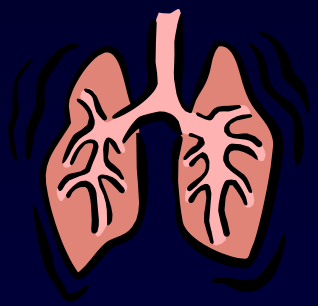


The Real world Conundrum in treating EGFR mutant NSCLC

Dr Ullas Batra MD, DM, ECMO

Senior Consultant Medical Oncologist

Chief, Thoracic Medical Oncology

Rajiv Gandhi Cancer Institute & Research Center

Delhi

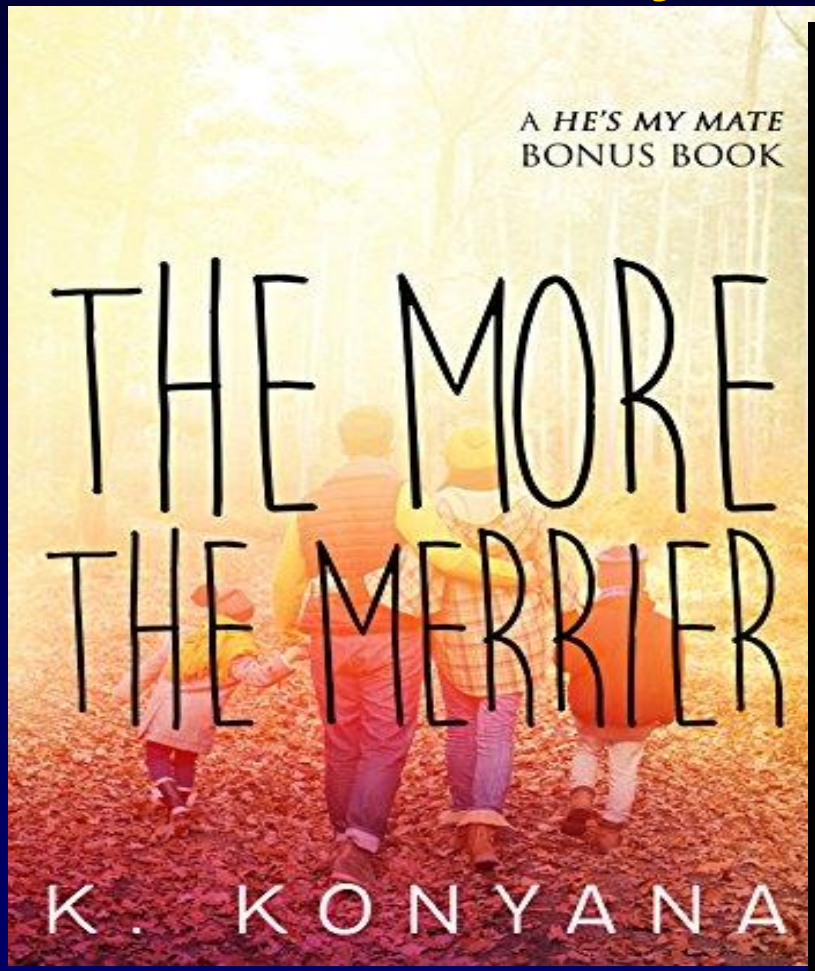
Case scenario…

- 60/female
- h/o cough and breathlessness 2 months
- PET CT done revealed right lung mass with bilateral pulmonary nodules, multiple liver and bony mets
- ECOG PS 1
- Lab parameters normal
- Biopsy from lung mass… adenocarcinoma
- What next??

Conundrums in Biomarker testing…

- Which all biomarkers do you send for and in what sequence??
- What are some peculiar challenges that you have faced in the covid era??

Do you (wish to) order NGS testing upfront routinely in your clinics??



More isn't
always merrier

What about liquid biopsy???

- Do you routinely use liquid biopsy for detection of EGFR mutations??
- How comfortable are you in treating a patient with EGFR mutation detected on Liquid biopsy??
- Does the type of test matter?
  - NGS
  - ddPCR
  - COBAS
- What about the status of liquid biopsy for detection of other oncogenes??

Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment With Targeted Tyrosine Kinase Inhibitors

