

Lung Cases: BCCA Annual Conference

Nevin Murray

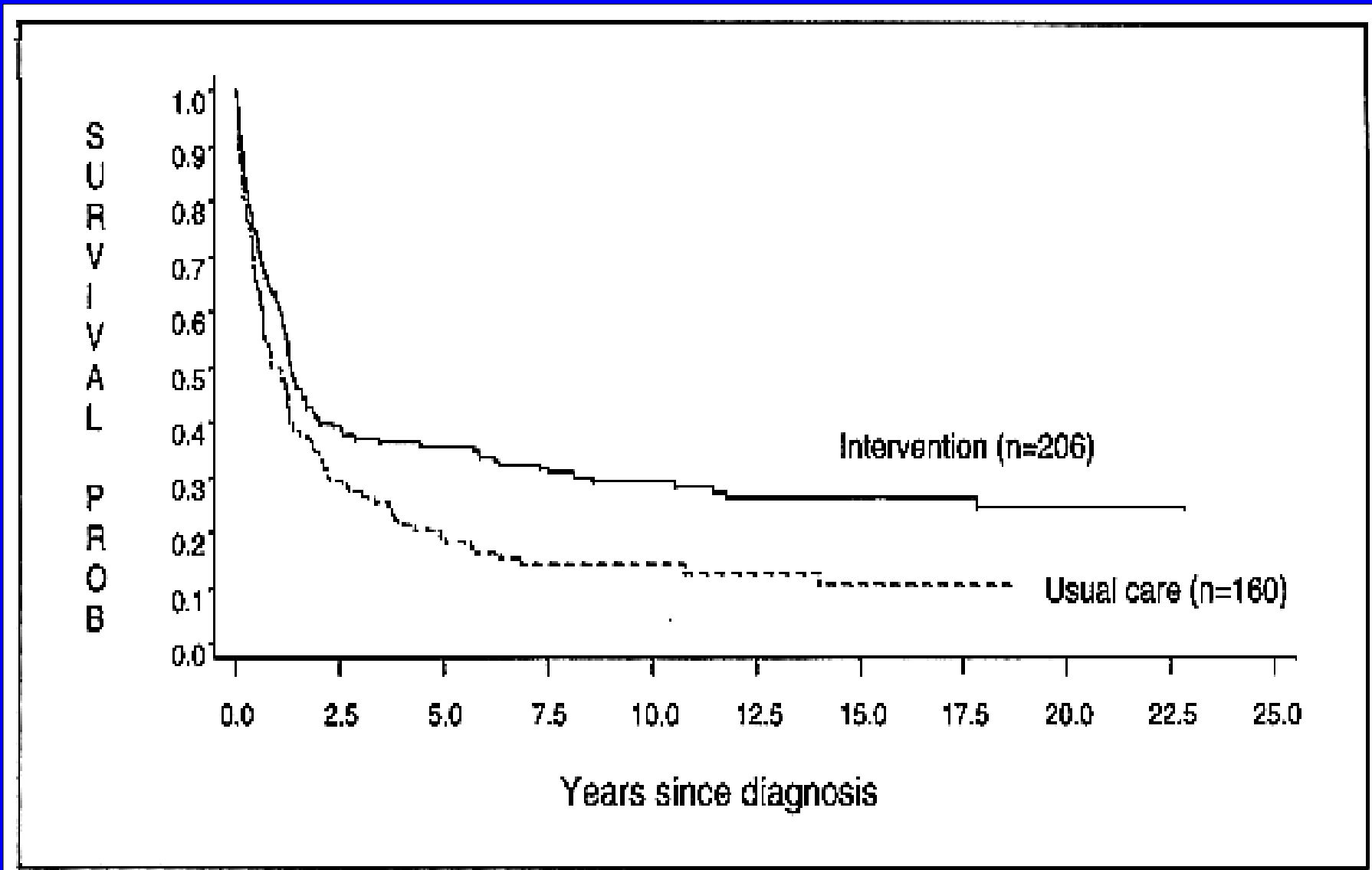
Vancouver Cancer Centre

Lung Cancer Case #1

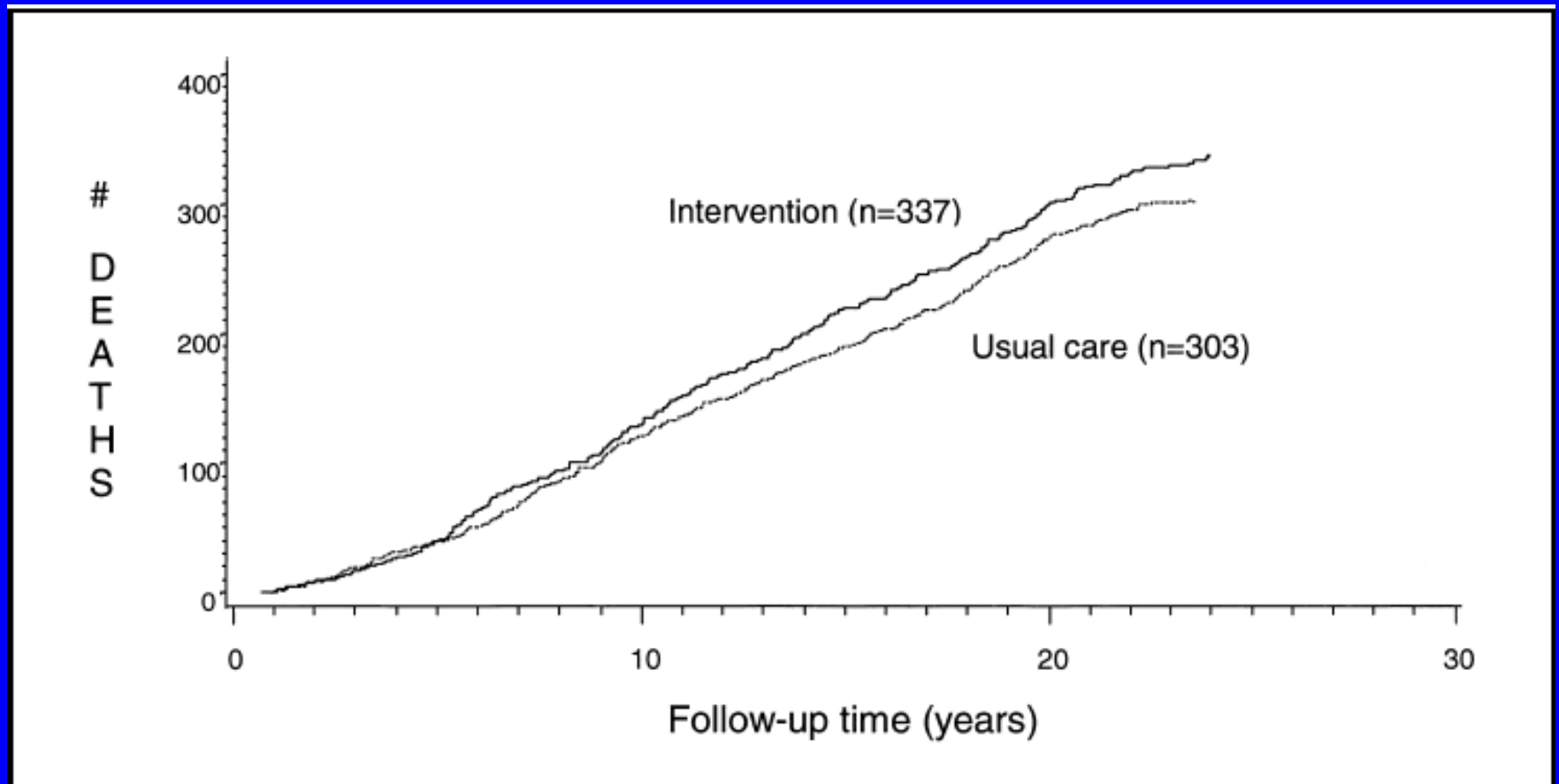
- A 60 year old man with a 30 pack year smoking history discontinued smoking 2 years ago.
- He is aware of a news report of lung cancer screening saving lives.
- He is free of co-morbidity, highly motivated and wants to start a lung cancer screening program.

