

Case #1

F/65

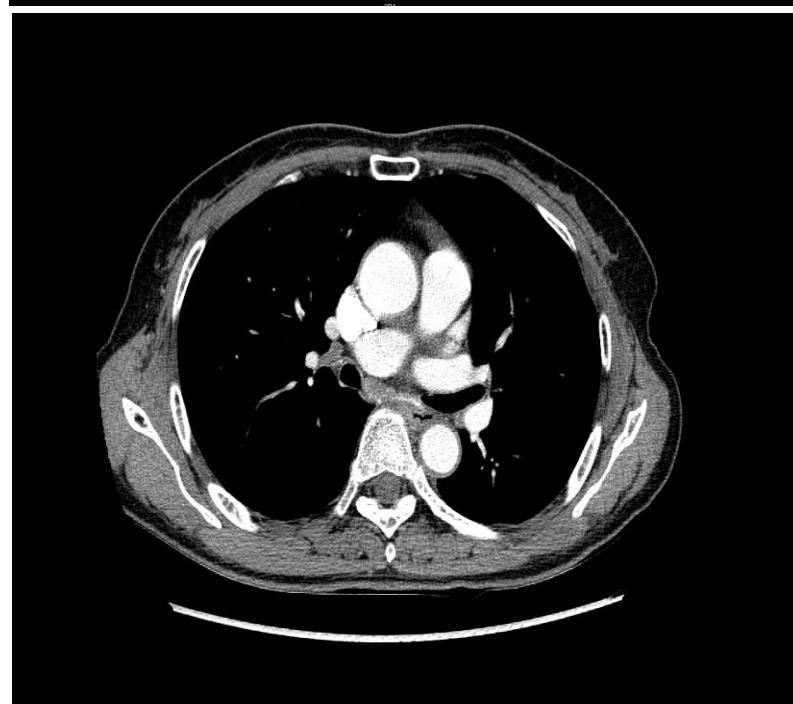
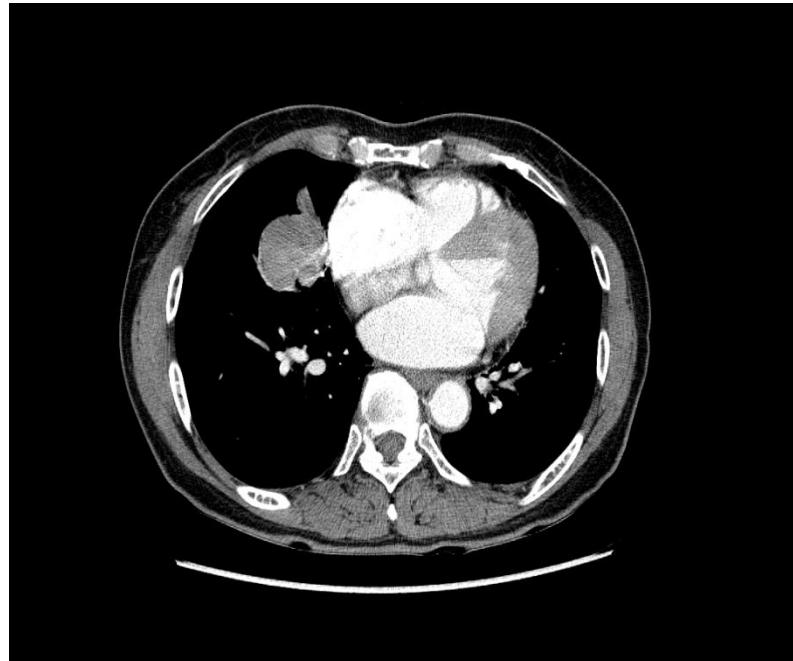
C.C: Persistent cough

onset > 1MA

Alcohol: Non-alcoholics,

Smoking: Never smoker

PMHx: DM/HT/TBc/Hepatitis (-/-/-/-)



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Bronchoscopy; Adenocarcinoma, moderately differentiated

PET-CT; LN7 - suspicious

What Next ?

- 1. Proceed to Thoracotomy**
- 2. Concurrent chemoradiotherapy**
- 3. Mediastinal nodal staging**
- 4. Chemotherapy**

VATS mediastinoscopy; LN 7 (+)
NSCLC, ADC, cT2N2M0, RML

EGFR – exon 19 deletion

Next Management Plan?

