International Association for the Study of Lung Cancer

IASLC

IASLC 15th World Conference on Lung Cancer

October 27 – October 30, 2013
Sydney, Australia

WCLC.IASLC.ORG

Welcome to WCLC 2013!

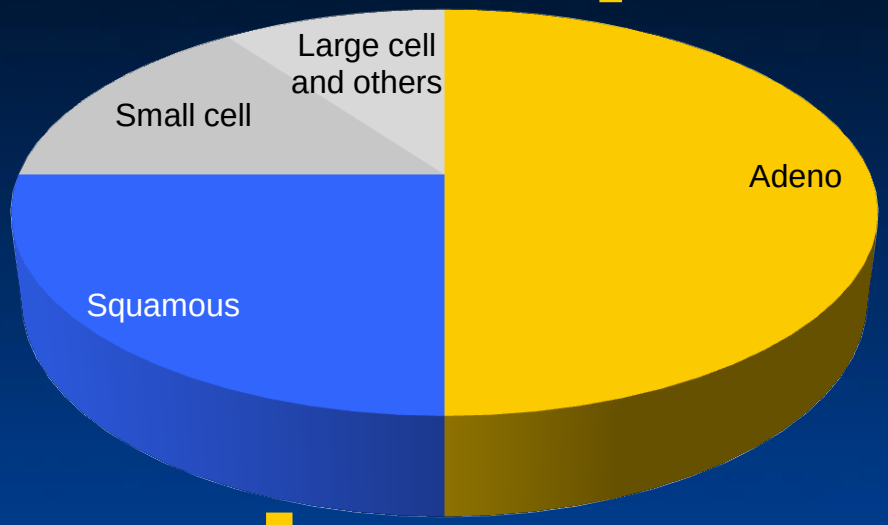
NEXT-GENERATION LUNG CANCER CARE

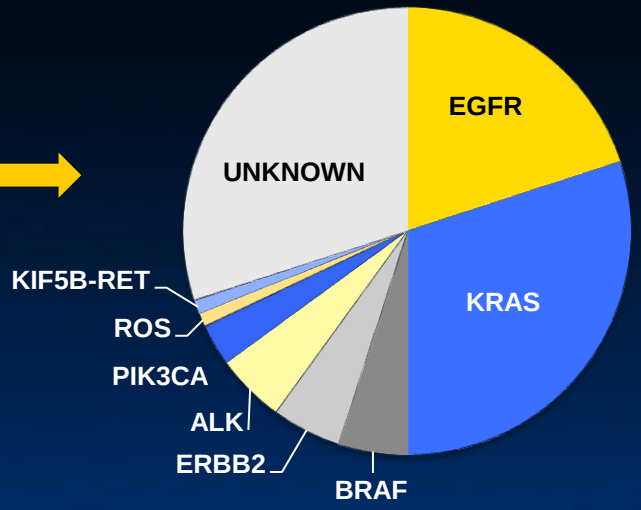
WCLC

Akciğer Kanserinde Yeni Gelişmeler

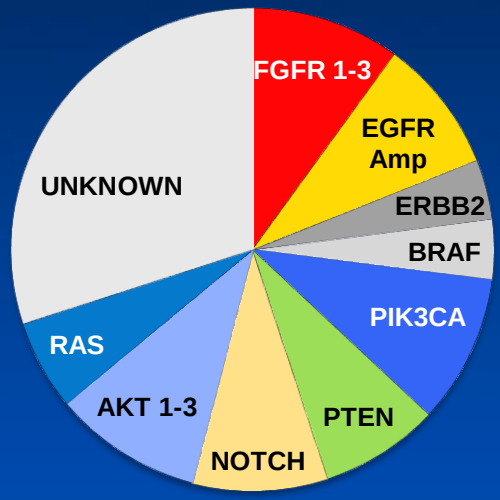
Prof Dr Nil MOLİNAS MANDEL

Large panels of genes will be routinely tested in the future





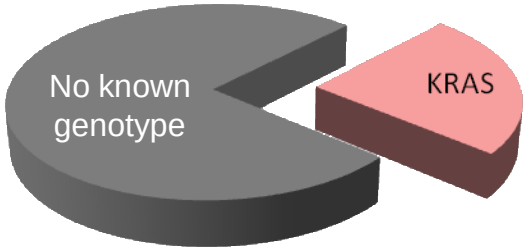
ADC



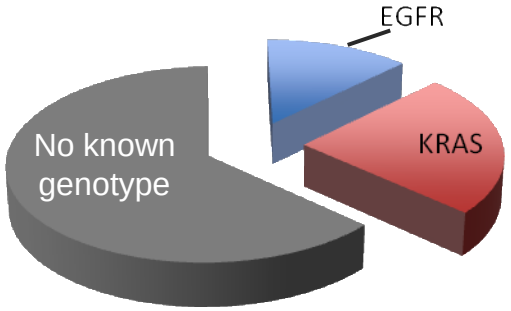
SQCC

TISSUE IS THE ISSUE!

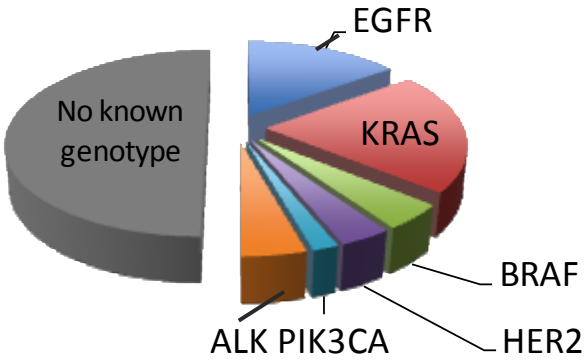
Discovery of genomic alterations in lung adenocarcinoma