The Lessons of History??

Mayo RCT: Post-diagnosis Survival. 4-monthly chest X ray and sputum cytology over 6 years as lung cancer screening; 4618 screened, 4593 usual care. 1971-83; Marcus et al., JNCI 92: 1308, 2000

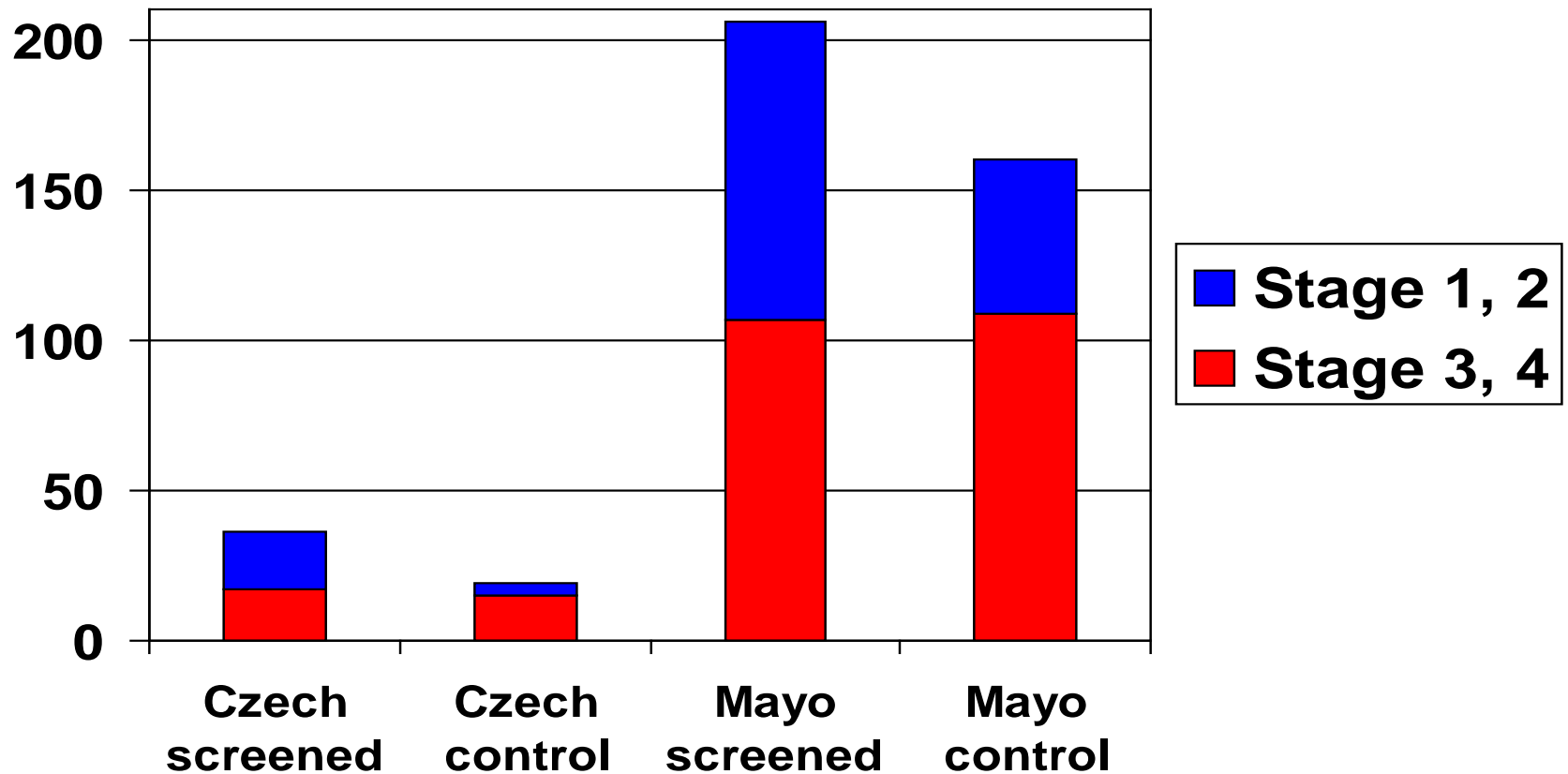


Mayo lung screening RCT: survival from study entry over 23 years



Marcus et al., JNCI 92: 1308, 2000

Numbers of Lung Cancers by Stage: Czech+Mayo Trials



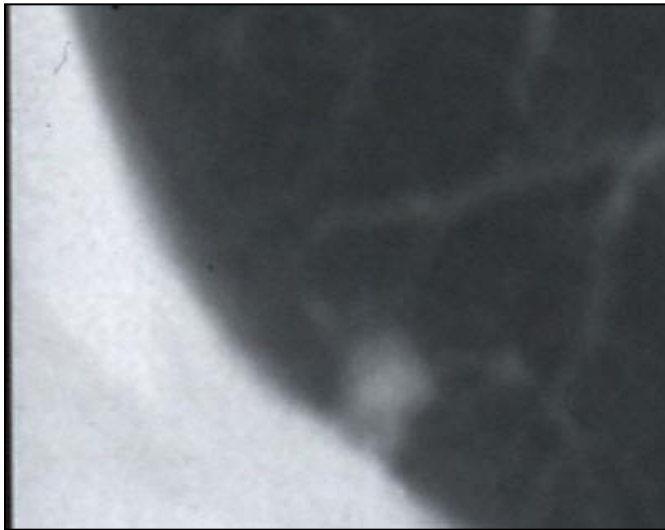
Over-Diagnosis Bias

- ↑ Stage I
- ↑ Resectability
- ↑ Survival
- ↑ Cancers
- Same # advanced cancers
- No ↓ lung cancer deaths

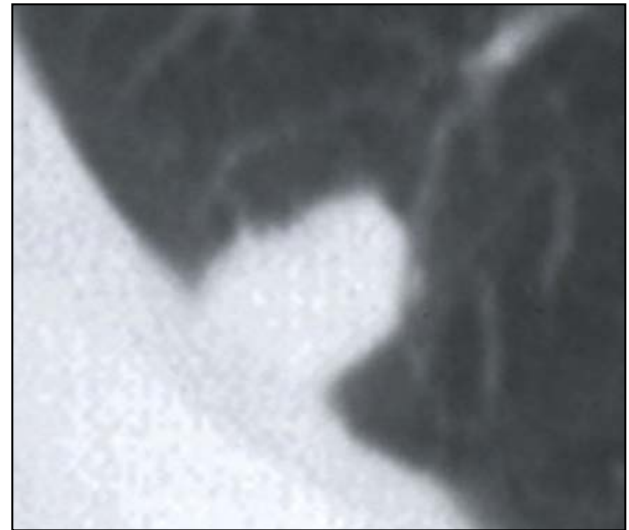
How long?