Guideline From the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology

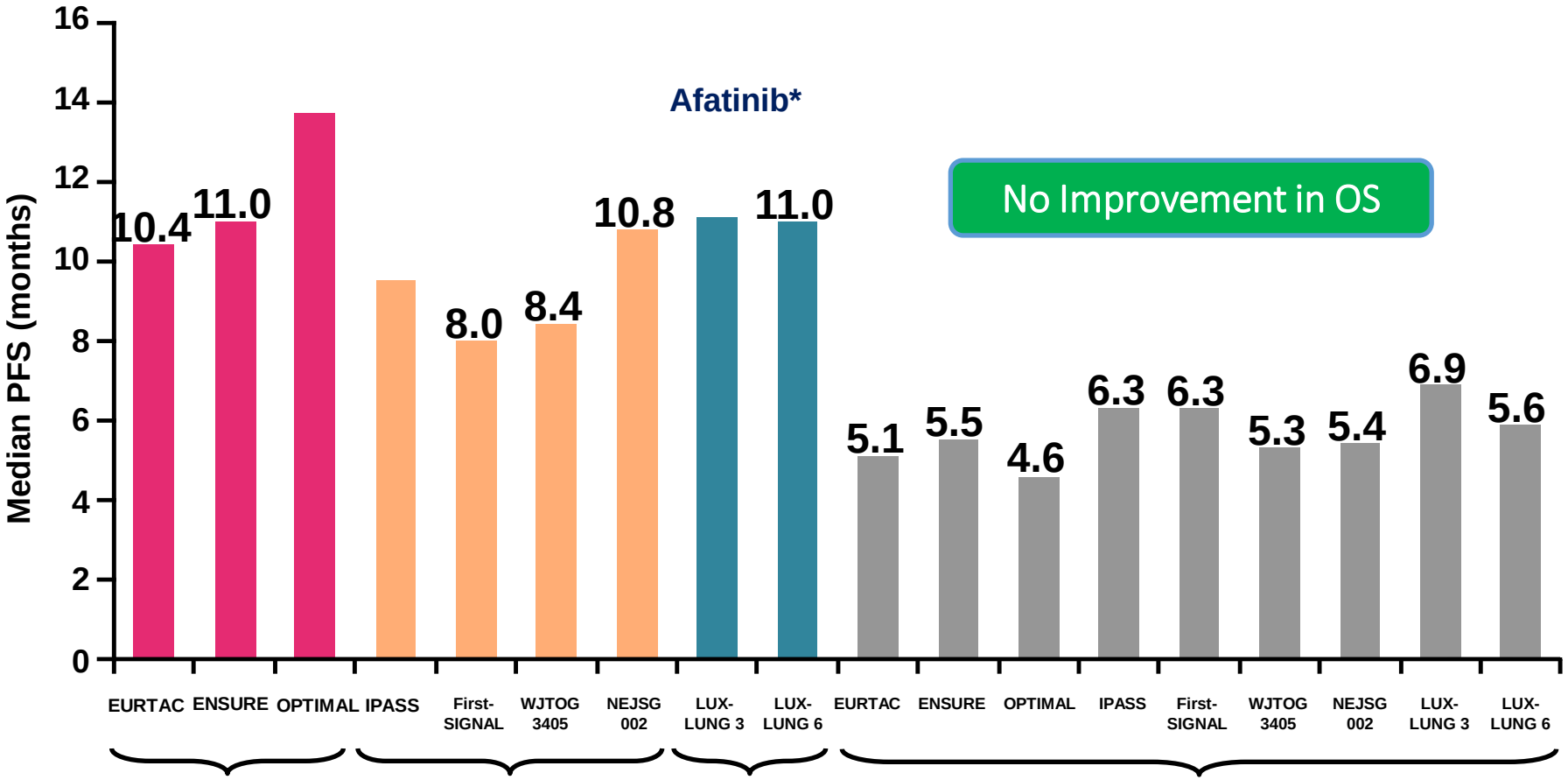
16. *Recommendation.*—In some clinical settings in which tissue is limited and/or insufficient for molecular testing, physicians may use a cfDNA assay to identify *EGFR* mutations.

Case scenario 1

- EGFR del 19 present
- ALK negative by IHC
- ROS negative by IHC
- PDL1 90%(22C3)
- Your choice of treatment??
- Is there a interaction between EGFR and PDL1??

Do you think that treatment of EGFR mutant NSCLC with first generation TKIs is sub optimal??

First-line EGFR TKIs demonstrate improved PFS vs chemotherapy in *EGFR* Mut+ NSCLC



Cross-trial comparison. Data should be interpreted with caution
*All *EGFR* mutations

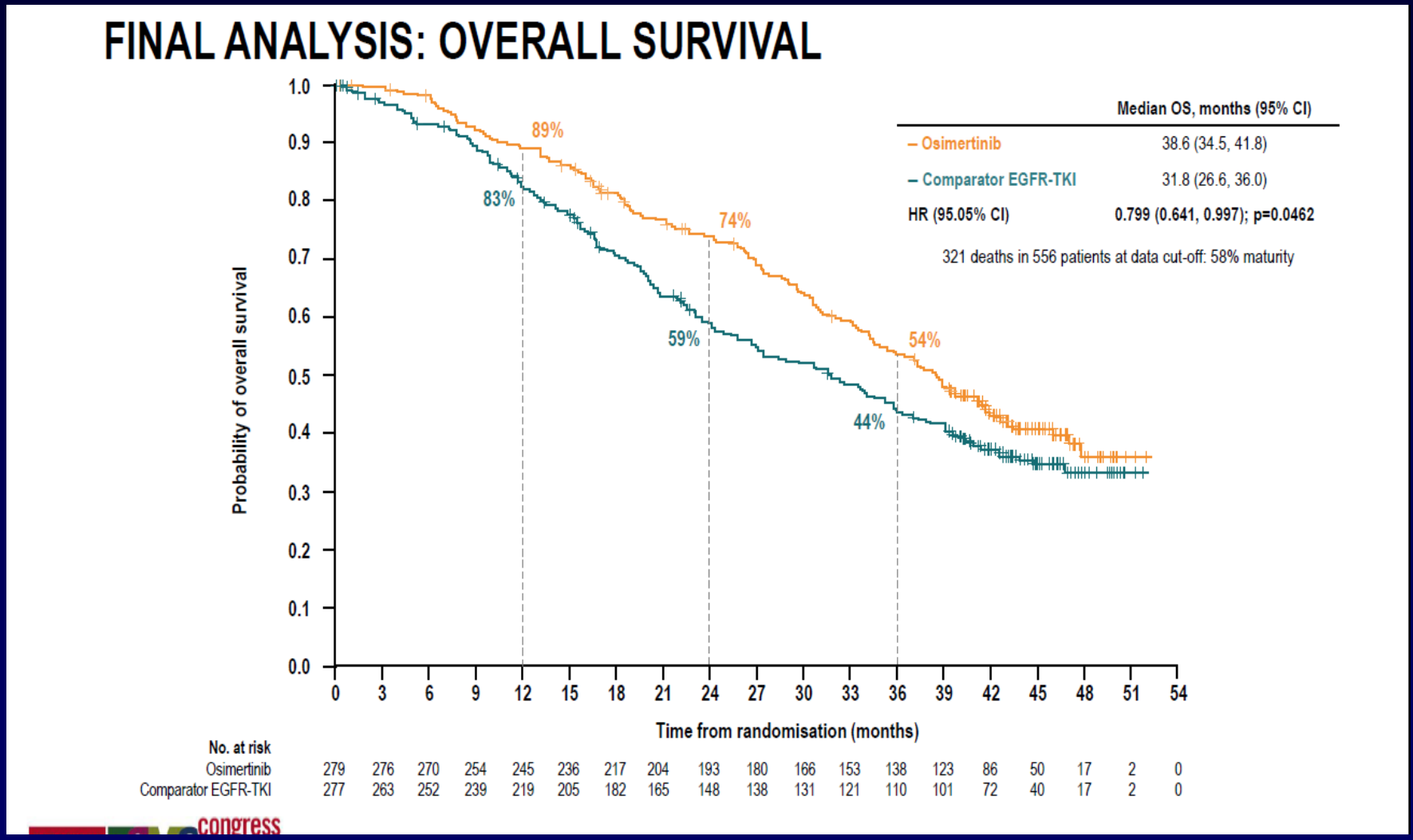
Costa, et al. Clin Cancer Res 2014; Wu, et al. WCLC 2013; Chen, et al. Ann Oncol 2013
Gefitinib SmPC 2010; Han, et al. J Clin Oncol 2012; Mitsudomi, et al. Lancet Oncol 2010
Maemondo, et al. N Engl J Med 2010; Sequist, et al. J Clin Oncol 2013; Wu, et al. Lancet Oncol 2014