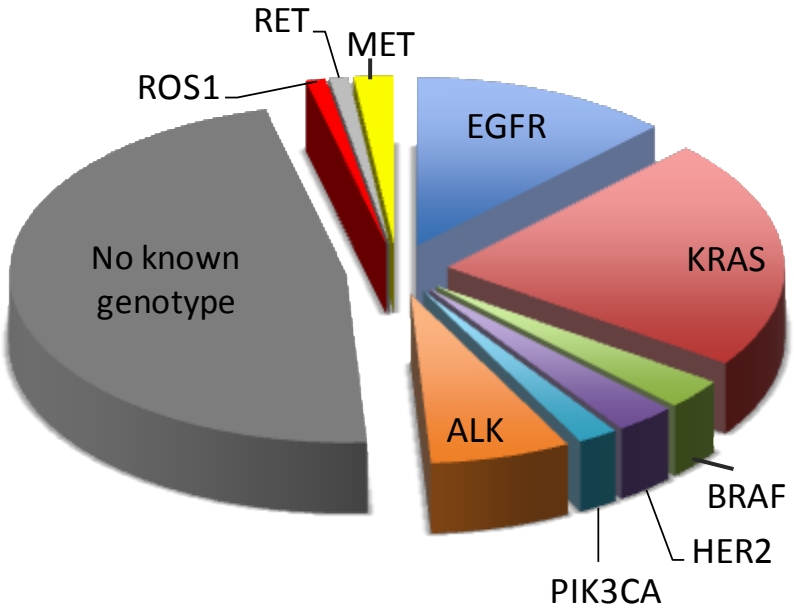
1984–2003



2004



2009



2013

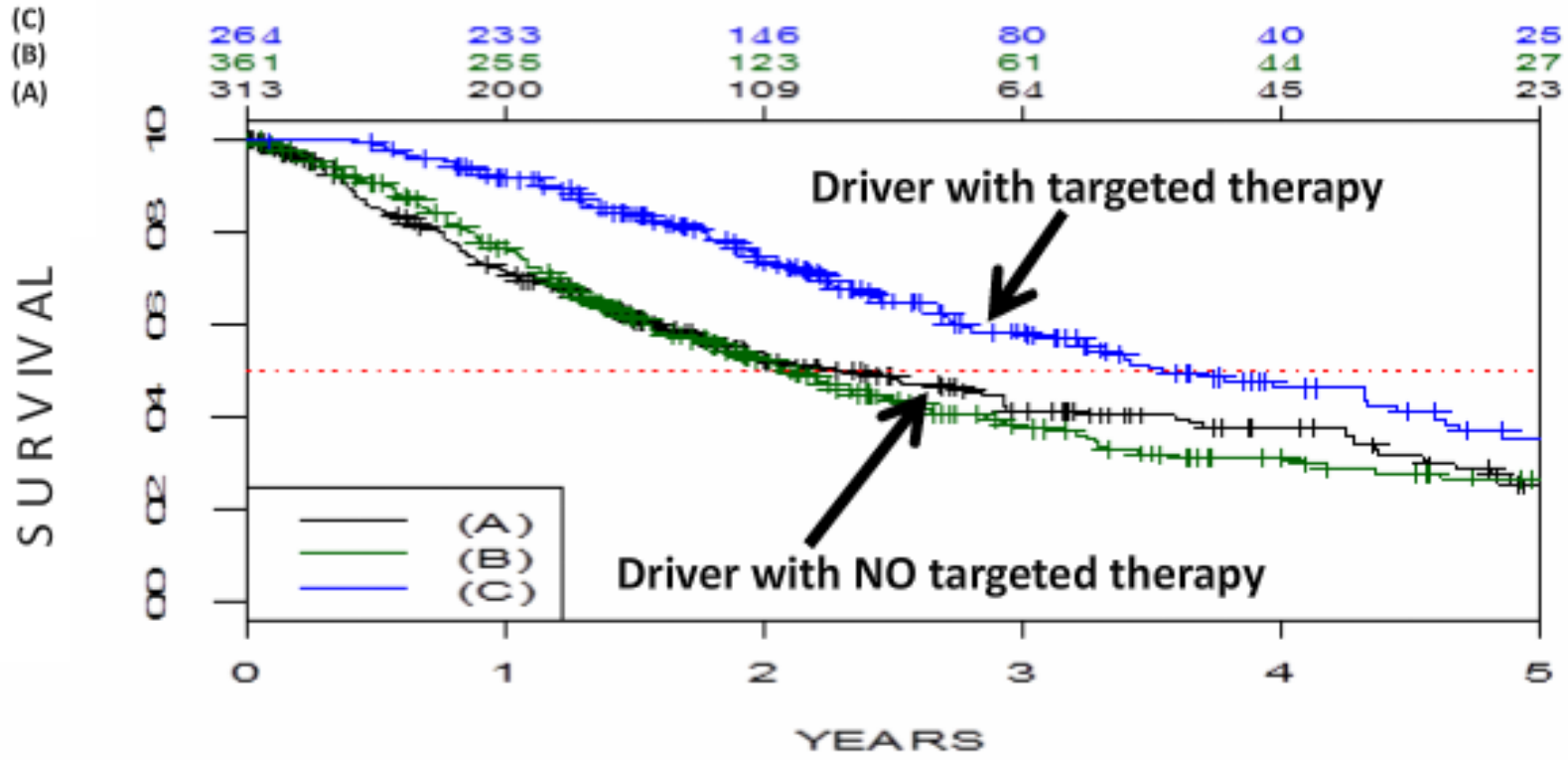
EGFR TKI as standard first-line therapy for patients with *EGFR*-mut NSCLC

Study	Drug	n (*EGFR* mutation+)	RR (TKI vs chemotherapy), %	Median PFS (months)
IPASS[1]	Gefitinib	132	**71.2** vs 47.3	9.8 vs 3.4
First-SIGNAL[2]	Gefitinib	26	**84.6** vs 37.5	8.0 vs 6.3
WJTOG 3405[3]	Gefitinib	86	**62.1** vs 32.2	9.2 vs 6.3
NEJGSG002[4]	Gefitinib	114	**73.7** vs 30.7	10.8 vs 5.4
EURTAC[5]	Erlotinib	86	**58.0** vs 15.0	9.7 vs 5.2
OPTIMAL[6]	Erlotinib	82	**83.0** vs 36.0	13.1 vs 4.6
LUX-Lung 3[7]	Afatinib	230	**56.1** vs 22.6	11.1 vs 6.9

1. Mok TS, et al. N Engl J Med 2009;361:947–57; 2. Han J-Y, et al. J Clin Oncol 2012;30:1122–8;
3. Mitsudomi T, et al. Lancet Oncol 2010;11:121–8; 4. Maemondo M, et al. N Engl J Med 2010;362:2380–8;
5. Rosell R, et al. Lancet Oncol 2012;13:239–46; 6. Zhou C, et al. Lancet Oncology 2011;12:735–42;
7. Sequist LV, et al. J Clin Oncol 2013;31:3327–34

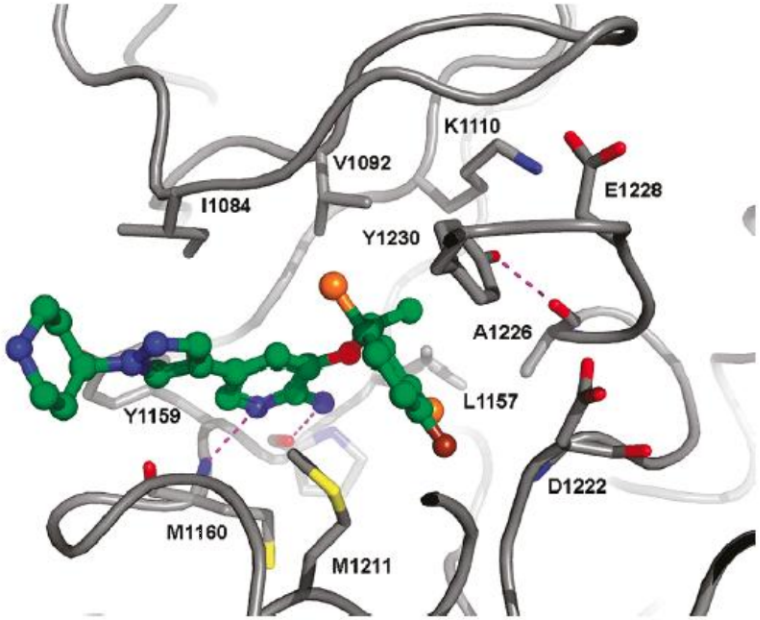
n = patients assigned to a TKI

Survival of Patients with Drivers: Targeted Therapy vs No Targeted Therapy



Group	N	Median Survival (95% CI)
Driver, no targeted therapy (A)	313	2.4 years (1.8 to 2.9)
No driver (B)	361	2.1 years (1.8 to 2.5)
Driver, targeted therapy (C)	264	3.5 years (3.2 to 4.6)

Crizotinib: A small molecule tyrosine kinase inhibitor of c-MET, ALK and ROS1



Co-crystal structure of crizotinib bound to c-MET

Kinase	IC_{50} (nM) mean*	Selectivity ratio
c-MET	**8**	**–**
ALK	40-60	5-8X
ROS1	**60**	**7X**
RON	80	10X
Axl	294	34X
	322	37X
Tie-2	448	52X
Trk A	580	67X
Trk B	399	46X
Abl	1,159	166X
IRK	2,887	334X
Lck	2,741	283X
Sky	>10,000	>1,000X
VEGFR2	>10,000	>1,000X
PDGFRβ	>10,000	>1,000X

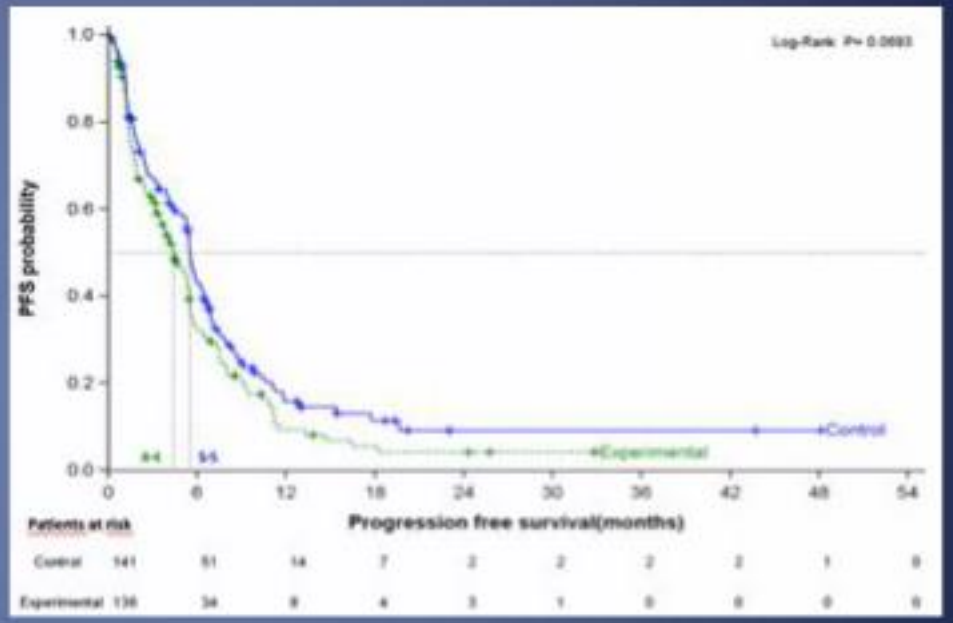
Mini oral presentation by Dr Ou at WCLC 2013:
Programme number: MO07.03
Targeted therapies II, Bayside Auditorium B
Monday October 28th; 4:15 pm–5:45 pm

Cui JJ, et al. J Med Chem 2011;54:6342-63; Pfizer data on file

Customized Chemotherapy

Treatment assignment based on BRCA-1 and RAP80 mRNA level

- Advanced NSCLC
- Customized chemotherapy versus standard therapy
- N=279 patients
- Chemotherapy regimens
  - Cisplatin, docetaxel
  - Cisplatin, Gemcitabine
  - Docetaxel alone

