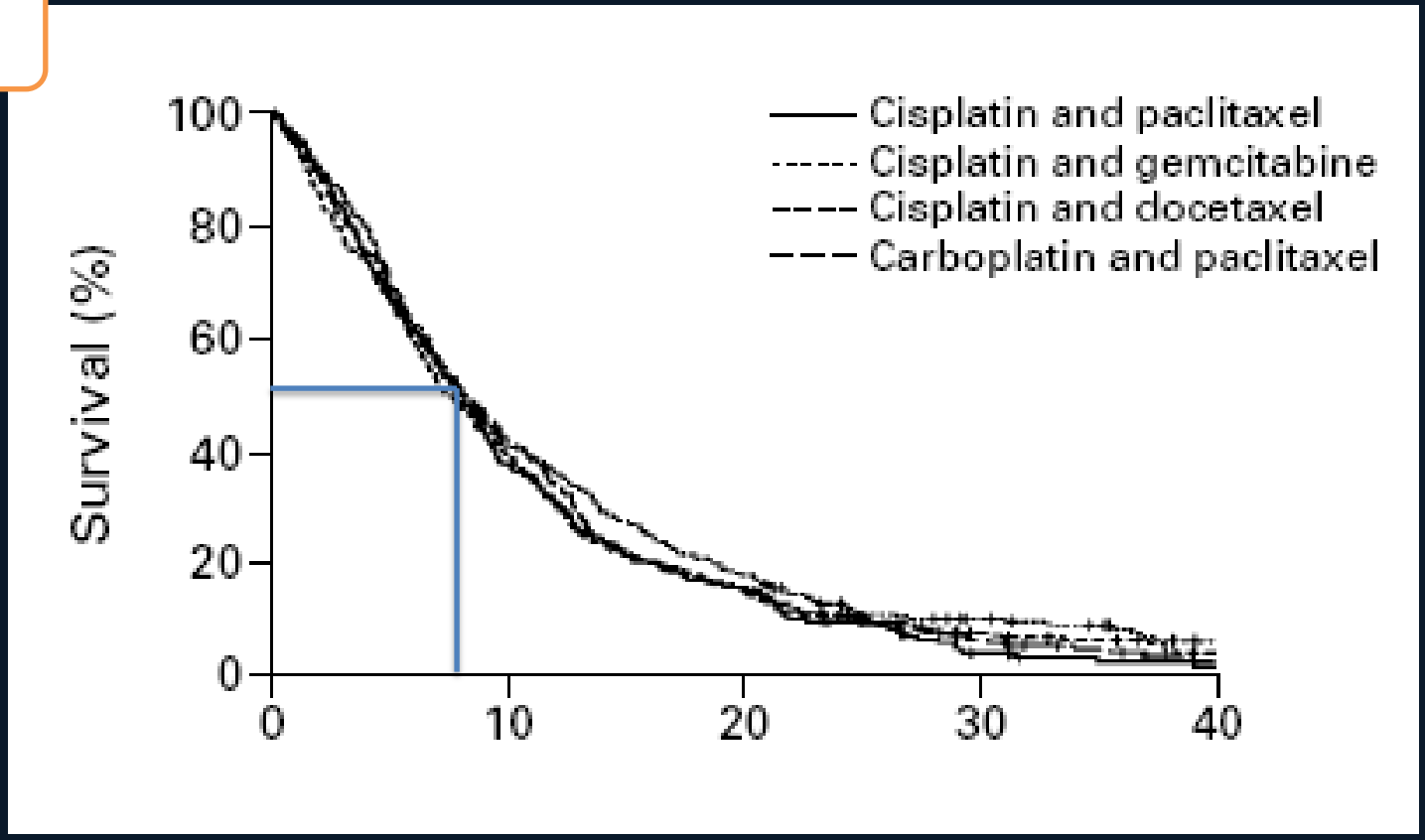
First line chemotherapy
General statements

- Several regimens have shown comparable efficacy
- The expected toxicity profile should contribute to the selection of the chemotherapy regimen
- Meta-analyses have shown higher RRs for cisplatin combinations when compared with carboplatin combinations