16 years

Doubling Time=813 days

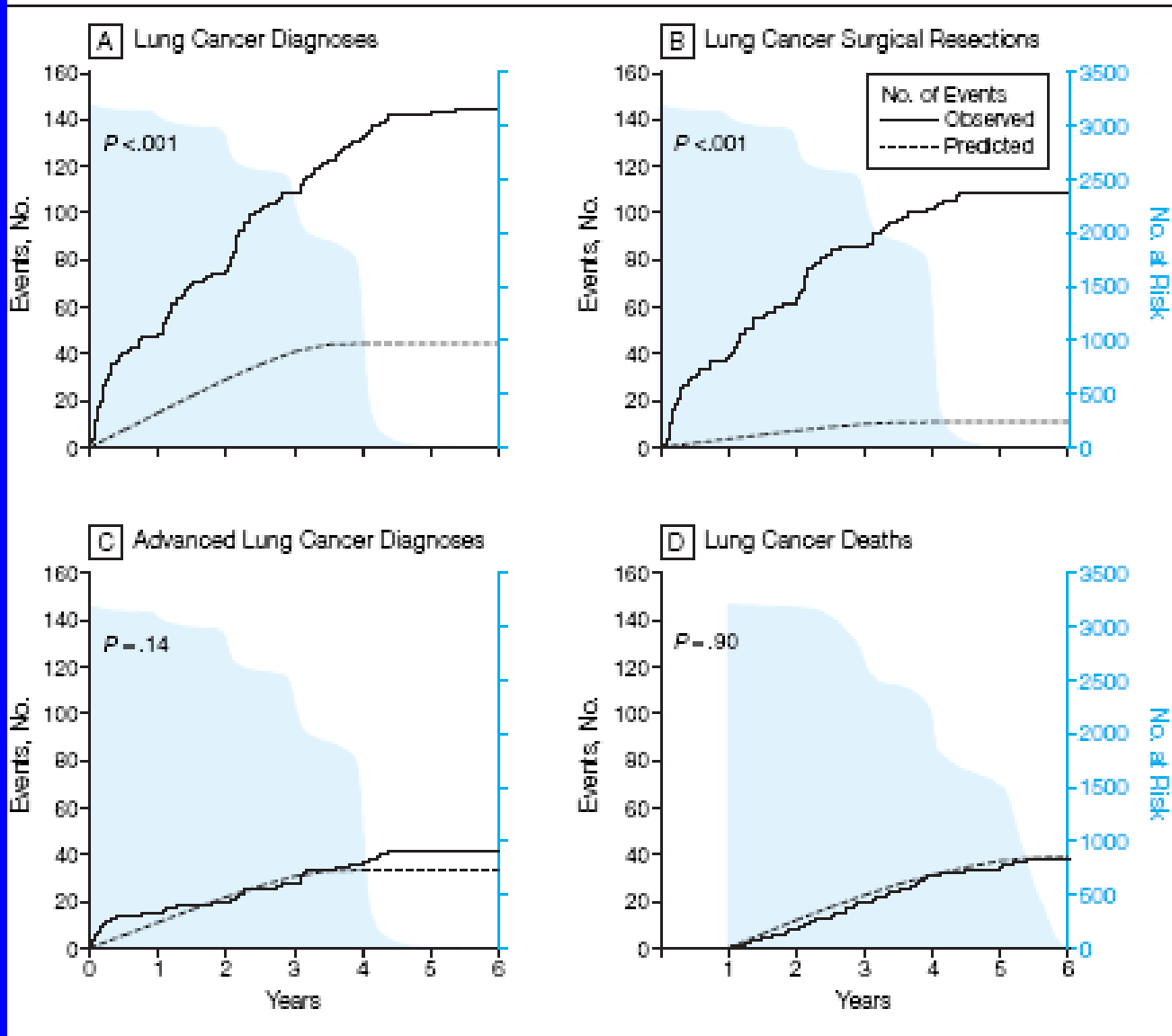


3mm



15mm

Figure 2. Combined Results for the Studies of Lung Cancer Screening With Computed Tomography



Conducted at the Istituto Tumori (Milan, Italy), the Mayo Clinic (Rochester, Minn), and the Moffitt Cancer Center (Tampa, Fla). The left axis shows the actual and predicted numbers of individuals with different lung cancer outcomes. The right axis shows the number at risk (blue tinted area). P values are for the difference between the observed and the predicted number of events over the course of the study.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

53,454 Participants

55 to 74 years;