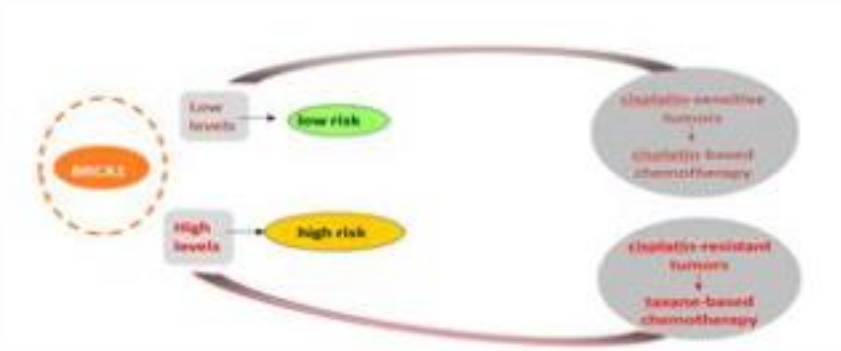


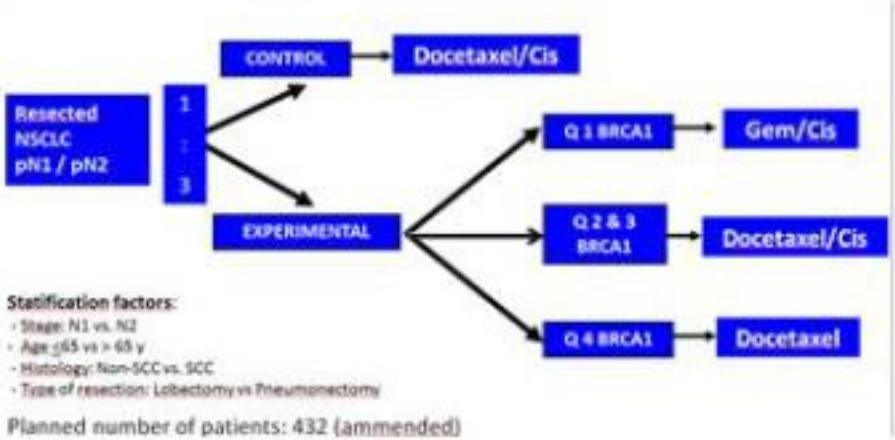
"Detrimental effect in the experimental arm"

Rosell et al, Abstract O15.02

First analysis of toxicity and treament compliance in customized postoperative chemotherapy based on BRCA1 levels after NSCLC resection: SCAT (Spanish Customized Adjuvant Therapy) trial. Spanish Lung Cancer Group/GECP

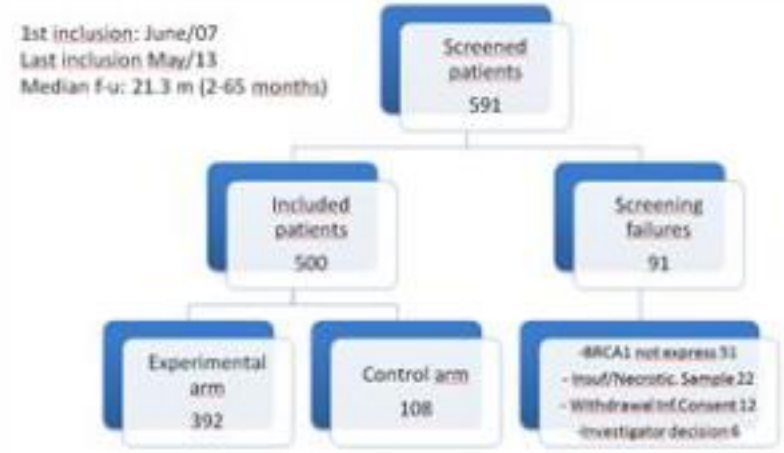
- Attempt to optimize currently available chemotherapy.
- Hypothesis: BRCA1 modulates platinum sensitivity.
  - Low levels: plat sensitive
  - Intermediate: combine with taxane
  - High levels: non-platinum

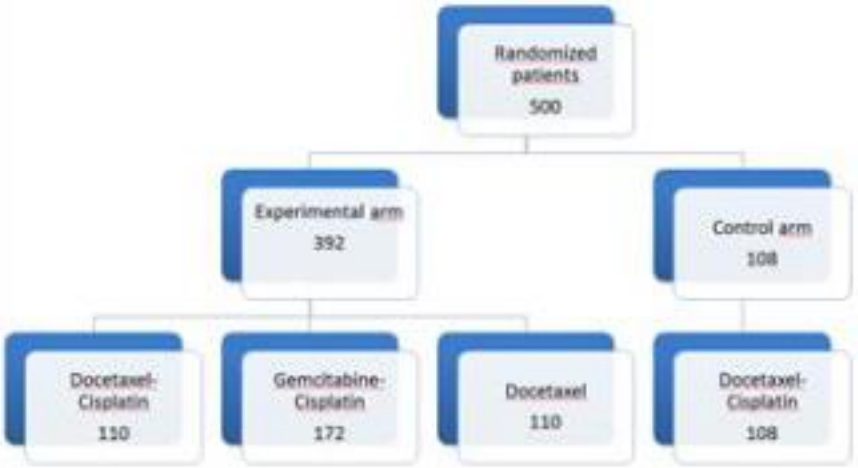




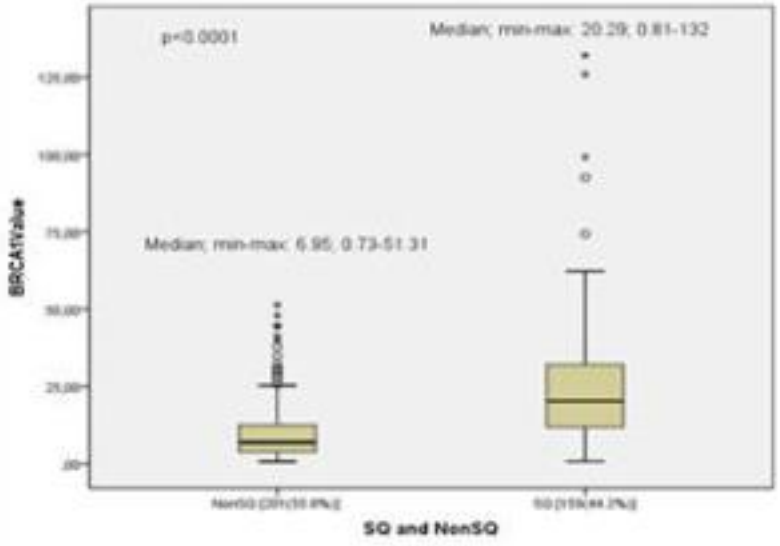
MO08.01 Massuti

Results





- Feasibility established
- Lower BRCA1 levels for nonsquamous vs. squamous
- More toxicity for CDDP/Docetaxel



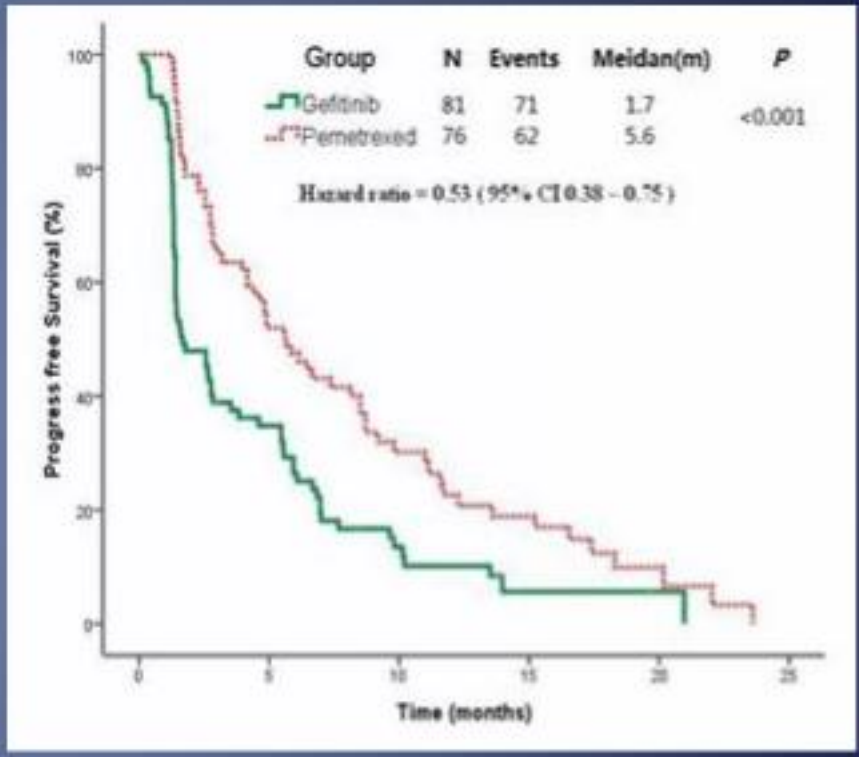
Customized Chemotherapy: Should it be Part of Standard Practice?