What is your first choice treatment in the treatment of EGFR mutant NSCLC??

Treatment options in NSCLC…

- What are the factors that you consider while deciding first line treatment options for EGFR Mutant NSCLC?
  - Cost
  - PFS
  - OS
  - Tolerability
  - Quality of life

Overall survival data…

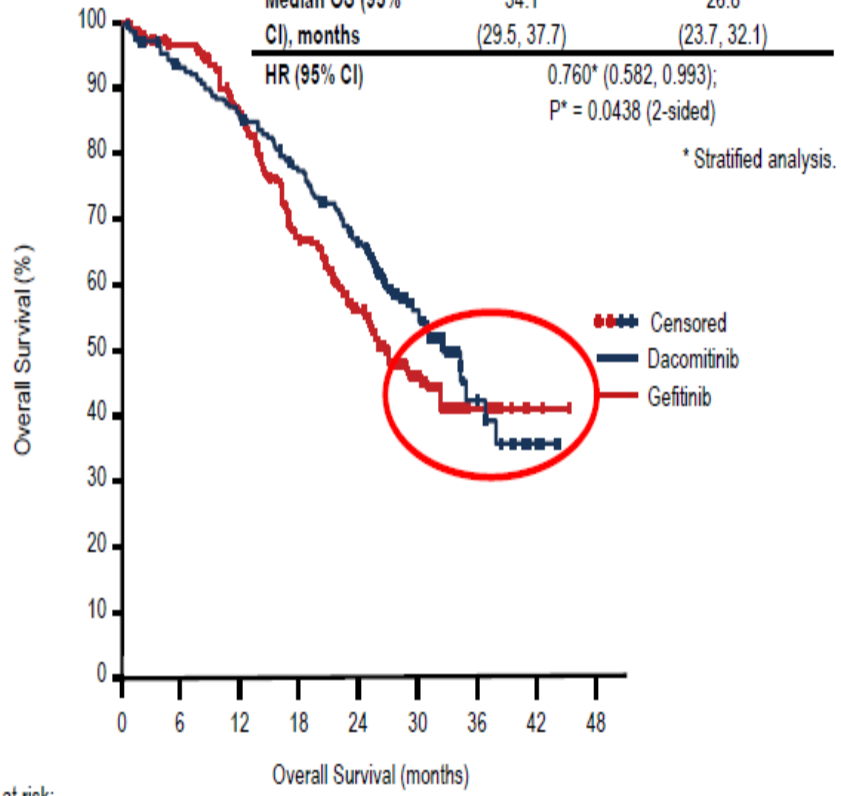


Overall Survival – Intention-to-Treat Population

Overall Survival (Feb. 17, 2017)

	Dacomitinib (n = 227)	Gefitinib (n = 225)
Events, No.	103	117
Median OS (95% CI), months	34.1 (29.5, 37.7)	26.8 (23.7, 32.1)
HR (95% CI)	0.760* (0.582, 0.993); P* = 0.0438 (2-sided)	

* Stratified analysis.