- 1. Proceed to Thoracotomy**
- 2. Neoadjuvant chemotherapy**
- 3. Concurrent chemoradiotherapy**
- 4. EGFR TKI**

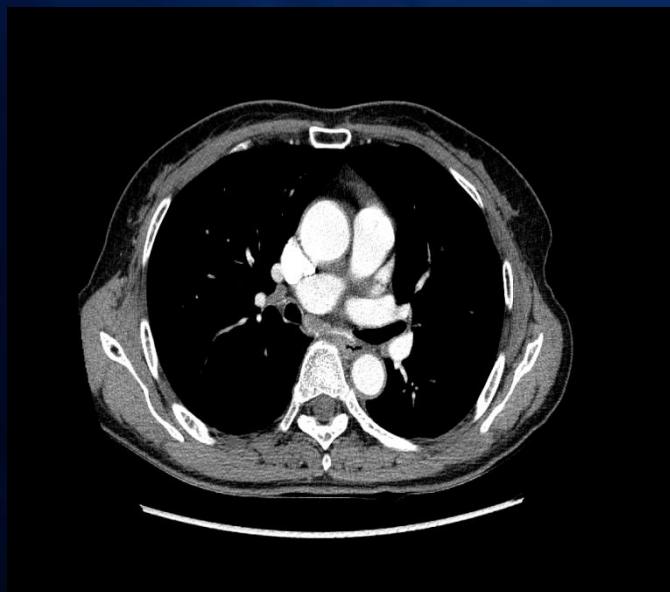
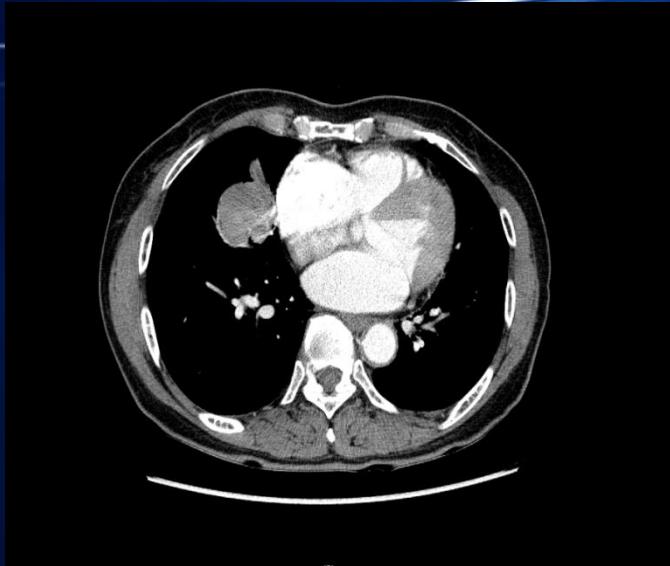
Neoadj Tarceva ; 2009.8.21-2009.10.19



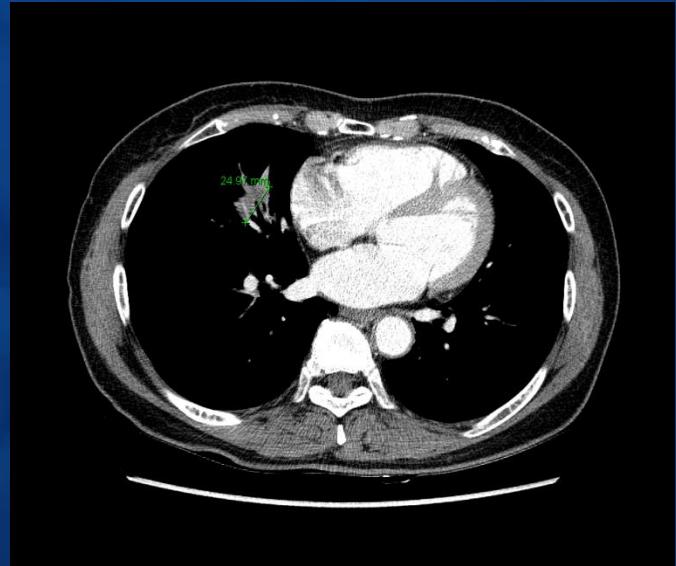
Tarceva
for 8 weeks



Neoadj Tarceva ; 2009.8.21-2009.10.19



Tarceva
for 8 weeks



CENTER

- Neoadjuvant Tarceva for 8 weeks
(2009.8.21-2009.10.19)
→ RMLobectomy with mediastinal LND
(2009.10.21)