- No Survival benefit with ERCC1 and RRM1 based treatment assignment
  - Bepler et al, ASCO 2013
- French adjuvant trial was discontinued due to unreliability of ERCC1 assay
  - Soria et al, ASCO 2013
- Presently there is no role for routine testing for ERCC1, RRM1 or TS for selection of chemotherapy

Optimal Salvage Therapy for Wt-EGFR

Advanced NSCLC
Prior Platinum-based therapy
EGFR-Wt

- Pemetrexed N=81
- Gefitinib N=76



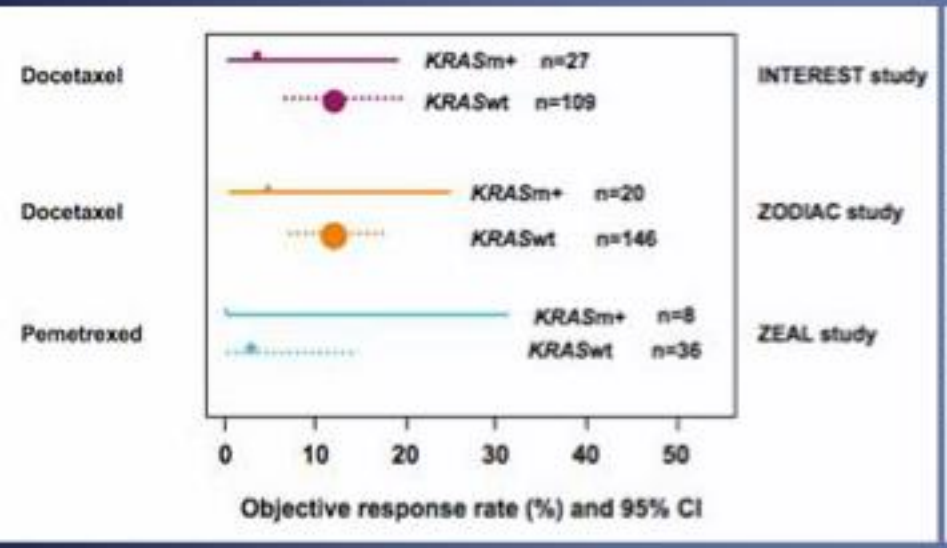
PFS by Independent Assessment

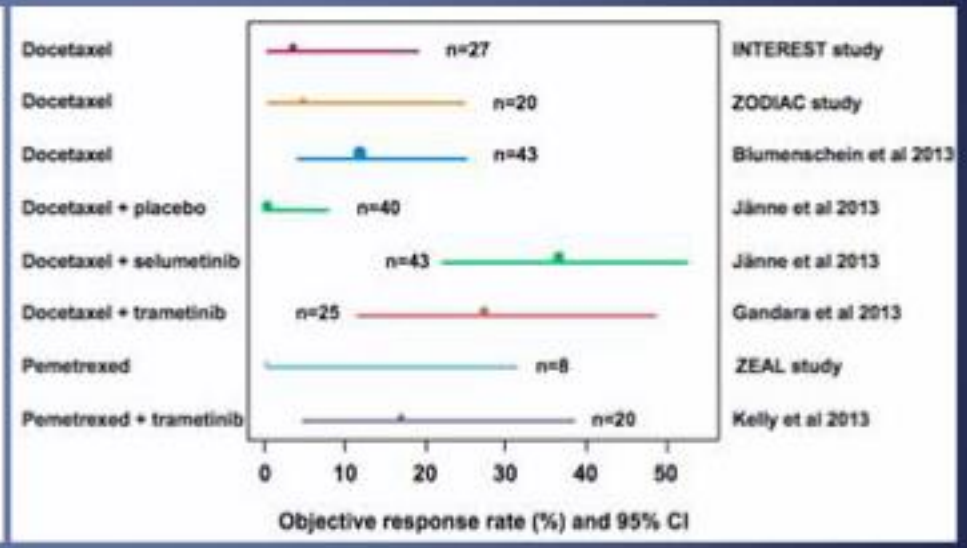
Retesting for EGFR mutation by ARMS detected mutation in 32/108 specimens!

Zhou et al, Abstract O15.07

MEK Inhibition to Treat K-Ras Mutated NSCLC

K-Ras mutation is observed in approximately 25% of lung adenocarcinoma

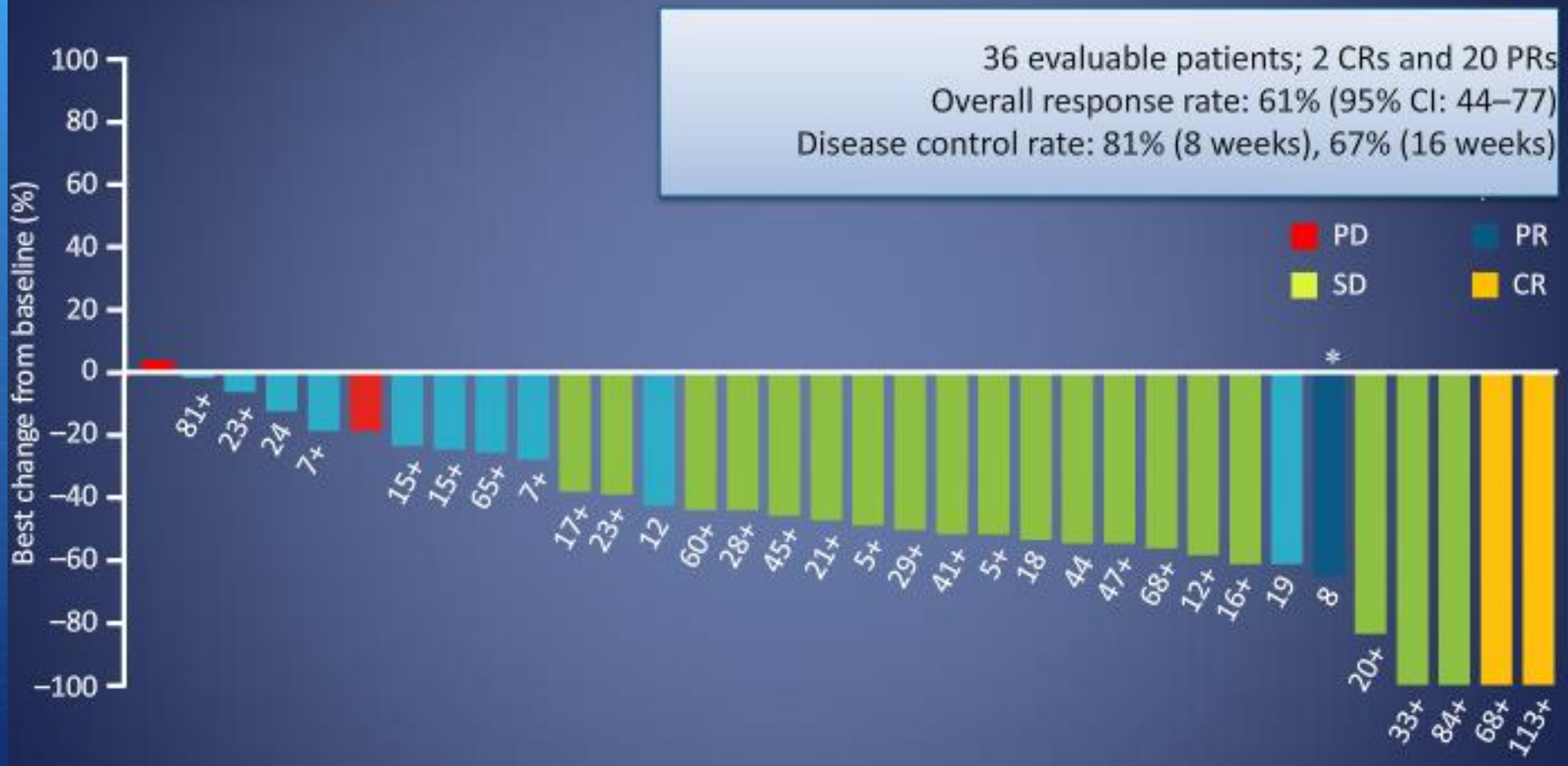




Ongoing studies will evaluate combination of chemotherapy with MEK inhibitors for patients with K-Ras mutation

Janne et al, Abstract # O16.02

Crizotinib in ROS1+ NSCLC: A Phase 2 Study



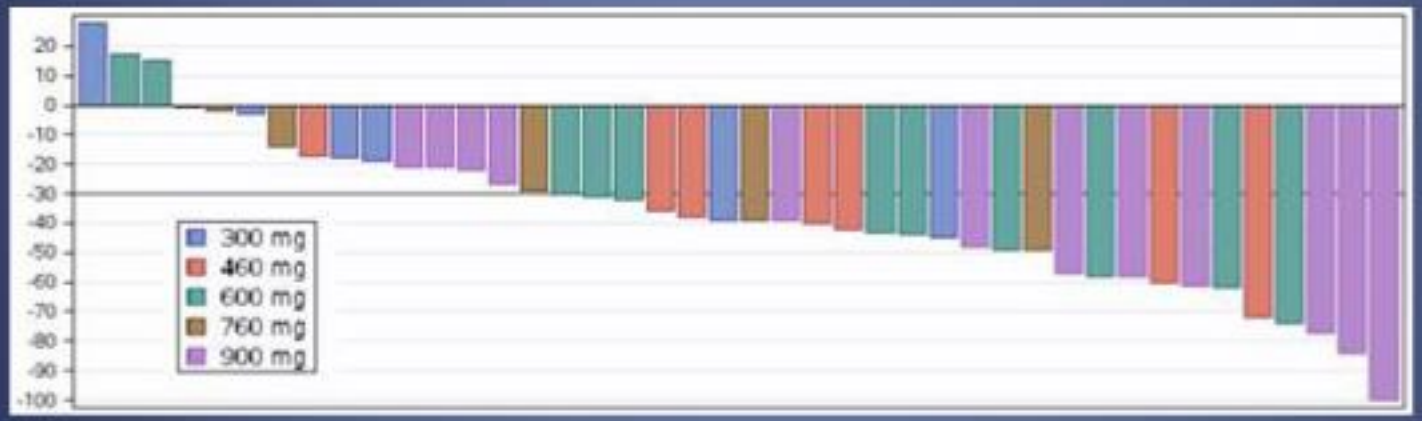
Ou et al, Abstract # O16.07

Alectinib (CH5424802): A Novel ALK inhibitor

- A potent ALK inhibitor
- Sustained tumor regression in xenograft models
- Activity in crizotinib-resistant cell lines
- Phase 2 study in Japan documented response rate of 93% in crizotinib-naïve patients
  - Nakagawa et al, ASCO 2013