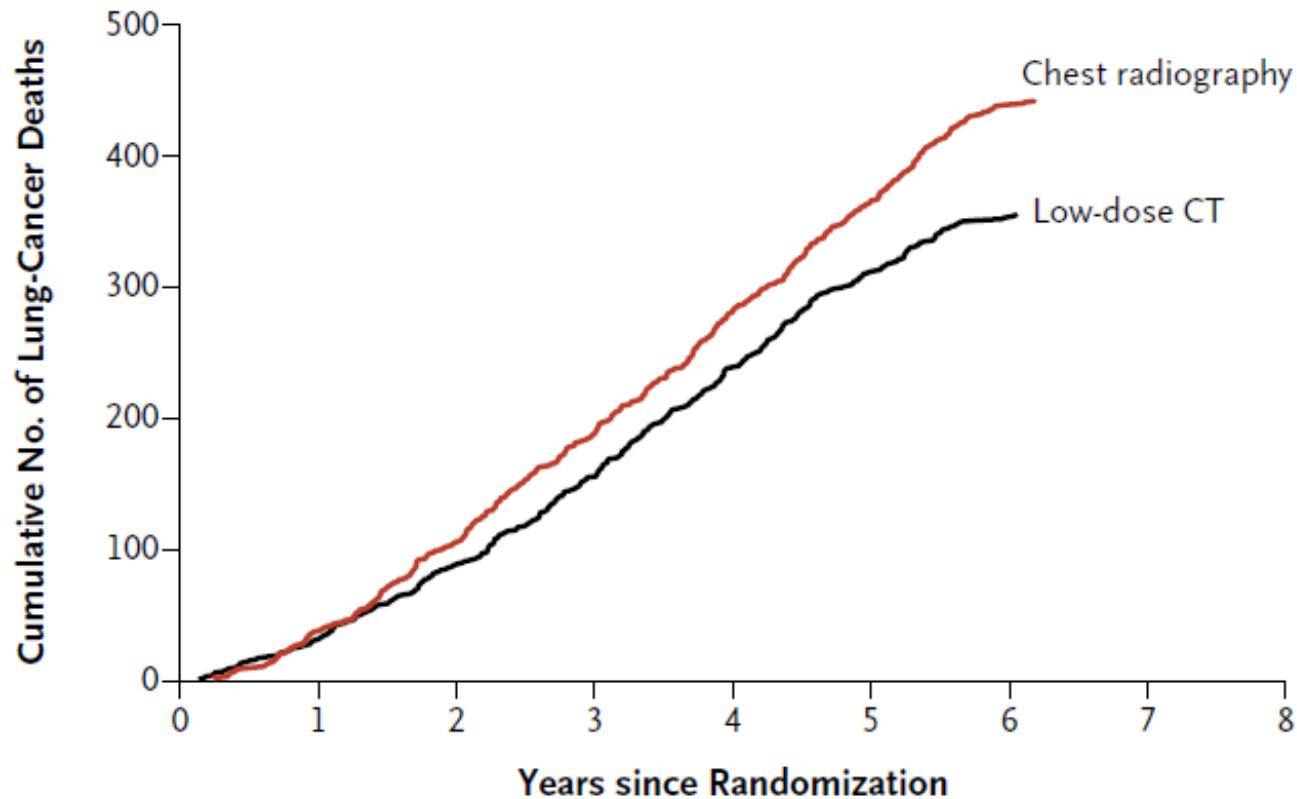
≥ 30 pack-years

Median follow-up 6.5 years

NEJM 2011; 365:395-409

Cumulative Lung Cancer Deaths

B Death from Lung Cancer



Prevalence Of Lung Cancer In Screening Trials Using Age & Smoking

	NLST	NELSON	Danish	ITALUNG
N=	26,312	7,557	2,052	1,406
Population	Age 55-74; ≥30 pack-yrs	Age 50-75; >15 cig/day >25 yr or >10 cig/day ≥ 30 yr	Age 50- 75; ≥20 pack-yrs	Age 55-69; ≥20 pack- yrs
Prevalence + (Incidence)	1.02% (CT – 1060 CXR - 941)	0.97% (CT - 134 after 2 + yrs)	0.8% (CT – 69 UC- 24)	1.4% (2.7% after 3+ yrs)

Estimation Of Proportion Of US Population Who Meets NLST Criteria

Age Strata (years)	Men	Women
55-59	0.218	0.119
60-64	0.231	0.130
65-69	0.213	0.115
70-74	0.165	0.094

What Is A Positive CT?

Study	Threshold	% Positive
NLST	$\geq 4\text{mm}$	27.3%
NELSON	$>500\text{ mm}^3$ ($>9.8\text{ mm}$) Intermediate: 50 to 500 mm^3 (4.6 mm to 9.8 mm)	1.6% 19.2%
Danish	$>15\text{ mm}$ Intermediate: 5 to 15mm	8.6%
ITALUNG	Solid : $\geq 5\text{ mm}$ GGO: $\geq 1\text{ cm}$	30%

Risk Of Unnecessary Biopsy/Surgery, Adverse Events Or Death

Event	Risk
Bronchoscopy/transthoracic needle biopsy	1.7%
Thoracotomy, thoracoscopy/mediastinoscopy	0.96%
Major complication	0.1%
Death within 60 days after the most invasive diagnostic procedure	0.035%

Lung Cancer Prediction Model

- Derived from PLCO study (Tammemägi et al. J Natl Cancer Inst 2011;103:1–11)
- Based on age, smoking history, family history of lung cancer, education level (socio-economic status), history of COPD (self-reported), chest X-ray in last 3 years and body mass index
- Pan-Canadian Study enrolled smokers with $\geq 2\%/3$ years lung cancer risk

How Should LDCT Screening Be Implemented?

- Opportunistic or adhoc screening
 - Risk of causing net harm if performed on patients who have only a low risk and therefore low probability of benefit
 - Risk of full dose/contrast CT instead of LDCT
 - Variation in expertise in diagnosis & management
- Organized or programmatic screening