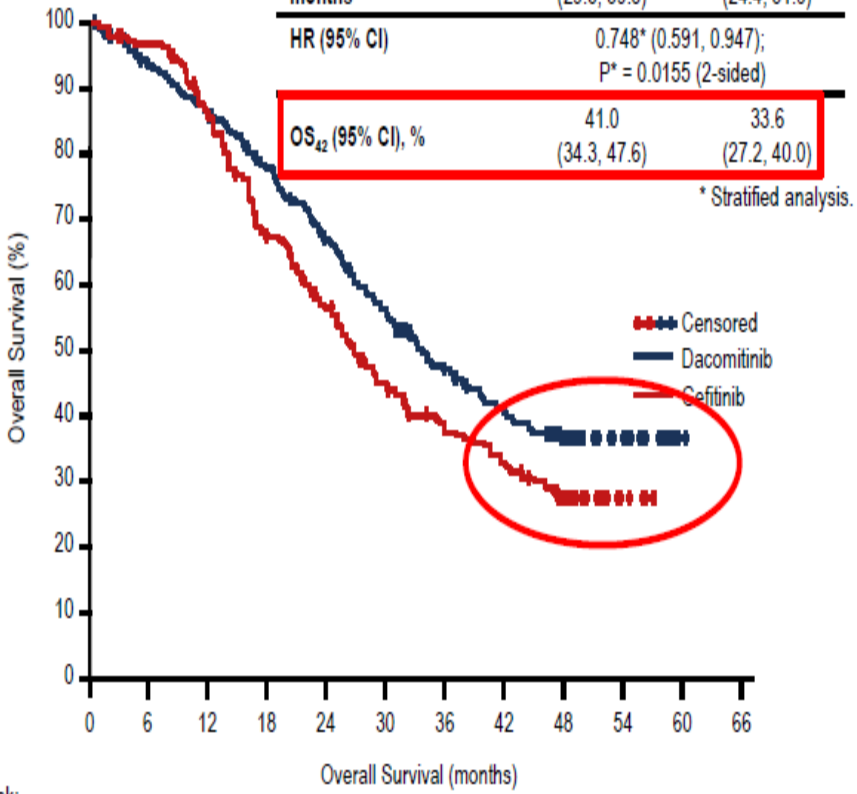


No. at risk:									
Dacomitinib	227	206	188	167	138	77	14	3	0
Gefitinib	225	213	186	144	113	63	12	3	0

Overall Survival (May 13, 2019)

	Dacomitinib (n = 227)	Gefitinib (n = 225)
Events, No.	133	152
Median OS (95% CI), months	34.1 (29.5, 39.8)	27.0 (24.4, 31.6)
HR (95% CI)	0.748* (0.591, 0.947); P* = 0.0155 (2-sided)	
OS_{42} (95% CI), %	41.0 (34.3, 47.6)	33.6 (27.2, 40.0)

* Stratified analysis.