Alectinib in Crizotinib-Resistant ALK$^+$ NSCLC

- N=47 patients
- 70% received $\geq$ 2 prior regimens



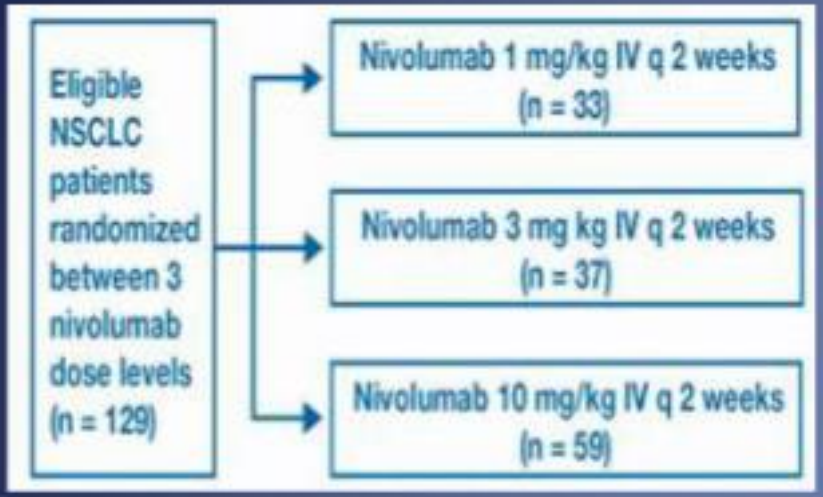
Objective response rate 60%

Adverse events: Myalgia, fatigue, peripheral edema, elevated CPK, nausea and Photosensitivity (Grades 1/2)

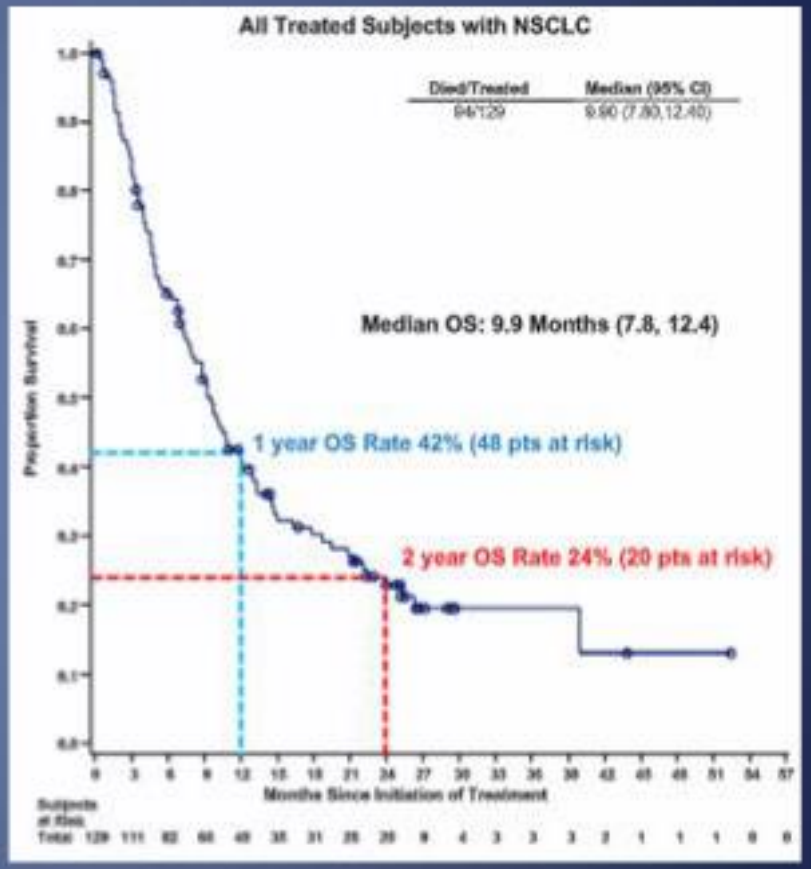
Gadgeel et al, Abstract # O16.06

Targeting PD-1/PDL-1

Nivolumab Phase 1 Study



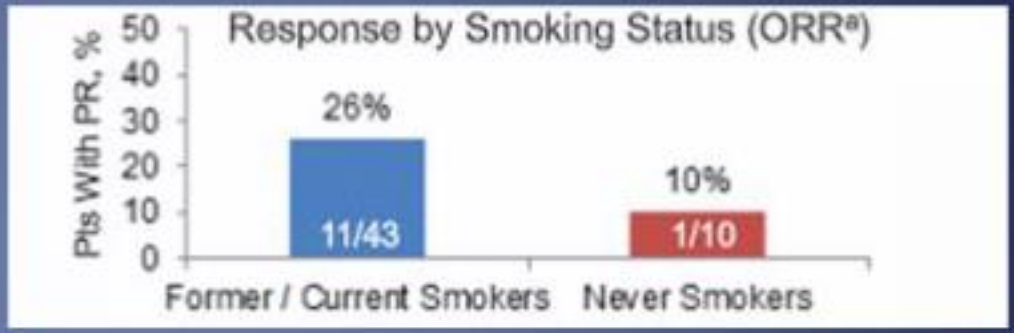
Dose mg/kg	ORR[a,b] % (n/N)	Estimated Median DOR Weeks (Range)	Stable Disease Rate ≥24 Wks % (n/N)	Median PFS Months (95% CI)	Median OS Months (95% CI)
All doses	17.1 (22/129)	74.0 (6.1+, 133.9+)	10.1 (13/129)	2.3 (1.9, 3.7)	9.9 (7.8, 12.4)
1	3.0 (1/33)	63.9 (63.9, 63.9)	15.2 (5/33)	1.9 (1.8, 3.6)	9.2 (5.6, 11.1)
3	24.3 (9/37)	74.0 (16.1+, 133.9+)	8.1 (3/37)	1.9 (1.7, 12.5)	14.9 (9.5, NE)
10	20.3 (12/59)	83.1 (6.1+, 132.7+)	8.5 (5/59)	3.6 (1.9, 3.8)	9.2 (5.2, 12.4)



Brahmer et al, Abstract # MO.18.03

MPDL3290A: An Anti-PDL1- Antibody

PD-L1 Status (n = 53)	ORR[a]	PD Rate
IHC 3 (n = 6)	**83%** (5/6)	**17%** (1/6)
IHC 2 and 3 (n = 13)	**46%** (6/13)	**23%** (3/13)
IHC 1/2/3 (n = 26)	**31%** (8/26)	**38%** (10/26)
All patients (IHC 0/1/2/3 and 7 patients with diagnostic unknown; n = 53)	**23%** (12/53)	**40%** (21/53)



- Tolerated well without dose-limiting toxicities up to 20 mg/kg
- 23% overall response rate
- PDL-1 expression is associated with higher response rate
- Median PFS not reached

Horne et al, Abstract MO 18.01

Targeting PD-1/PDL-1

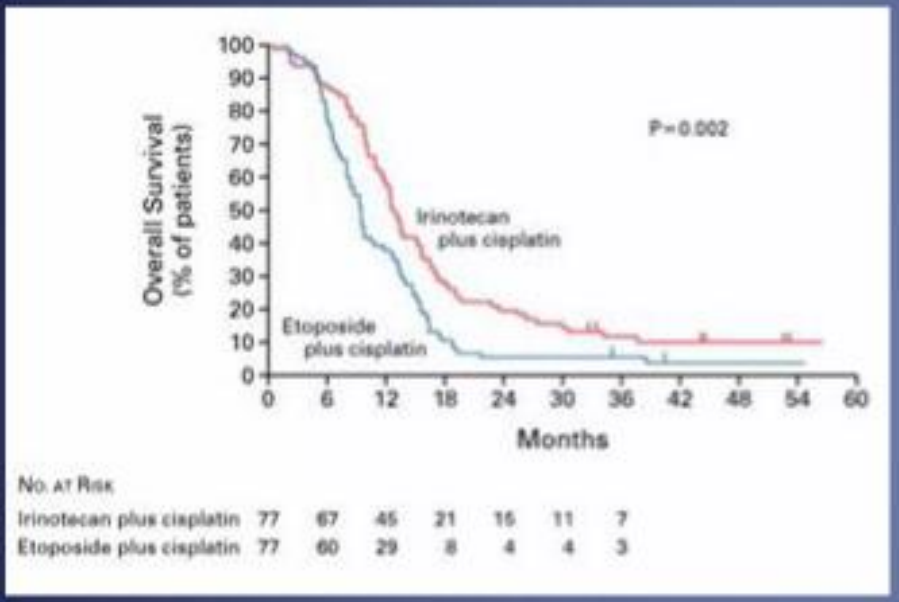
- Clear evidence of activity with three different therapeutic antibodies
  - Good tolerability
- Efficacy in both squamous and non-squamous histology
- Unclear if targeting PD-1 versus PDL-1 might result in variable efficacy
- Phase III studies are ongoing