ESMO guidelines, Reck M. et al., Ann Oncol 2014

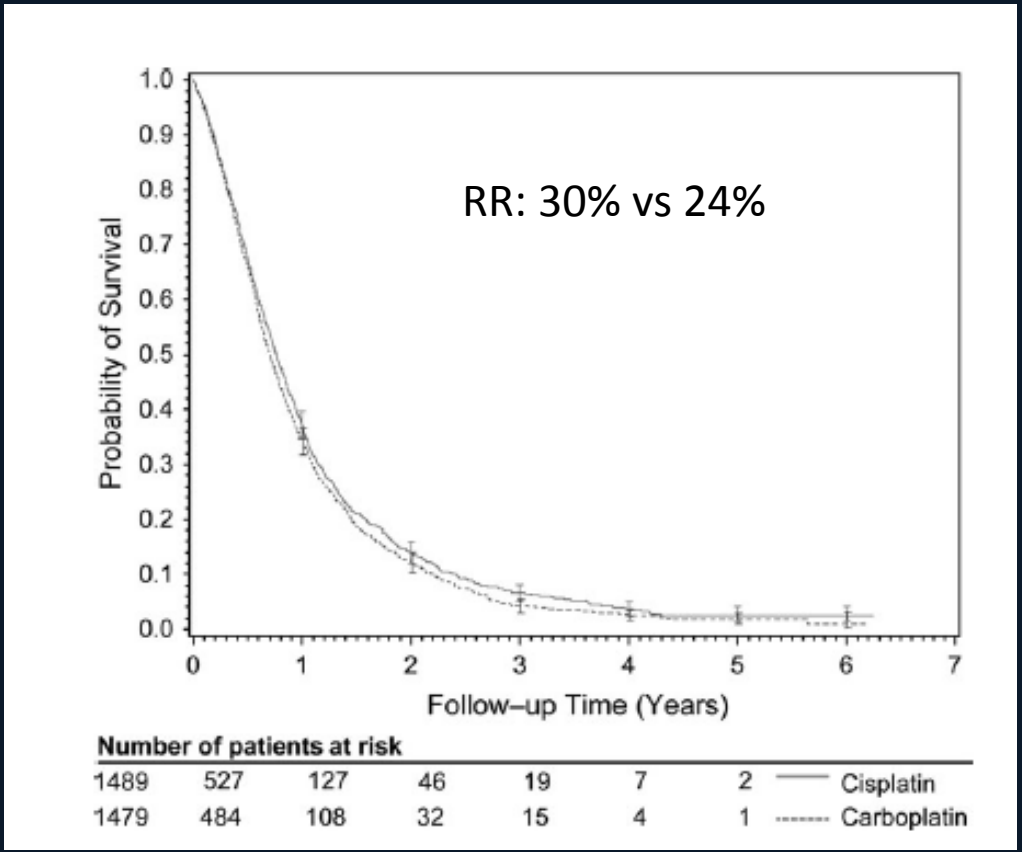
First line chemotherapy PS 0-1

2002



Schiller, NEJM 2002

Cisplatin as the European standard

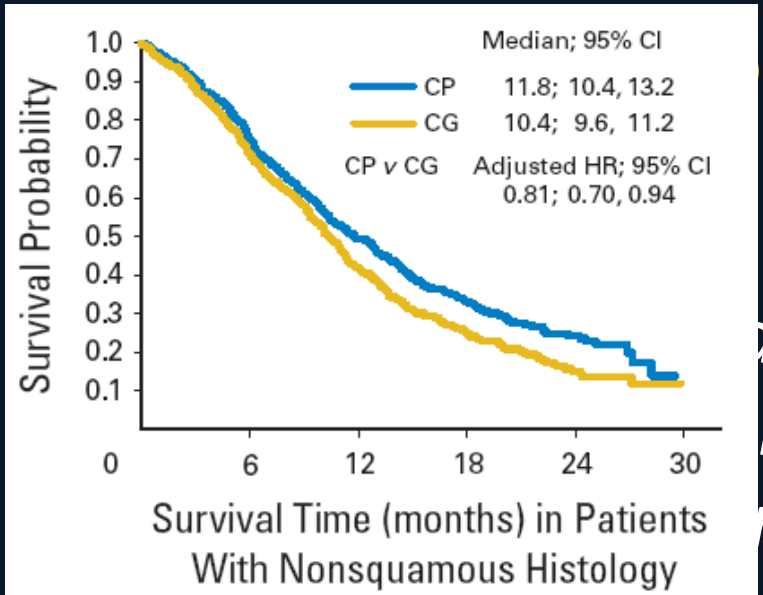


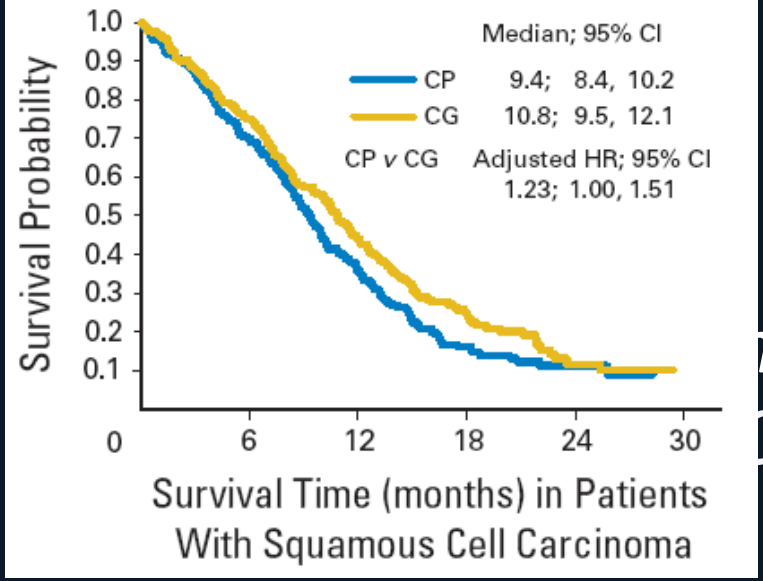
mOS 9.1 vs 8.4 mos (p=NS), absolute benefit 3% at 1yr