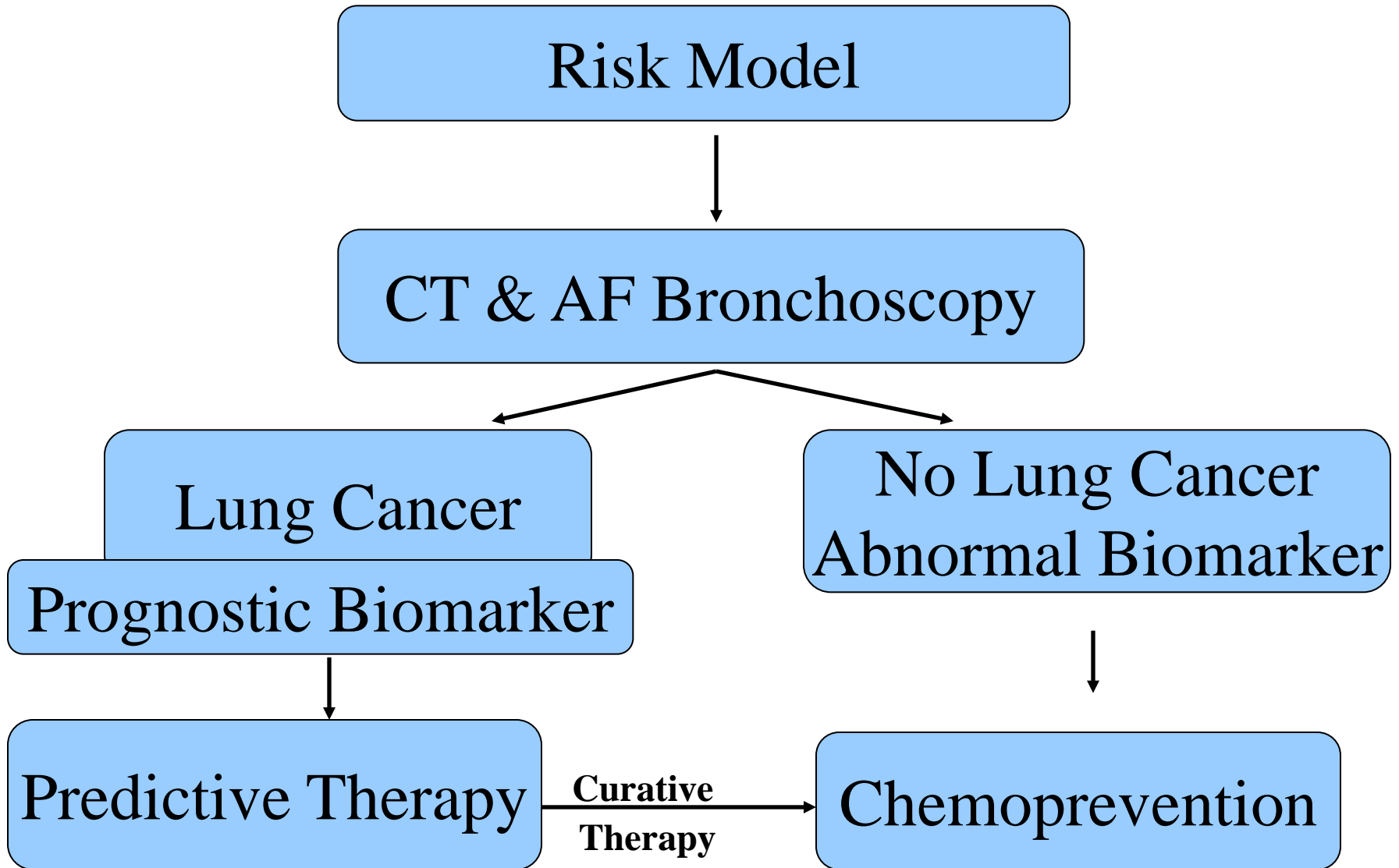
Organized Program

- A defined screening population
- An explicit policy regarding method and interval for screening
- Coordinated multi-disciplinary team approach
- Quality assurance
- Outcome evaluation

Lung Cancer Screening

- Opportunity to significantly improve outcome of patients with lung cancer
- Dual strategy of tobacco control and early detection likely the most effective
- Canadian contribution to international collaboration to better define the screening process and most cost-effective diagnostic and treatment pathways

Pan-Canadian Lung Health Study



Lung Case #2

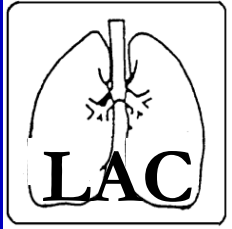
- A 58 year old dentist presents with cough and a 6 cm RLL mass.
- PET scan shows uptake in the lesion with no uptake in the mediastinum or distant sites.
- Cervical mediastinoscopy negative.
- Surgical pathology shows 6 cm squamous carcinoma with visceral pleural penetration.

Lung Case #2

- N1 lymph node stations are negative but a posterior subcarinal node is replaced with squamous cell carcinoma and there is microscopic extension beyond the capsule.
- Performance status 0 four weeks post-op.
- Blood work normal. Creatinine clearance 70 cc/minute.
- Anxious to pursue any treatment that could minimize risk of recurrence.

Lung Case #2

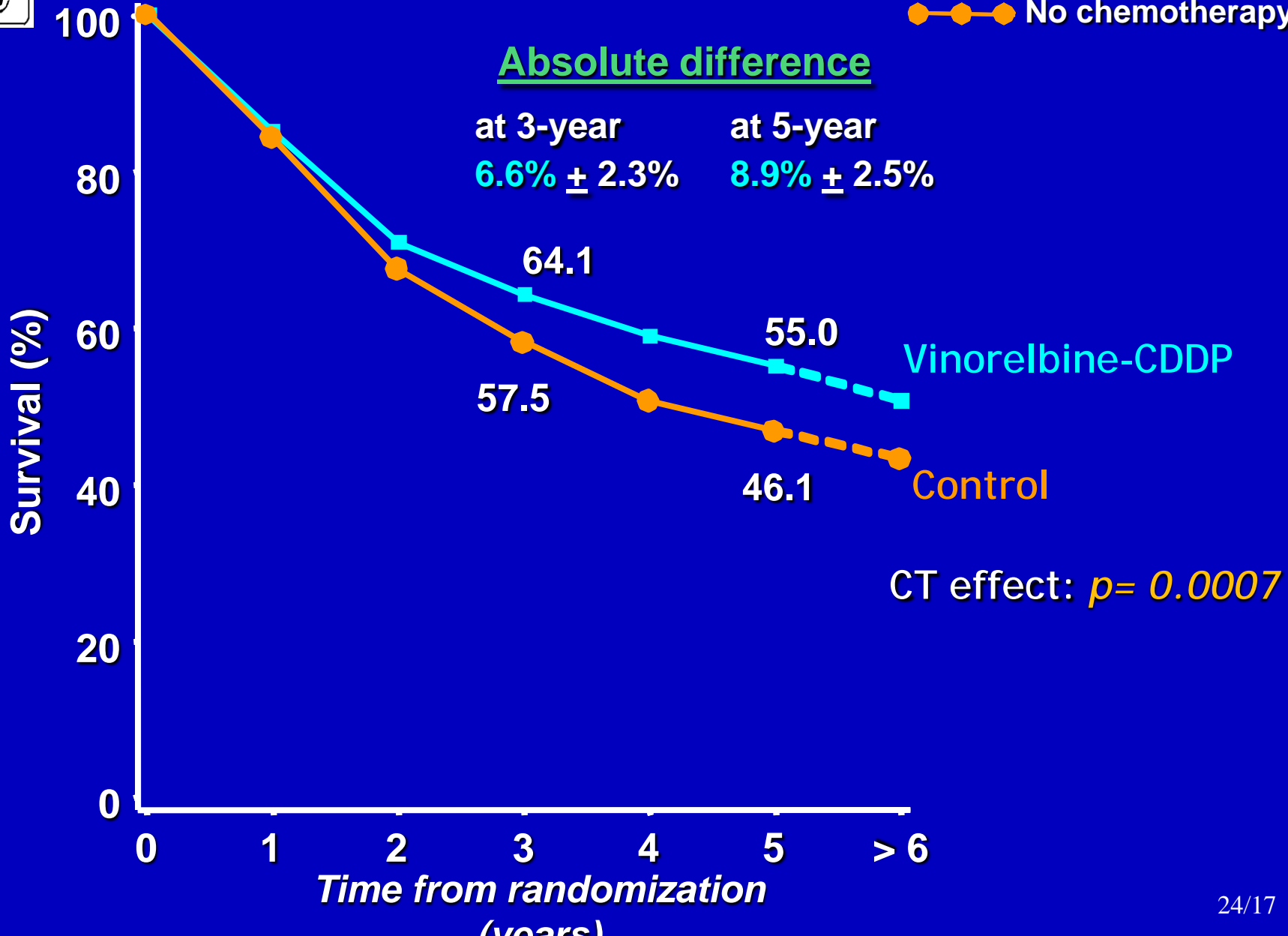
1. Estimate risk of recurrence.
2. Chemotherapy recommendation?
3. Role for post-op radiotherapy?
4. Patient is adamant that follow-up should include regular CT scans and possibly additional PET scans. Your response?