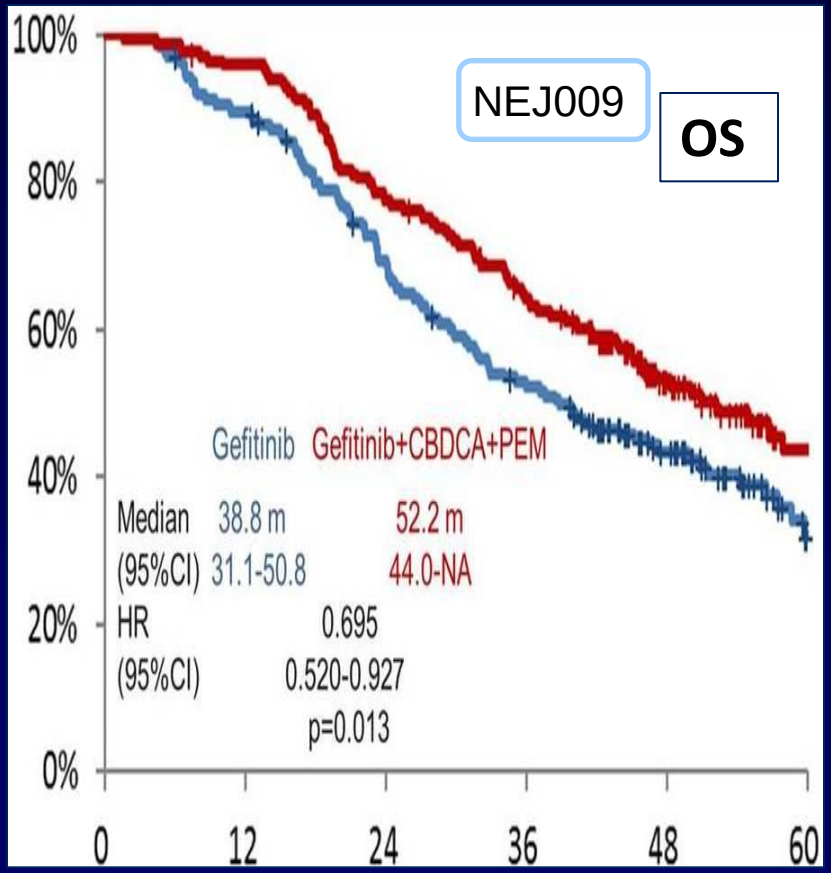


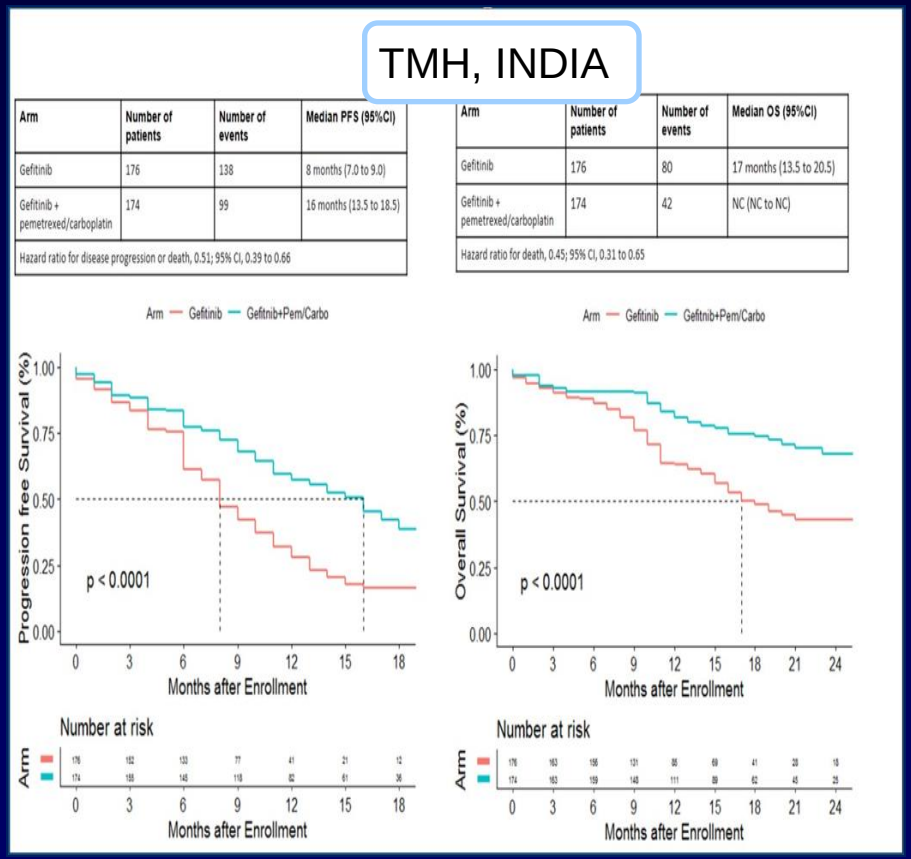
No. at risk:												
Dacomitinib	227	208	190	169	144	119	95	80	39	15	2	0
Gefitinib	225	216	189	147	122	95	76	65	29	4	0	0

Mok TS et al. *J Clin Oncol*. 2018:36(22):2244–2250.

What about combination of chemotherapy and TKIs??

Addition of Chemotherapy to TKI





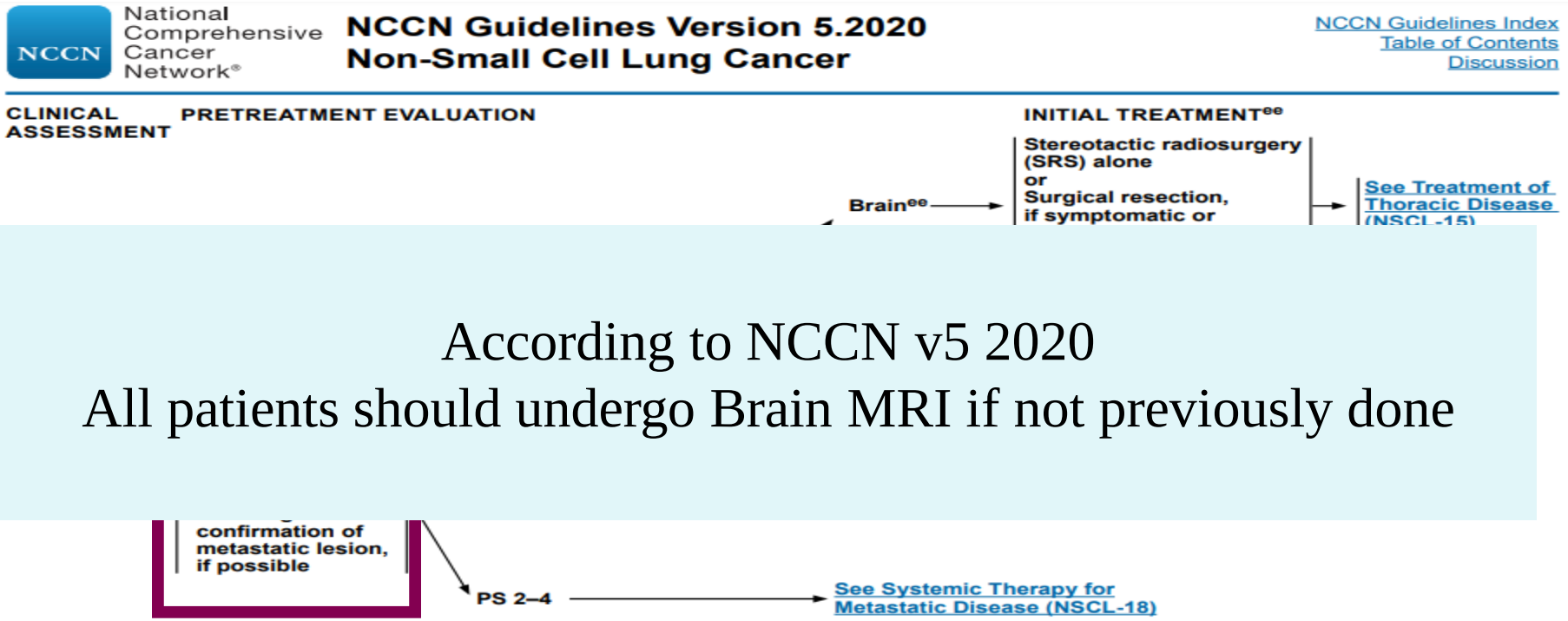
OS benefit of first line EGFR-TKI mono/combo treatment

	phase, n	Gefitinib	Erlotinib	Afatinib	Dacomitinib	Osimertinib	Gefitinib +CBDCA +PEM	Erlotinib +BEV	*HR*
FLAURA [1)]	III, 556	31.8				38.6			*0.80*
LUX-LUNG 7 [2)]	IIB, 319	24.5		27.9					
ARCHER1050 [3)]	III, 452	26.8			34.1				*0.76*
NEJ005 [4)]	II, 80						41.9*		
JO25567 [5)]	II, 154		47.4					47.0	
NEJ009 [6)]	III, 342	38.8					50.9		*0.72*
Noronha V, et al. [7)]	III, 350	17					n.r.		*0.45*

OS (months)

1) Ramalingam SS et al. N Engl J Med 2020; 2) Paz-Ares L et al. Ann Oncol. 2017; 3) Mok TS et al. J Clin Oncol 2018; 4) Oizumi S et al. ESMO Open 2018, * concurrent regimen; 5) Yamamoto N, et al. ASCO Annual Meeting 2018; Oral session #9007; 6) Hosomi Y et al. J Clin Oncol. 2020 7) Notonha V et al. J Clin Oncol. 2020

Do you routinely do MRI Brain in all your patients of NSCLC???