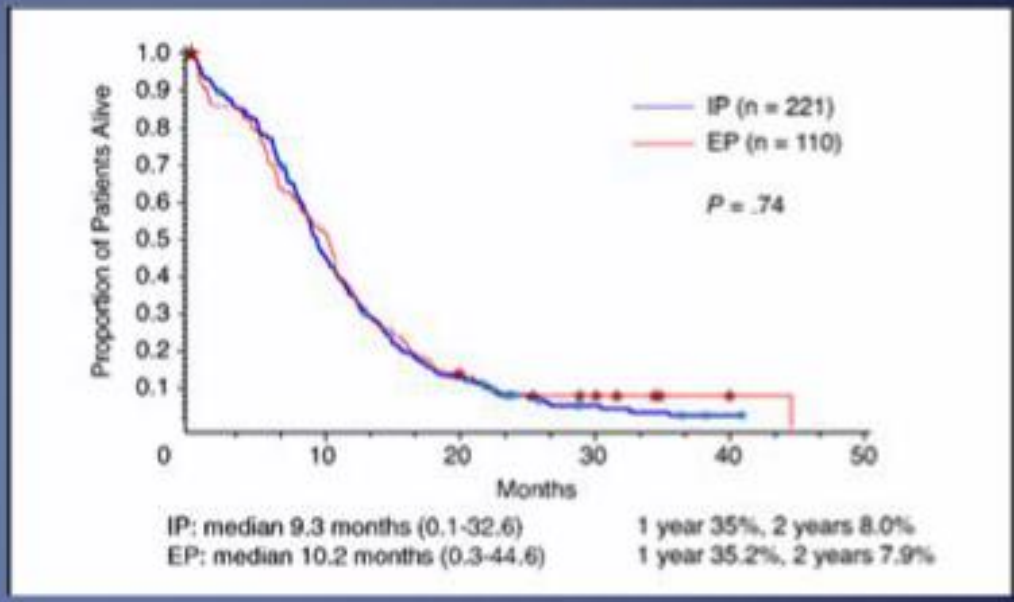
Small Cell Lung Cancer

Targeted Agents Studied in SCLC

- Lack of efficacy with the addition of chemotherapy with
  - Anti-angiogenic agents
  - IGF-1R inhibitors
  - MMP inhibitors
  - Hedgehog inhibitors
  - HGF inhibitors
  - Statins
- Mirrors our experience in NSCLC before the advent of biomarker evaluation

Is IP Superior to EP for SCLC-ED?

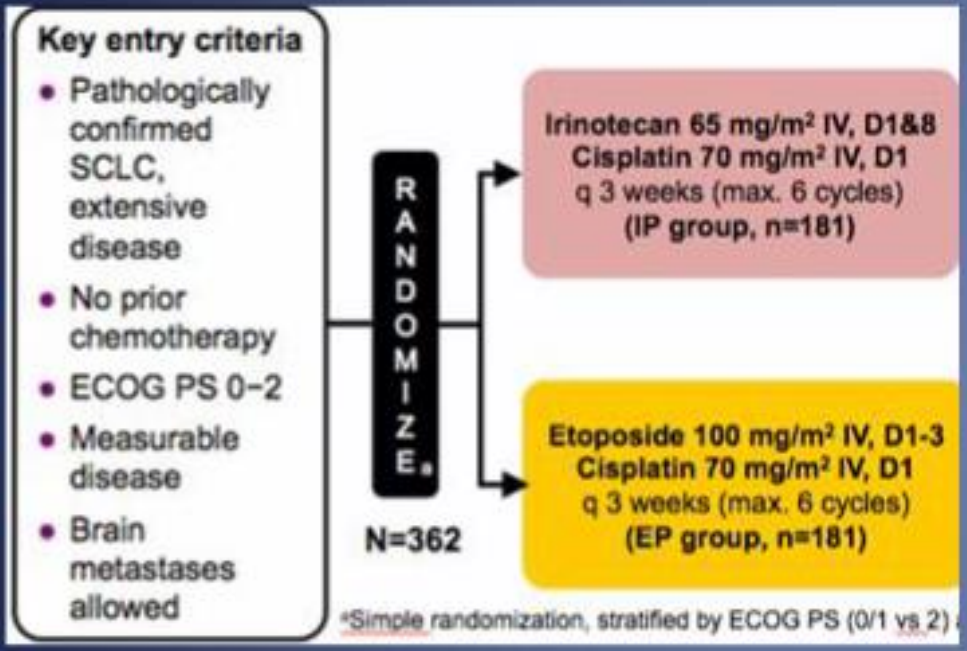


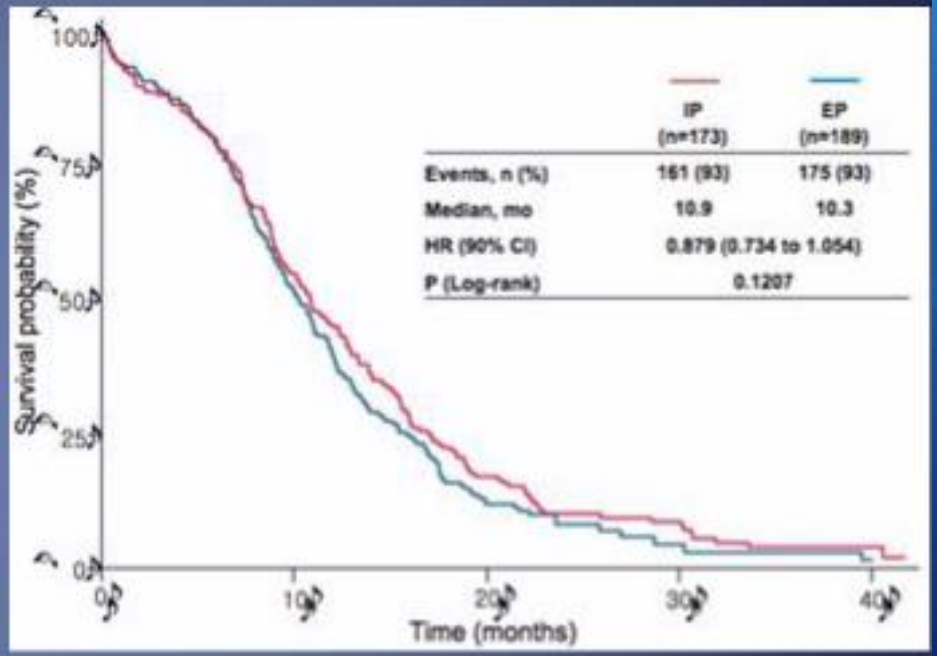


Japanese patient population
Noda et al, N Engl J Med, 2002

Western patient population
Hanna et al, J Clin Oncol, 2006

IP in Korean Patient Population





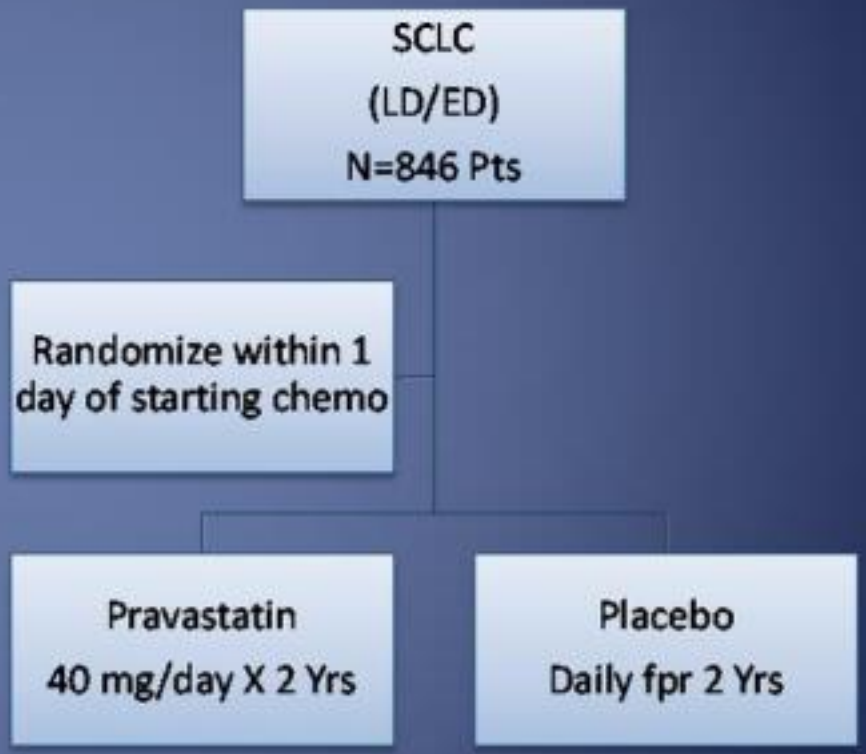
- Response rate was higher with IP (62% vs. 48%)
- More anemia, nausea and diarrhea with IP