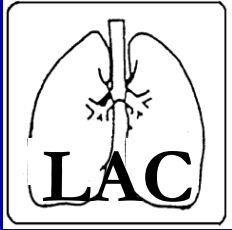


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Survival curves

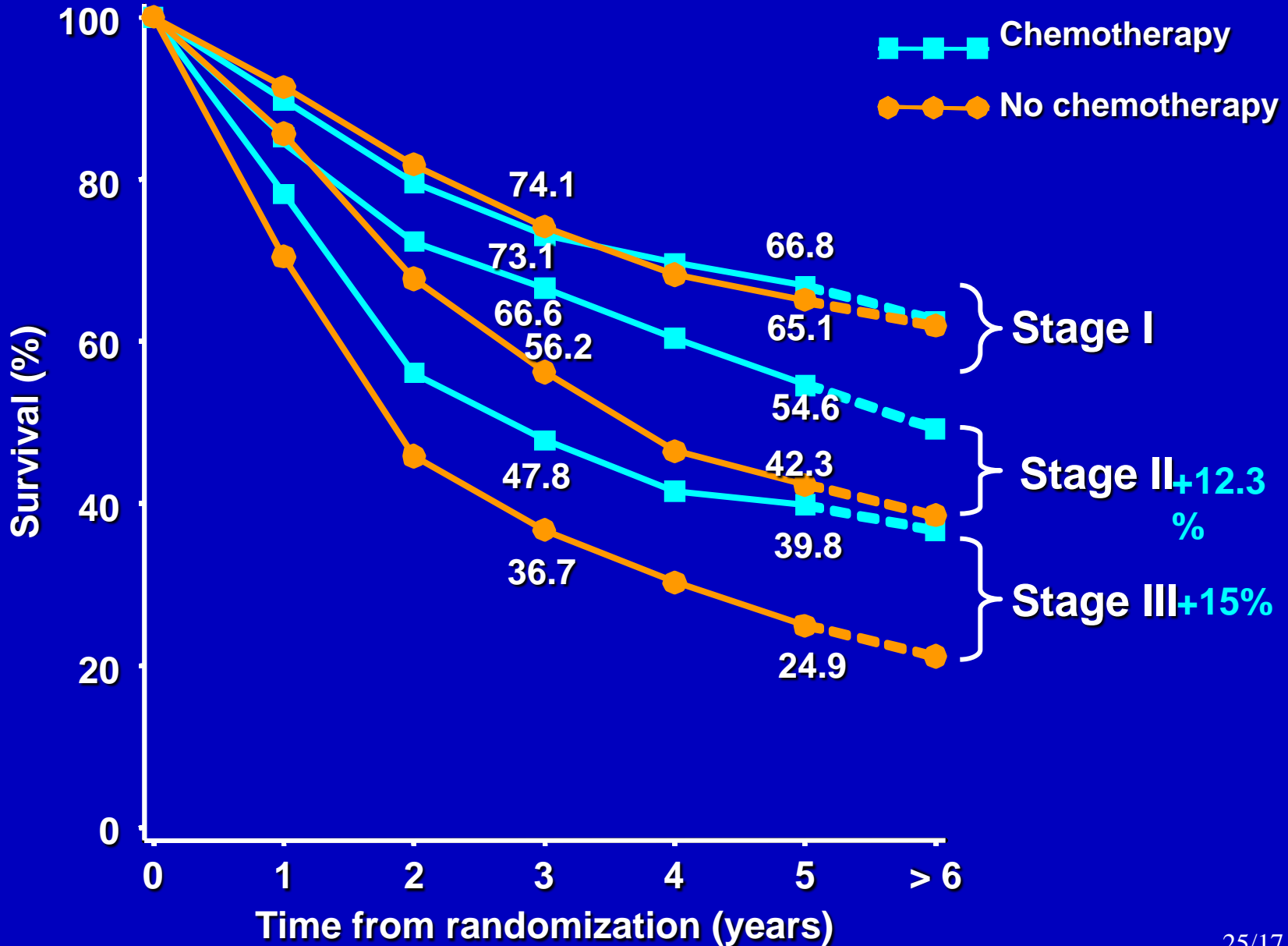
- Chemotherapy
- No chemotherapy





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CT effect and Stage



Lung Case #2

- A 53 year old woman presents with persistent cough.
- Chest X-ray: a right upper lobe (RUL) mass.
- 30 pack-year smoking history.
- Fully functional, excellent performance status (PS=1)
- No weight loss.

Lung Case #3

- Subsequent CT scan reveals a 2.8 cm RUL mass and a 2 cm precarinal (N2) lymph node.
- No other enlarged mediastinal nodes and no evidence of distant metastases.
- Fine needle aspiration (FNA) of the RUL mass discloses poorly differentiated adenocarcinoma.
- Bronchoscopy: no other lesions.
- Volumes allow “radical” thoracic irradiation.

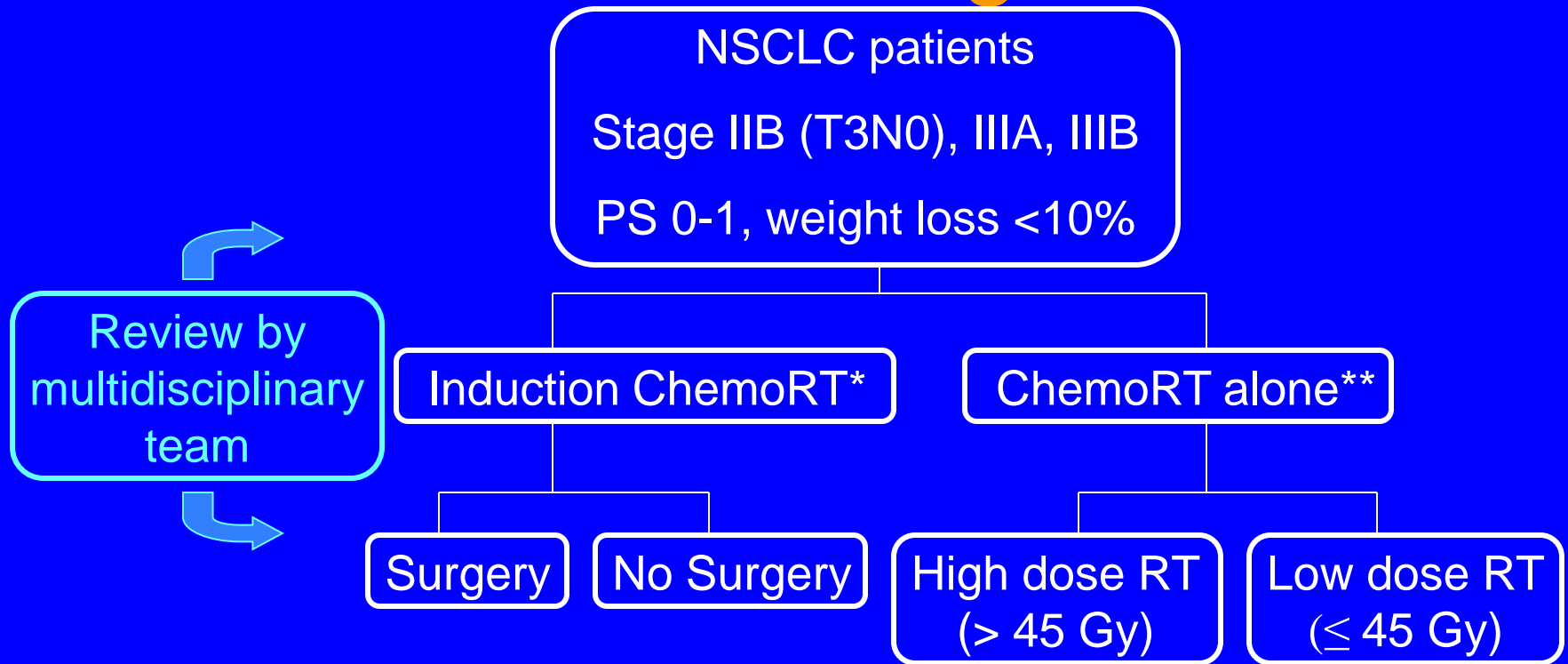
The patient undergoes **PET scan** which is positive in the RUL lung mass, shows “equivocal uptake” in the precarinal node, and no evidence of distant metastases.