According to NCCN v5 2020
All patients should undergo Brain MRI if not previously done

[j] PET/CT performed skull base to knees or whole body. Positive PET/CT scan findings for distant disease need pathologic or other radiologic confirmation. If PET/CT scan is positive in the mediastinum, lymph node status needs pathologic confirmation.

[o] If MRI is not possible, CT of head with contrast.

[dd] Including selected patients with stage M1c and limited number and volume of metastatic lesions amenable to definitive local therapy. Limited number is undefined but clinical trials have included up to 3 to 5 metastases.

This patient is 65 years female: Adeno Ca lung, LLL, cT3N3M1-left pleura metastases. PDL-1 expression: 55% and EGFR Exon19del mutation

Q: What would be your treatment approach in this patient if Brain MRI shows…..

1. Isolated CNS metastatic lesion (asymptomatic)

2. Multiple small metastases (asymptomatic)

3. Symptomatic CNS mets

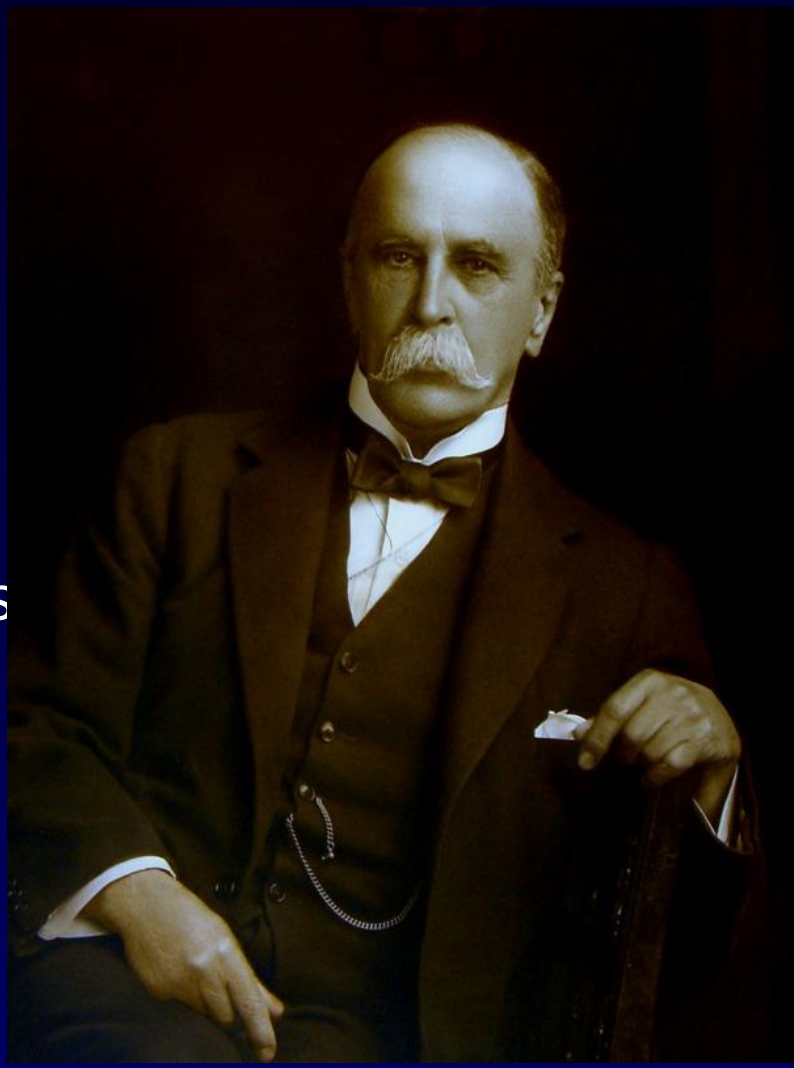
4. Large CNS metastatic lesion near a sensitive site

- Surgery or Stereotactic radiosurgery (SRS)
- Only EGFR TKI
- Role of WBRT?
- Any Role of Steroids?
- Any other

Rationale……?

“If it were not for the great variability among individuals, medicine might as well be a science and not an art.”