Pathologic reports

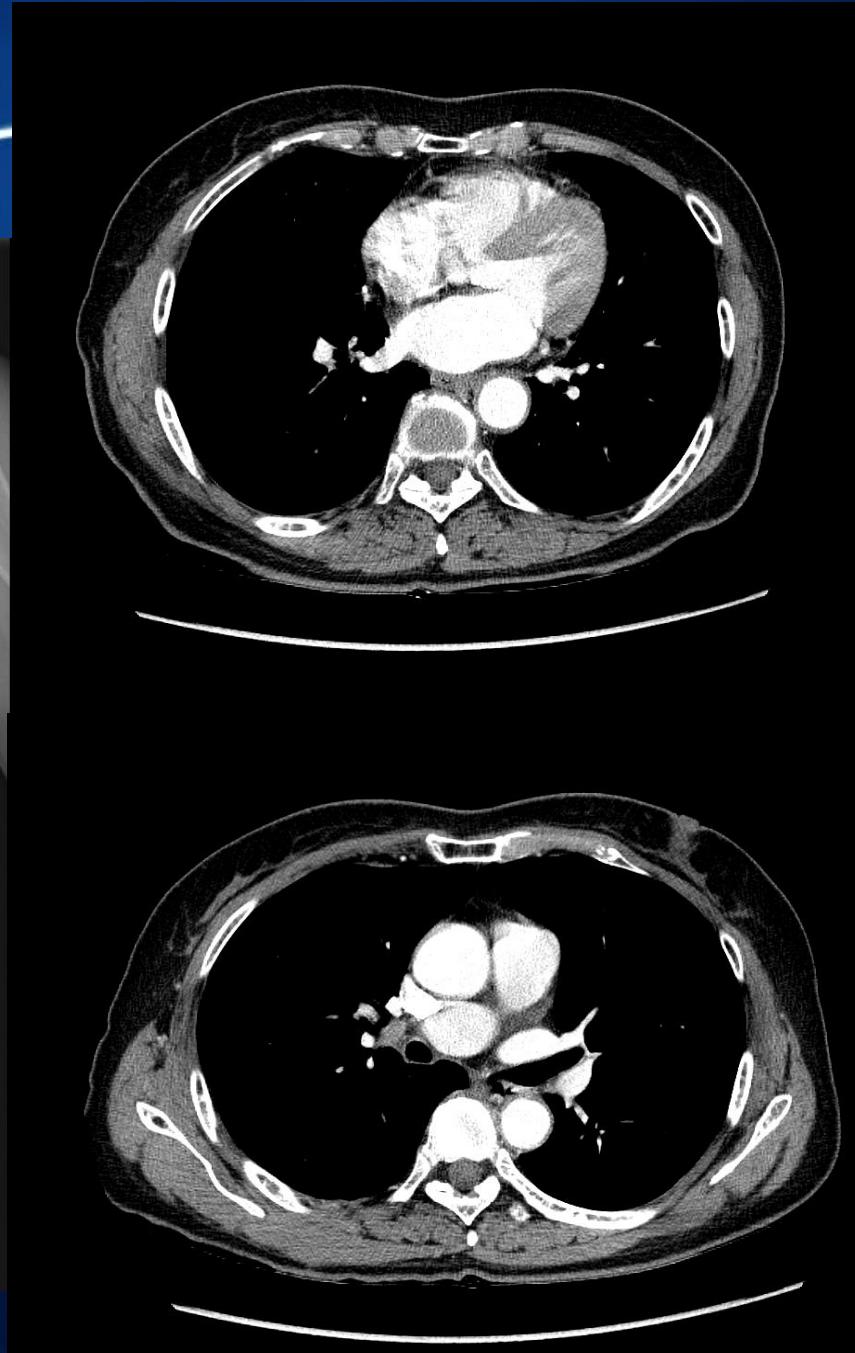
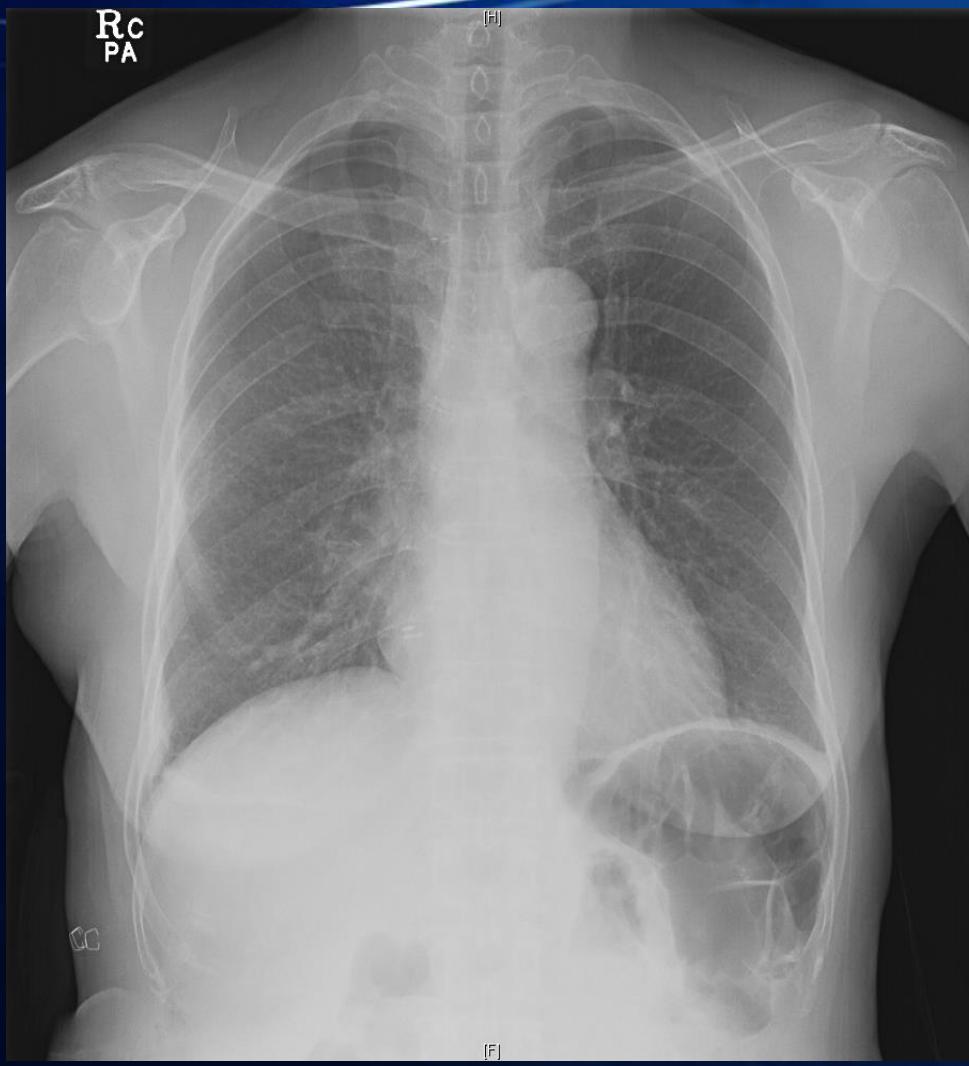
- **Lung, right middle lobe, RMLobectomy with mediastinal LN dissection**
Adenocarcinoma, moderately differentiated, mixed acinar and BAC pattern
lateral segment