Mediastinoscopy is positive for adenocarcinoma in the subcarinal node.

Lung Case #3: Recommendation

- A) Proceed to Surgical Resection
- B) Radical radiotherapy
- C) Preoperative Chemotherapy
- D) Preoperative Chemoradiotherapy
- E) Sequential Chemotherapy followed by Radiotherapy without Surgery
- F) Concurrent Chemoradiotherapy without Surgery

Treatment Algorithm



*Cisplatin 25mg/m²/day D1-3, Etoposide 100mg/m²/day D1-3 q28d x 2, q21d x 2; RT 45Gy (1.8Gy/d) D1

**Same chemotherapy with 40-61 Gy RT D1

Lung Case #4

- A 50 year old female presents with stage IV adenocarcinoma of the lung.
- Staging demonstrates an adrenal lesion and several small liver metastases.
- Brain scan is negative.
- Biochemistry and hematology are normal.
- Performance status is 1.
- Weight loss <5%.

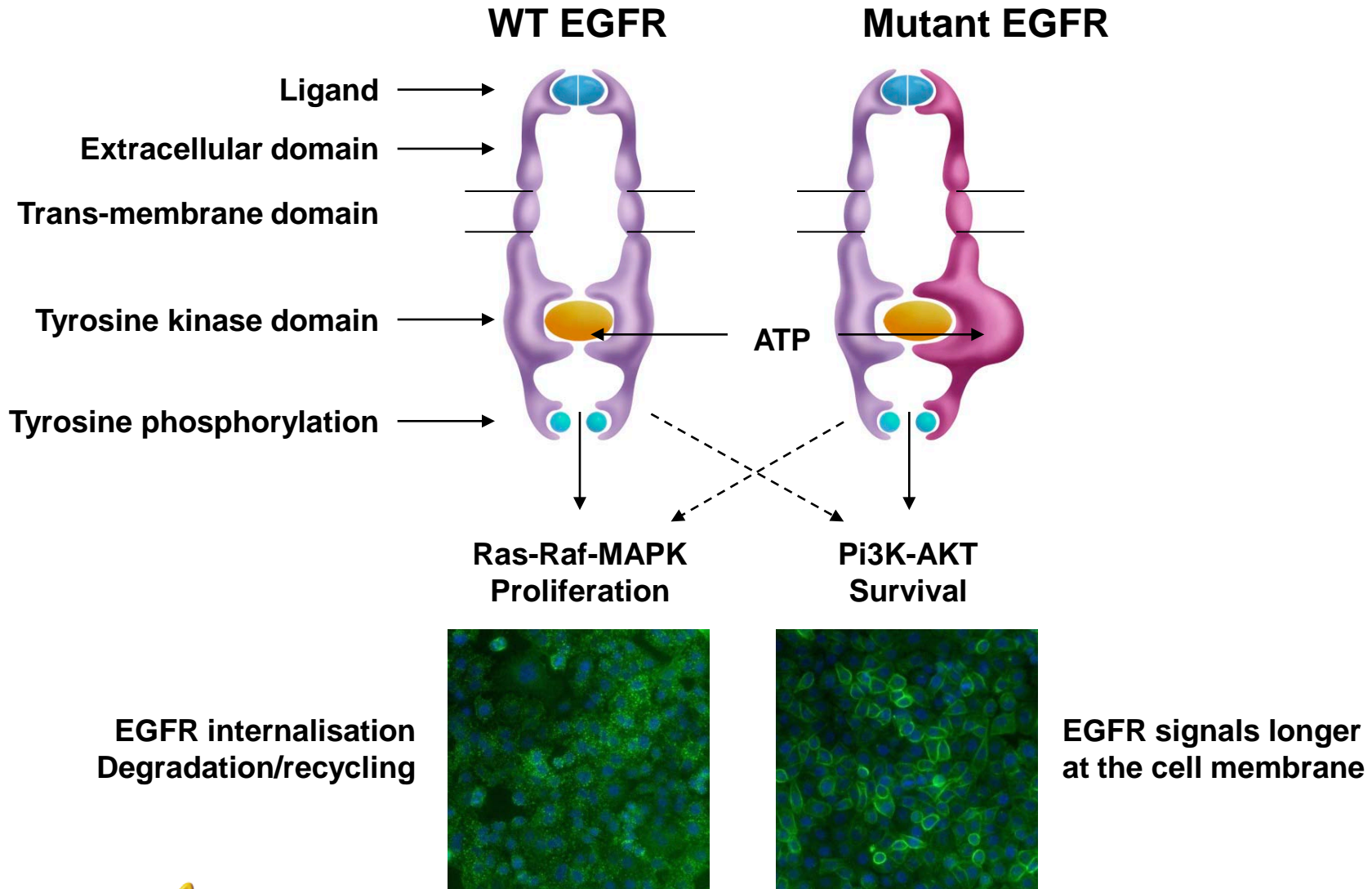
Lung Case #4

- The patient received 4 cycles of a platinum doublet and had a partial response documented on CT scan.
- Eight months after completion of chemotherapy, blood tests show a rising CEA and progression of liver metastases.
- Options?