Kim et al, Abstract O21.02

Pravastatin in SCLC

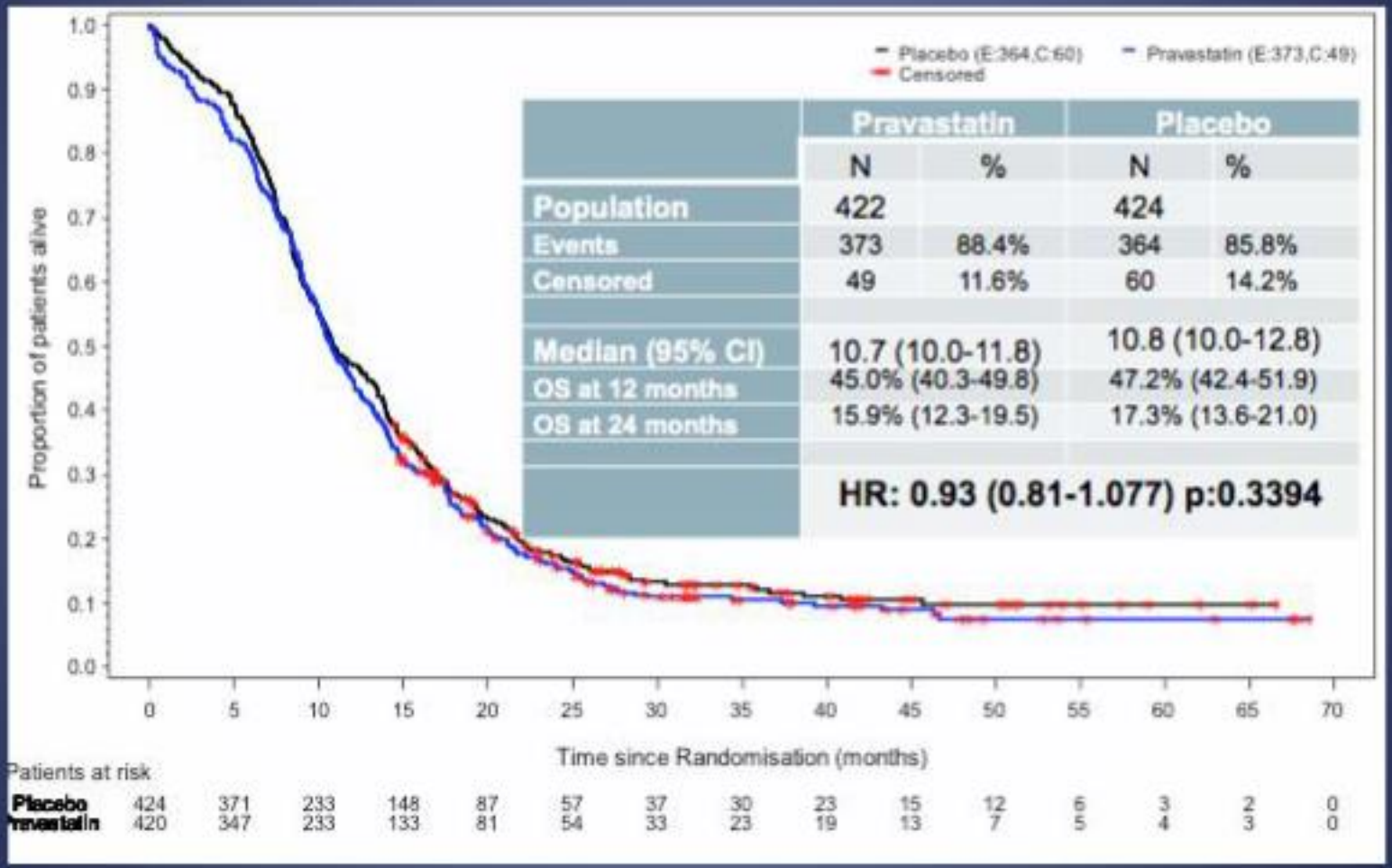
Rationale

- Statins are cytotoxic to SCLC in vitro
- Enhance efficacy of chemotherapy
- May have a role in prevention of cancer



Secki et al, Abstract # O21.01

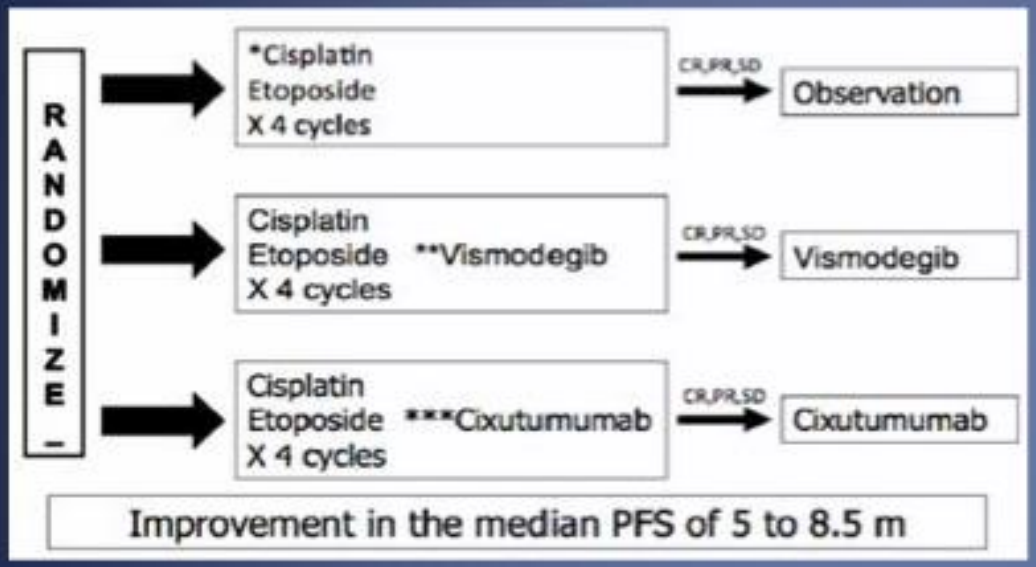
Results

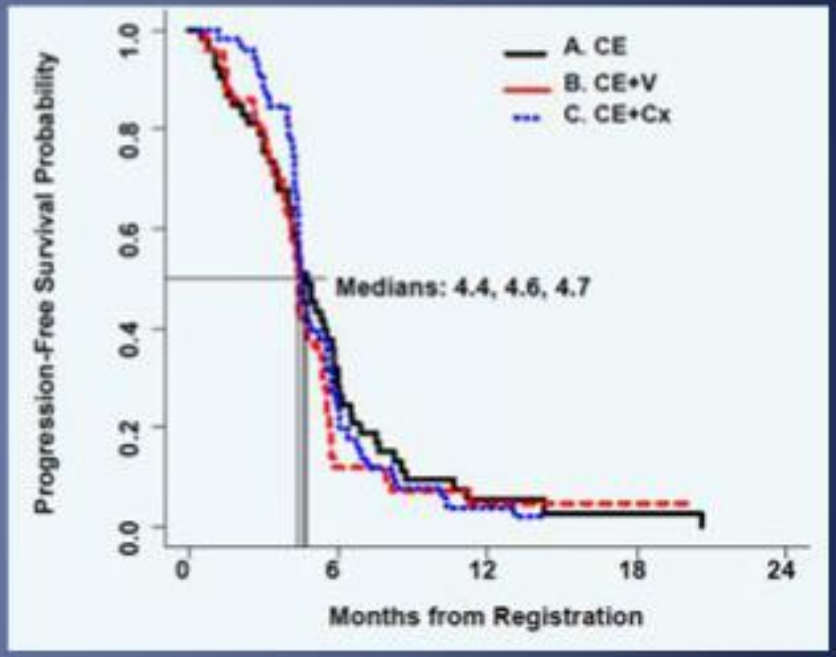


	Pravastatin		Placebo	
	N	%	N	%
Population	422		424	
Events	373	88.4%	364	85.8%
Censored	49	11.6%	60	14.2%
Median (95% CI)	10.7 (10.0-11.8)		10.8 (10.0-12.8)	
OS at 12 months	45.0% (40.3-49.8)		47.2% (42.4-51.9)	
OS at 24 months	15.9% (12.3-19.5)		17.3% (13.6-21.0)	
	HR: 0.93 (0.81-1.077) p:0.3394			

Bottom-line: Statins are effective lipid lowering agents!