- (1) **Size: 4x3x1.5cm**, invasive carcinoma (1.1cm in diameter)
(tumor volume 50%; fibrosis 30%; necrosis and calcification 20%)
- (2) Vascular invasion (arteriolar or venous): not identified
- (3) Lymphatic invasion: not identified
- (4) Perineural invasion: not identified
- (5) Margins Bronchial 1.2cm
- (6) Pleural/extrapleural : tumor located within the lung parenchyma (PLO)
- (7) Lymph nodes included in main specimen
 - a. Total number examined 6
 - b. **Number involved by tumor 0**

Soft tissue labeled " LN 7", biopsy :

- . Dense collagenous tissue with foreign body granuloma (no residual tumor)
- **ypT2N0M0 ;**

Image (post-Op)

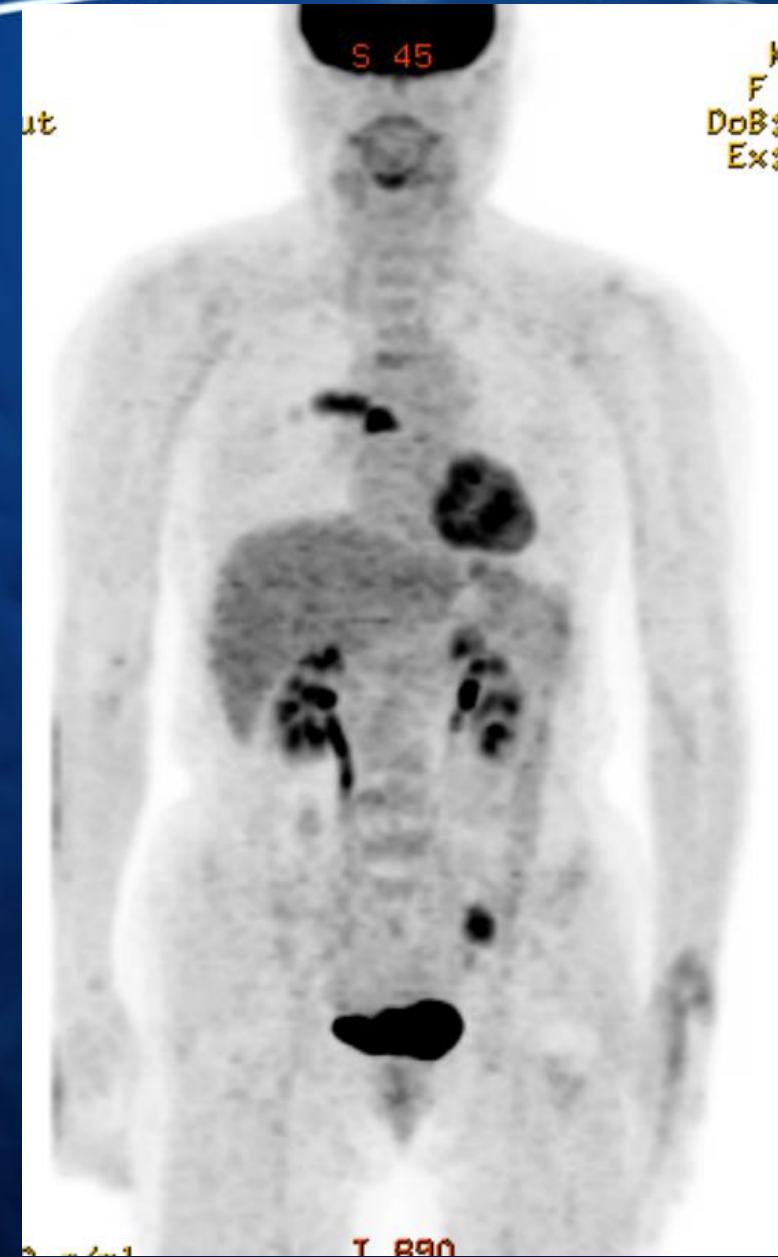
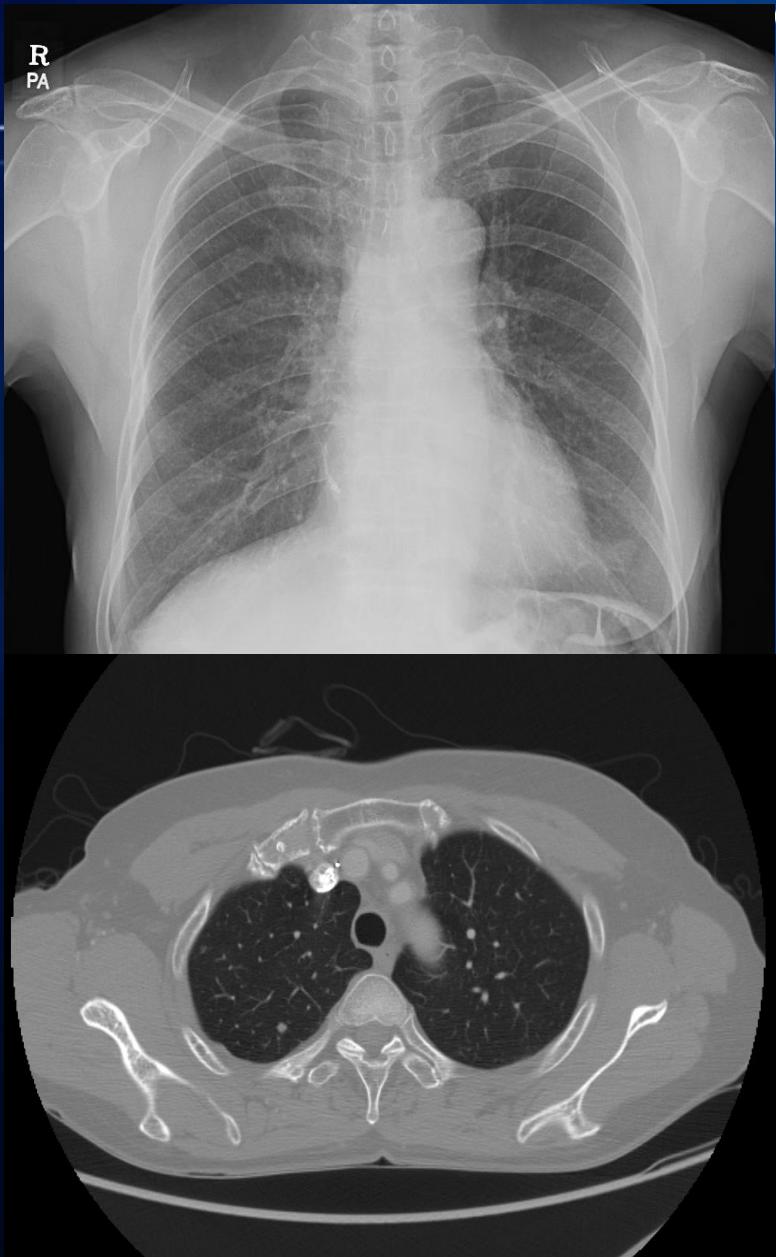