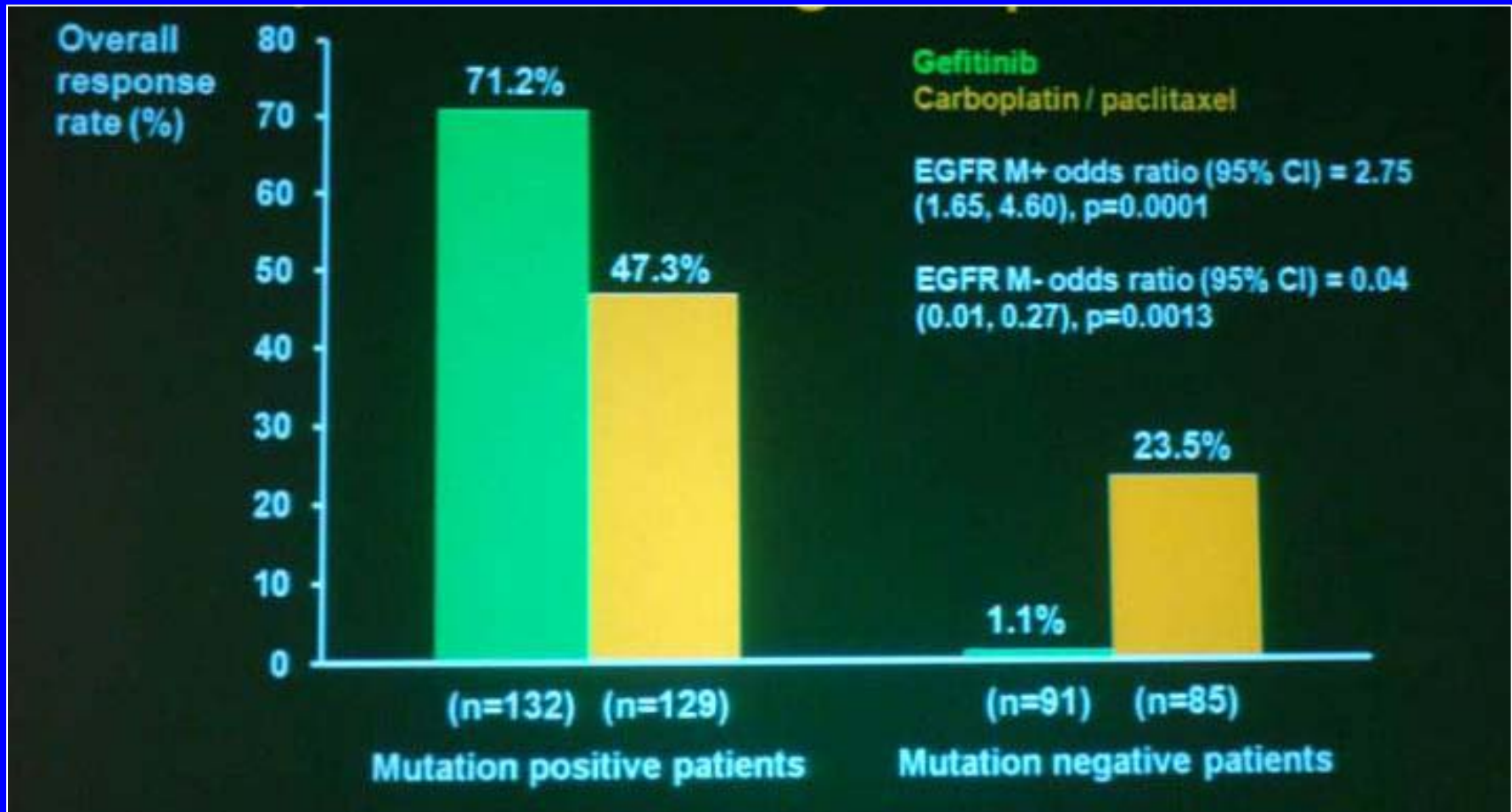
Lung Case #5

- An 82 year old Chinese lifetime non-smoking female has a history of resection of a T2N0M0 adenocarcinoma with bronchioalveolar features 18 months previously.
- A follow-up CXR now shows bilateral pulmonary nodules.
- Although elderly, this family matriarch has been in good health over the years. She certainly tolerated the surgery well and continues to drive her car several times per week.
- Recommendation?

Mutation status causes conformational change and increased activation



Objective Response Rate in EGFR Mutation Positive and Negative Patients



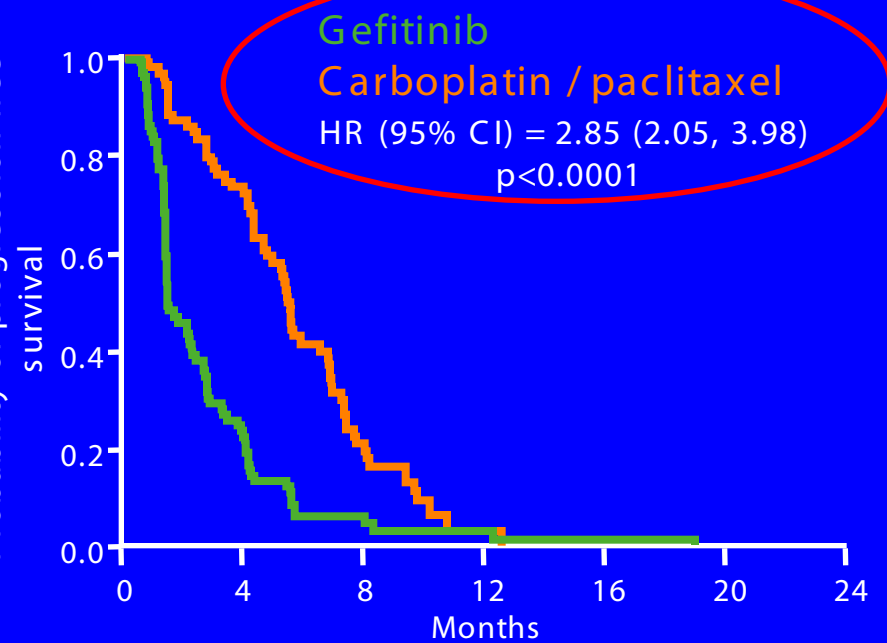
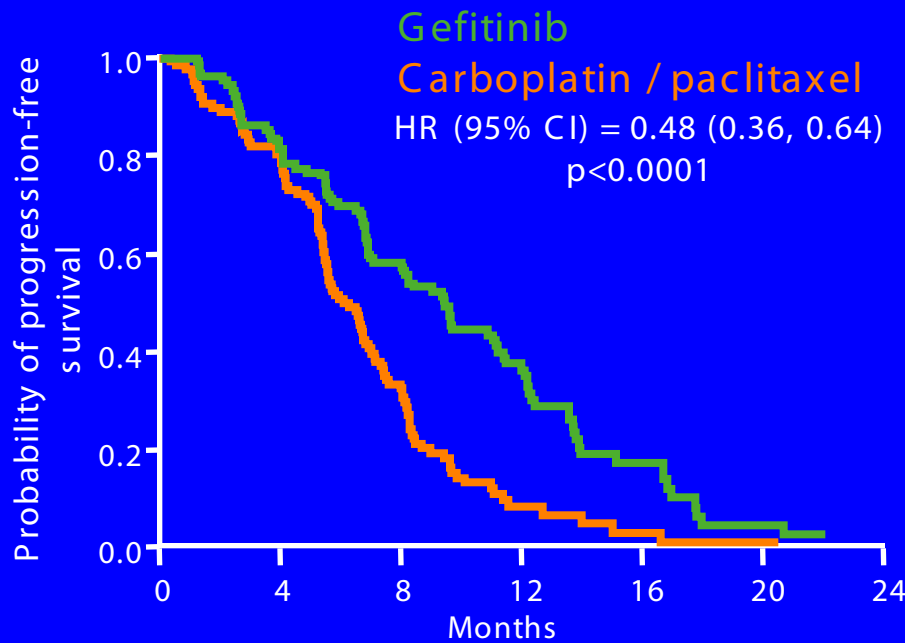
Odds ratio >1 implies greater chance of response on Gefitinib

IPASS Trial

PFS EGFR Mutation

EGFR mutation positive

EGFR mutation negative



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

Interaction test: p < 0.0001

IPASS Trial

Overall survival in ITT population