Sir William Osler



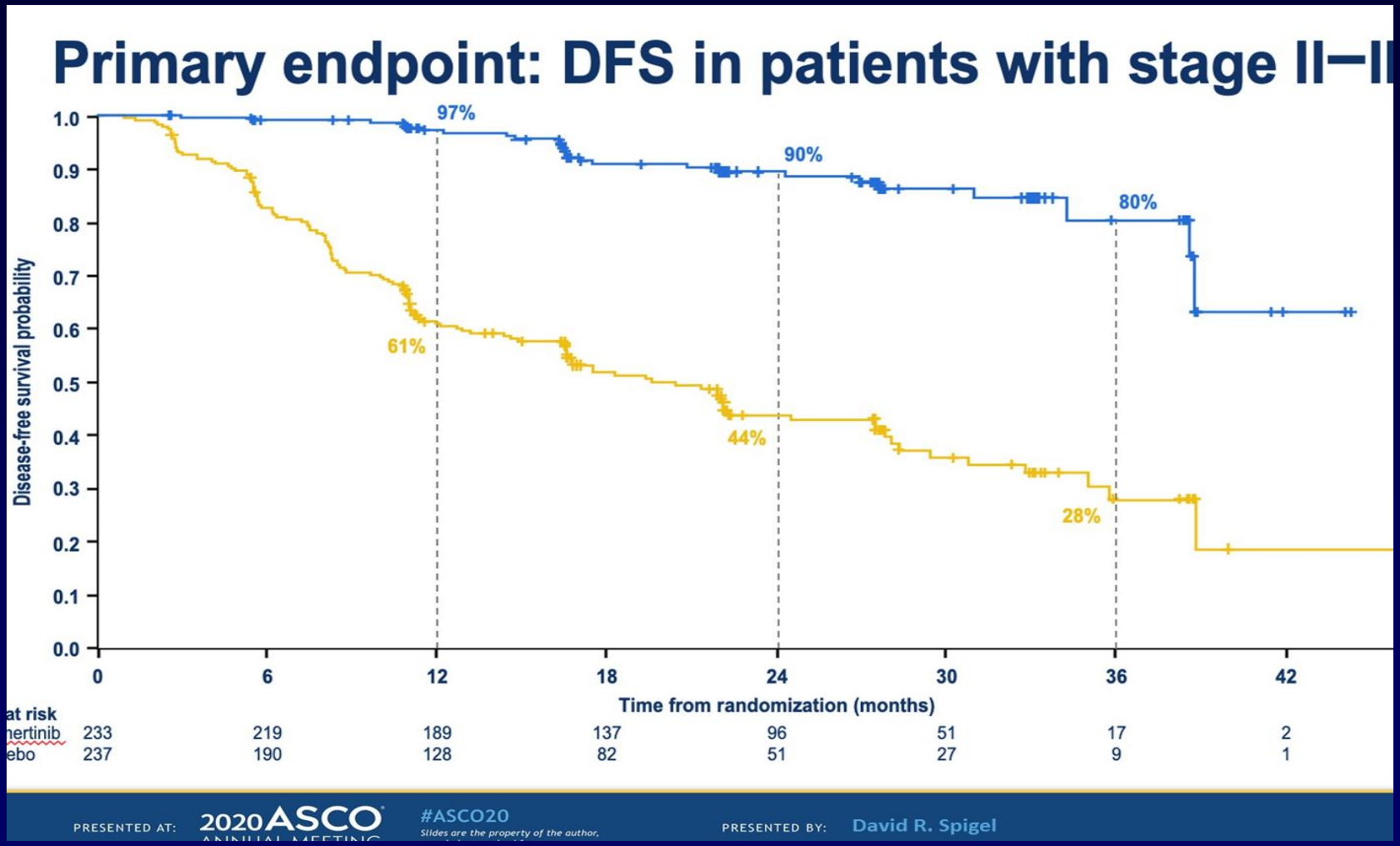
Case 3…

- 55 year old male, never smoker
- Diagnosed as NSCLC
- Underwent surgery
- pT2N1M0

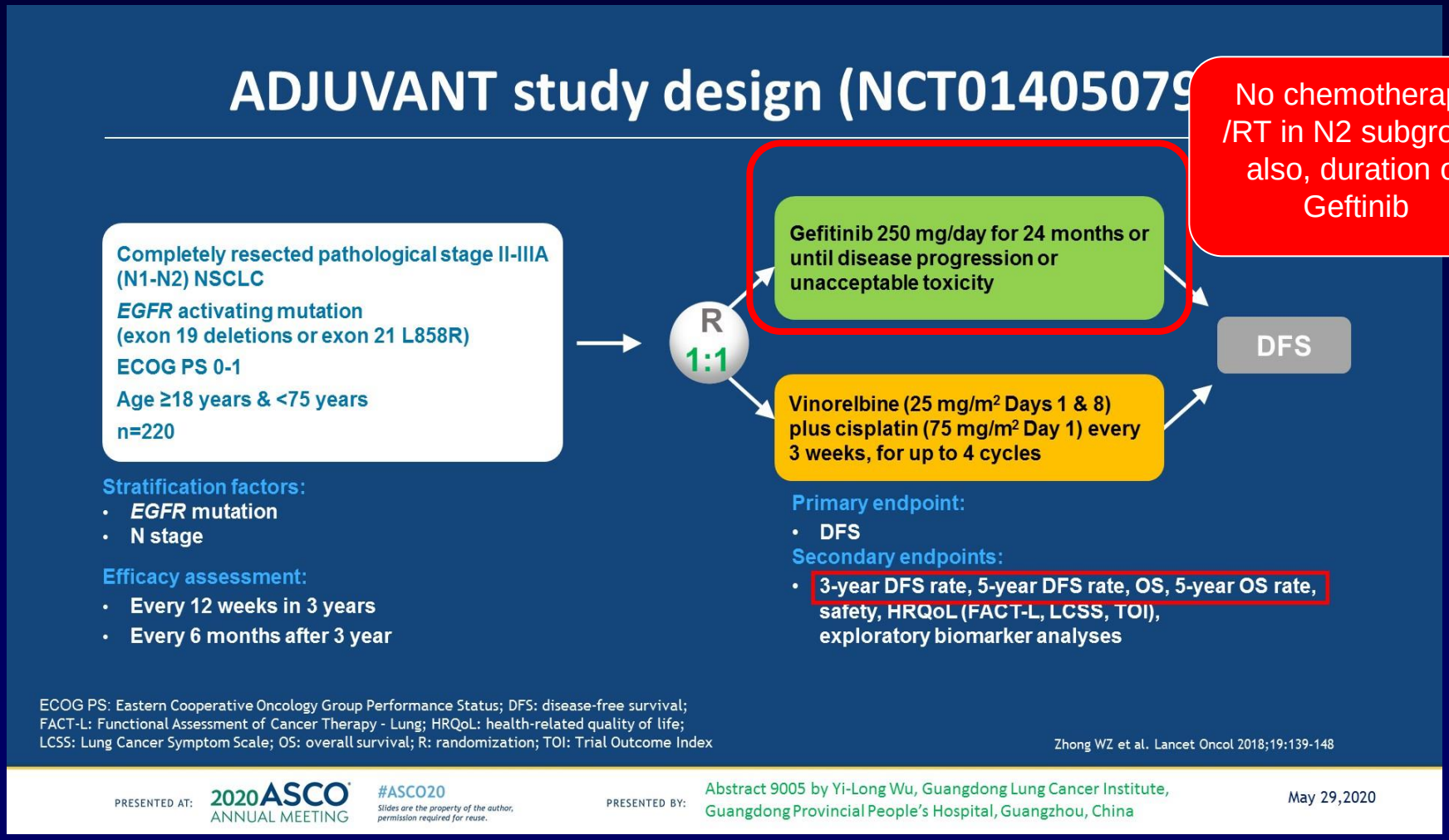
- What would be your choice of treatment??