Next Management Plan?

- 1. Observation**
- 2. Adjuvant radiotherapy**
- 3. Adjuvant chemotherapy**
- 4. Adjuvant chemoradiotherapy**
- 5. Adjuvant EGFR TKI**

- Neoadjuvant Tarceva for 8 weeks
(2009.8.21-2009.10.19)
 - RMLobectomy with mediastinal LND
(2009.10.21)
 - Adjuvant Taxol/Carbo x 4
(2009.11.11-2010.1.19)

2011. 8 ; Pelvic pain for 2 months



2011. 8 ; Pelvic pain for 2 months

- Recurrence with
lung-to-lung metastasis
bone mets; T6 vertebra,
left iliac bone metastasis
s/p palliative RT 30Gy (2011.8.10-8.19)
- Palliative Gefitinib (2011.9.29-
--> PR > 4 years

Tumor Response and Toxicity of Neoadjuvant Erlotinib in Patients With Early-Stage Non-Small-Cell Lung Cancer

Table 3. Tumor Response According to Study Design (N = 60)

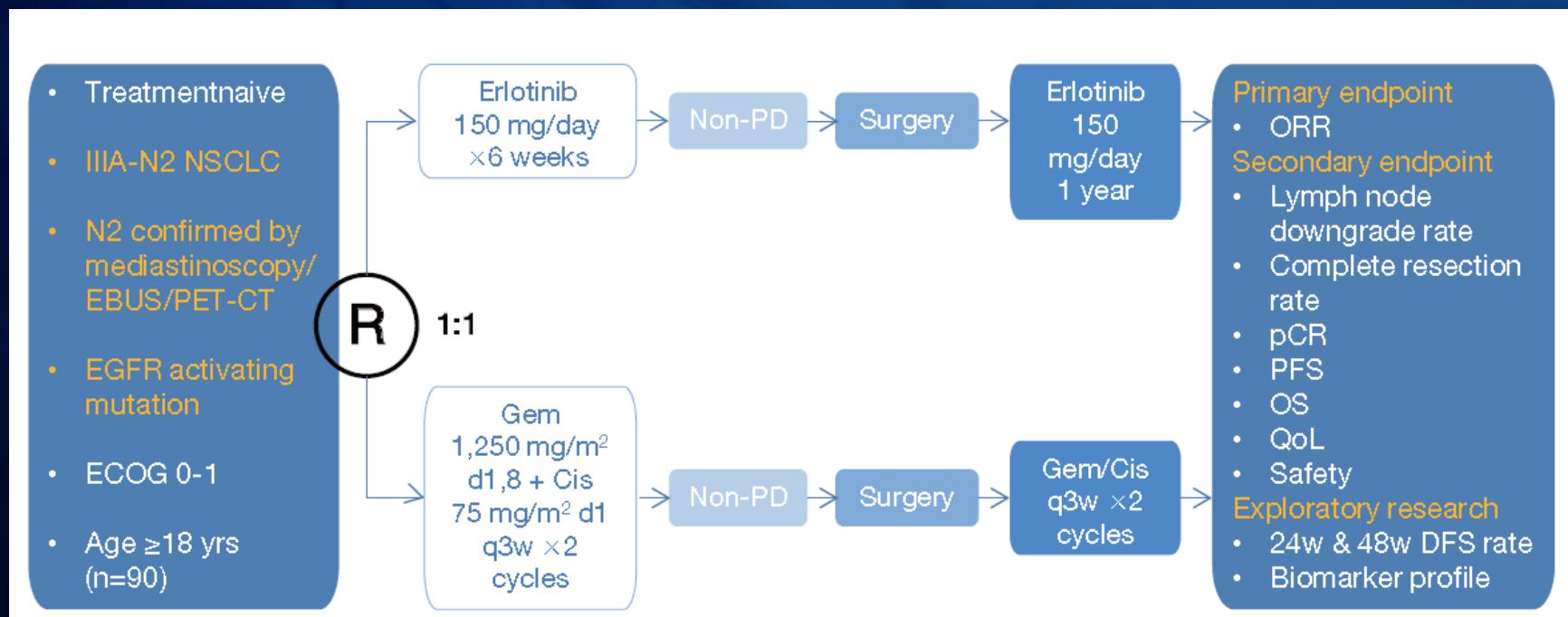
Response	Total Population		Enriched Population		Unselected Population	
	No. (N = 60)	% or Range	No. (n = 29)	% or Range	No. (n = 31)	% or Range
Median erlotinib treatment, days	20	3 to 28	20	3 to 28	19	8 to 26
Median follow-up, months	30	3 to 58	36	5 to 58	24	3 to 52
Median change SUV _{max} , % (n = 59)	-10	-78 to 76	-20	-78 to 43	0.7	-56 to 76
Metabolic response, EORTC criteria						
PR	16	27	10	34	6	20
SD	36	61	16	55	20	66
PD	7	12	3	10	4	13
Median change in tumor size, mm (n = 59)	0.7	-10 to 16	0.5	-10 to 16	0.9	-8 to 10
Radiologic response, RECIST criteria						
PR	3	5	3	10	0	0
SD	54	92	24	83	30	100
PD	2	3	2	7	0	0
Pathologic evaluation (n = 56)						
Median % necrosis	29	0 to 97	40	0 to 97	18	0 to 60
> 50% necrosis	14	23	11	38	3	10
< 50% necrosis	42	70	18	62	24	77
No resection	4	7	0	0	4	13

Tumor Response and Toxicity of Neoadjuvant Erlotinib in Patients With Early-Stage Non-Small-Cell Lung Cancer

Table 4. Tumor Response According to Mutation Status (n = 54)

Response	EGFR Mutated		KRAS Mutated		Double Wild-Type	
	No. (n = 7)	% or Range	No. (n = 12)	% or Range	No. (n = 35)	% or Range
Median erlotinib treatment, days	21	13 to 27	19	11 to 26	19	8 to 28
Median follow-up, months	35	7 to 54	26	3 to 45	29	7 to 58
Median change SUV _{max} , %	-40	-78 to 17	-7	-45 to 24	-3	-66 to 74
Metabolic response, EORTC criteria						
PR	4	57	2	17	8	23
SD	2	28	10	83	20	57
PD	0	0	0	0	7	20
Median change in tumor size, mm	-5	-8 to 1	2	-2 to 16	0	-10 to 11
Radiologic response, RECIST criteria						
PR	2	28	0	0	1	3
SD	4	57	11	92	33	94
PD	0	0	1	8	1	3
Pathologic evaluation						
Median % necrosis	46	0 to 97	29	0 to 60	26	0 to 95
> 50% necrosis	3	43	3	25	8	23
< 50% necrosis	4	57	9	75	24	69
No resection	0	0	0	0	3	8

CTONG1103 (EMERGING)