-> Statistically significant in patients with non-squamous tumors or treated with third-generation chemotherapy

Ardizzoni, J Natl Cancer Inst 2007

therapy after EGFR TKI failure





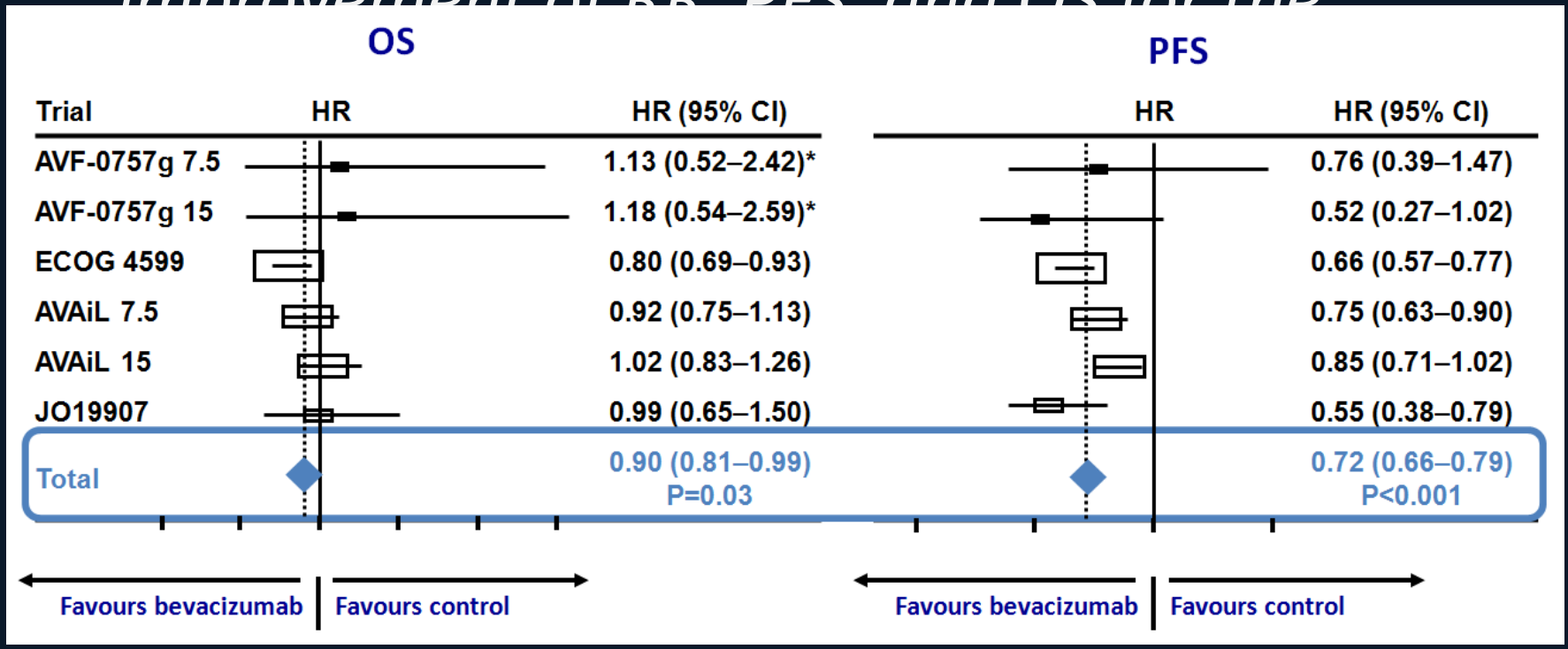
alysis showed a slight but
l benefit with pemetrexed-
n chemotherapy compared
or docetaxel-based
of a pre- planned subgroup
randomised phase III trial

hould be restricted to
CLC in any line [I, A]

ESMO guidelines, Reck M. et al., Ann Oncol 2014;
Scagliotti JCO 2008

Bevacizumab with platinum based chemotherapy

- *Two meta-analyses showed a significant improvement of RR, PFS, and OS for the*



ESMO guidelines, Reck M. et al., Ann Oncol 2014

Thanks for your attention!