- Do you ask for EGFR/ALK/ROS in this setting??

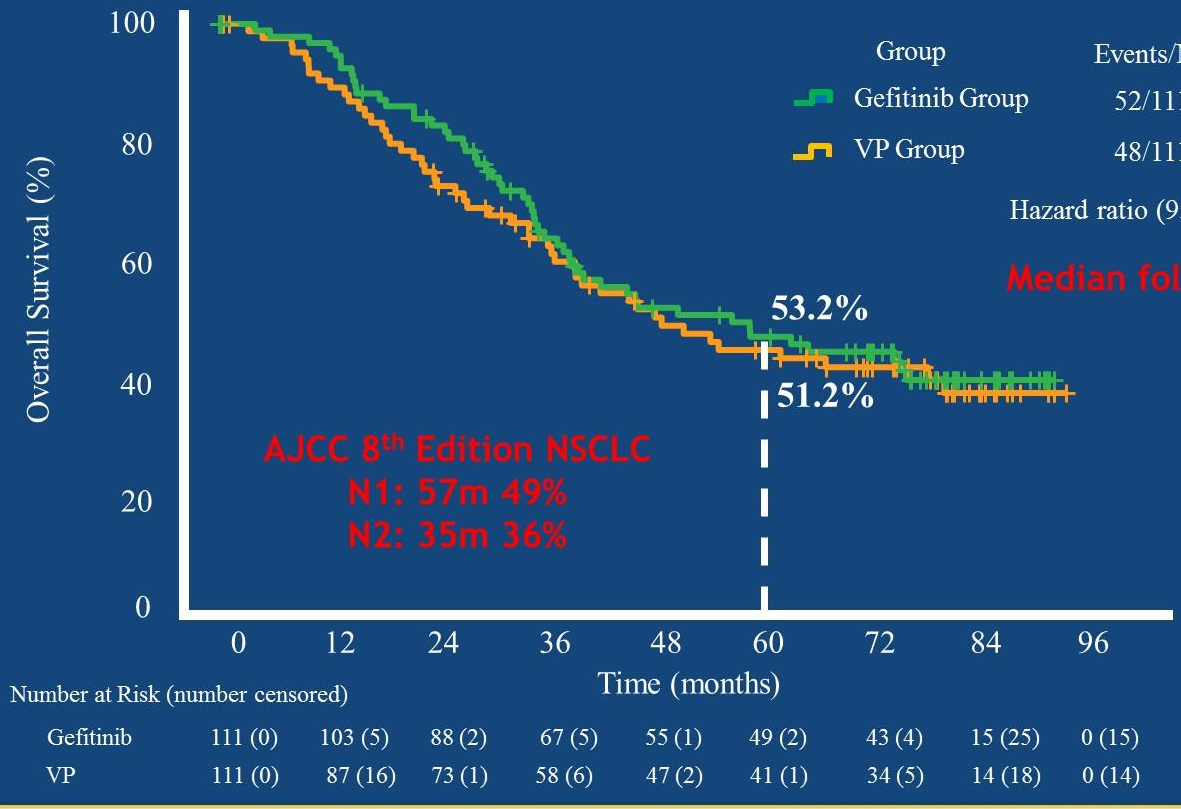
Will you change your practice??



Another positive trial in 2017…



Overall survival (ITT population)



Group	Events/N	Median (m ,95% CI)
Gefitinib Group	52/111	75.5 (46.6 - NC)
VP Group	48/111	62.8 (45.8 - NC)

Hazard ratio (95% CI) = 0.92 (0.62 -1.36) $p = 0.674$

Median follow-up 80 months

Number at Risk (number censored)

Gefitinib	111 (0)	103 (5)	88 (2)	67 (5)	55 (1)	49 (2)	43 (4)	15 (25)	0 (15)
VP	111 (0)	87 (16)	73 (1)	58 (6)	47 (2)	41 (1)	34 (5)	14 (18)	0 (14)

lung cancer

DESERVES A CURE TOO

The woods are lovely, dark and deep, but I have promises to keep, and miles to go before I sleep, and miles to go before I sleep.

Robert Frost

quotefancy


HOPE