Reported trials of neoadjuvant and adjuvant therapy

Trials	Delete column, use ref #	Study design	Stage and/or pathologic type	NAd	Ad	N	2-year DFS	Median DFS	2-year OS	Median OS
Gold KA	WCLC	II	Stage IB-III NSCLC	DOC + DDP x3 cycles	Erlotinib x1 year	46				
Rizvi NA	Clin Cancer Res	II	Stage I or II NSCLC (T1-2 N0-1 or T3N0M0); adenocarcinoma	Gefitinib x21 days	Gefitinib x2 years (EGFR mutation+ or with effective neoadjuvant therapy)	21	95%	NR		
					None (patients without effective neoadjuvant therapy)	29	78%	NR		
Janjigian YY	JTO	Re	Stage I-III; adenocarcinoma with EGFR 19 or 21 exon mutations	21 cases: Gefitinib x21 days	G/E (median medication time: 24 months)	56	89%		96%	
					None	111	72%		90%	
D'Angelo SP	JTO	Re	Stage I-III NSCLC; adenocarcinoma with 19-exon and 21-exon (L858R) mutation @@	G/E neoadjuvant therapy x21 days	G/E x2 years	84@				
Waterhouse DM##	ASCO07035	II	Staging IB-IIIA* NSCLC; any pathological types	None	CBP (AUC =5) + DOC + BEV day 1, q21d x4 cycles; then BEV day 1 + E q21d x8 cycles	54	1-year DFS: 78%	2-year DFS: 77.6%	3-year OS: 81%	
					CBP (AUC =5) + DOC day 1, q21d x4 cycles	52	88%	86.8%	63%	
BR19	JCO	III	Staging IB/II/IIIA NSCLC	None	G x2 years	251		4.2 years		5.1 years
					Placebo x2 years	252		NR		NR
Wang SY	ASCO 7519	II	Staging IIIA-N2 NSCLC; (19-exon deficiency or L858R point-mutation)	None	PEM + CBP (AUC =5) q3w x4 cycles; then G, 6 months	30	78.9%	39.8 months	92.4% months	41.6 months
					PEM + CBP (AUC =5) q3w x4 cycles; without G	30	54.2%	27.0 months	77.4% months	32.6 months
Waterhouse		II	Randomized	Maintenance treatment	Arm A: BEV + erlotinib, q21d x8 cycles	54		1-year DFS: 78%	3-year OS: 81%	
					Arm B: CBP (AUC5) + DOC, q3w x4 cycles	52		88%	63%	
				Induction treatment: CBP AUC5, DOC, BEV, q21d x4 cycles						

Ongoing trials of TKI adjuvant therapy

Trials	Registration number	Phase	Stage	Selected patients	N	NAd	Ad	Medication time	Primary endpoint	Secondary endpoint	Study start time	Estimated study completion date	Primary completion time	Reports about data
RADIANT	NCT00373425	III	IB-IIIA	EGFR-positive by various tests (IHC and/or FISH)	1,252	None	Erlotinib* vs. placebo*	2 years	DFS	OS; DFS and OS in EGFR mutation+; AEs	2006.9	2016.6	2013.4	2009 ASCO7520; 2014 ASCO7501, 7513
SELECT	NCT00567359	II	IA-IIIA	NSCLC; complete resection; EGFR mutation+; PS 0-2	100	Erlotinib (single arm)	None	28 days before surgeries	2-year DFS	Safety, OS	2006.5	2015.6	2014.5	2010 ASCO 7078; 2012 ASCO7010; 2014 ASCO7514
WJOG6410L		III	II-III	19, L858R mutation+; without T790M mutation	230	None	Gefitinib 250 mg/day vs. NVB + DDP	2 years vs. 4 cycles	DFS	OS, safety, patterns of recurrence	2011.9	3 years of enrolment and 5 years of following up	2012 ASCO TPS7110	
ADJUVANT	NCT01405079	III	II-IIIA	Completely resected (N1-N2) pathological NSCLC with EGFR exon 19 deletions and exon 21 L858R activating mutation; PS 0-1	220	None	Gefitinib vs. NVB + Cis	2 years vs. 4 cycles	DFS	OS, 3-year DFS, 5-year DFS/OS, safety, QoL, AE	2011.7	2018.8	2016.8	
ML28280	NCT01683175	II	IIIA	19, L858R mutation+	94	None	Erlotinib vs. NVB + Cis	2 years vs. 4 cycles	2-year DFS	DFS, OS, safety, QoL, AE, SAE	2012.8	2019.3	2019.3	