Integration of Targeted Agents: E1508

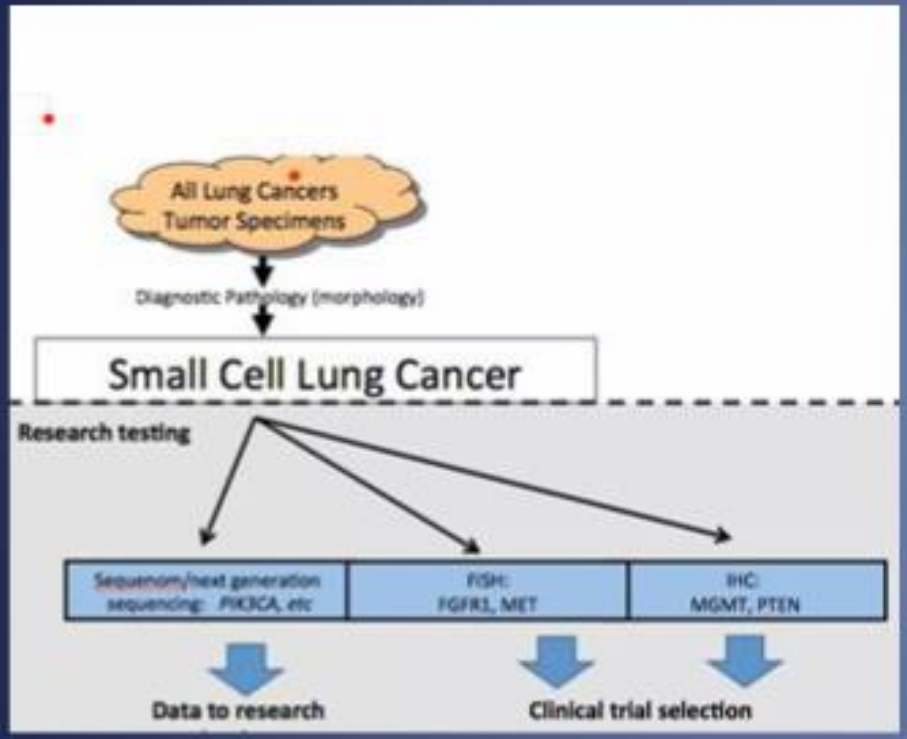




- No improvement in efficacy with the addition of a hedgehog inhibitor or an IGF-1R antibody

Belani et al, ASCO 2013.

Molecular Evaluation of SCLC



Sequenom (N=32)	IHC		FISH (N=26)	IMPACT (N=26)	
	MGMT (N=25)	PTEN (N=24)		Mutations	Amplifications
AKT1 E17 (N =1)	Loss (N=13)	Loss (N=19)	FGFR1 (N=2)	TP53 (N=25)	EIF4BP1 (N=5)
PIK3CA E542K (N =1)				RB1 (N=21)	FGFR1 (N=4)
				MLL3 (N=10)	GOLPH3 (N=2)
				EPHA5 (N=8)	GNAS (N=2)
				ERBB4 (N=7)	MYC (N=2)
				Notch1 (N=7)	SRC (N=2)

Pietanza et al, Abstract # MO13.10

Aurora A Kinase Inhibition in SCLC

Alisertib (MLN8237)

- Small molecule inhibitor of Aurora A Kinase
- AAK is a critical mitotic regulator
- Single agent activity in solid organ and hemtological malignancies

Phase 2 cohort in SCLC	
N	48 pts
Median age	62
Prior lines of therapy	1- 52% 2- 48%
Response Rate Chemo-sensitive Chemo-refractory	21% 19% 25%
Median PFS	2.11 m

Common AEs: Fatigue, Neutropenia, Diarrhea, Nausea, Stomatitis

Havel et al, Abstract # O21.06

Pazopanib in SCLC

- Setting: Second line therapy of SCLC
- Treatment: Pazopanib 800 mg/day
- N= 19 pts with sensitive relapse
- Response rate 21%
- Median PFS 3.6 m

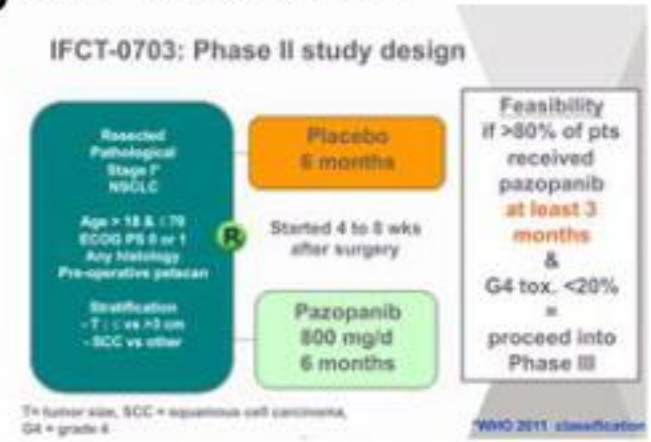
Kotsakis et al, Abstract # M13.04

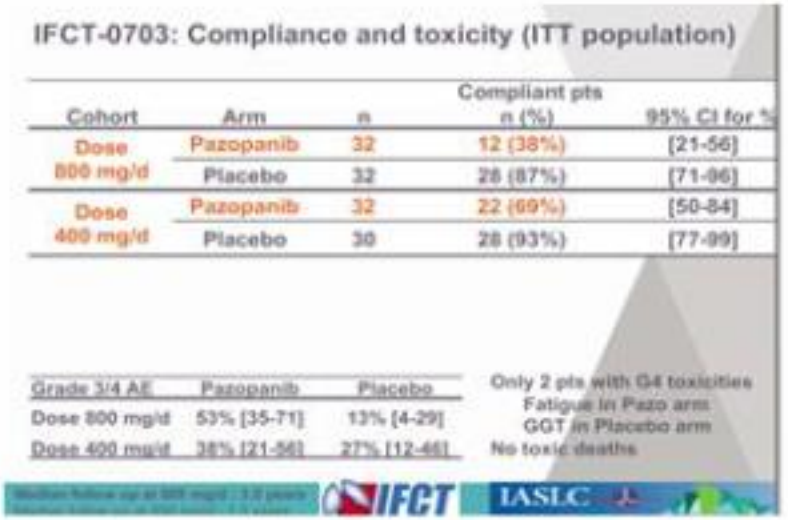
SCLC: Take Home Messages

- Progress in the treatment of SCLC continues to be dismal
- Treatments based on molecular sub-typing are urgently needed
- The efficacy of IP regimen is restricted to the Japanese patient population
- Aurora kinase inhibitors are active and poised for further development

Adjuvant pazopanib or placebo in resected stage I NSCLC

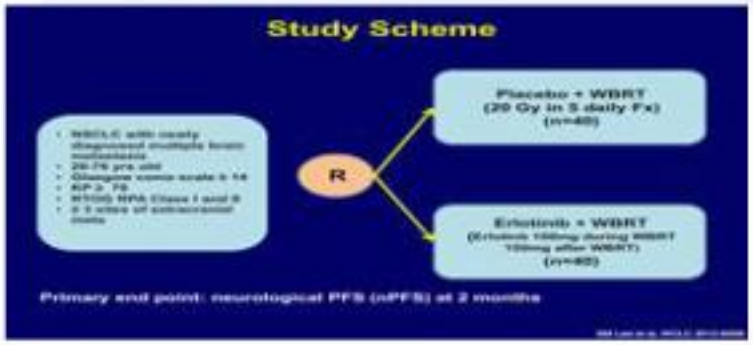
- Pazopanib: small molecule inhbitor of VEGFR
- Feasibility study
- Not feasible due to poor compliance.



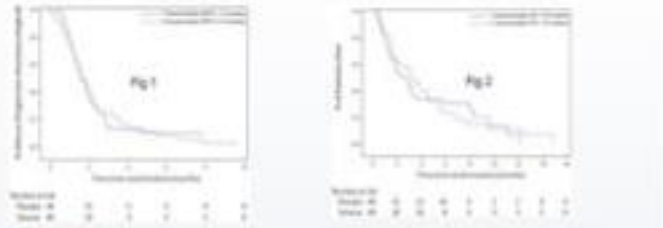


EGFR TKIs as Radiosensitizers

A randomised placebo-controlled multicentre phase II trial of erlotinib plus whole brain radiotherapy for patients with advanced non-small cell lung cancer with multiple brain metastases (TACTIC)



Neurological Progression-Free Survival (Fig 1) and Overall Survival (Fig 2) – ITT population



Results

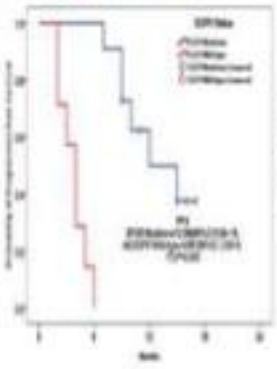
- Fifteen patients (37.5%) from each arm were alive and without neurological progression 2 months after WBRT.
- Median nPFS was 1.6 months in both arms; nPFS HR 0.95 (95% CI, 0.59-1.54; p=0.84).
- Median overall survival (OS) was 2.9 and 3.4 months in the placebo and erlotinib arms; HR 0.95 (95% CI, 0.58-1.55; p =0.83).
- Frequency of EGFR mutations was low with only 1 out of 35 (3%) patients with available samples had activating EGFR-mutations.
- Grade 3/4 adverse event rates were similar between the two groups (70% in each arm), except for rash 20% (erlotinib) vs. 5% (placebo), and fatigue 17% vs. 35%.
- No significant QoL differences were found.

A phaseII study of Icotinib and whole brain radiotherapy (WBRT) for Patients With Brain Metastases from NSCLC

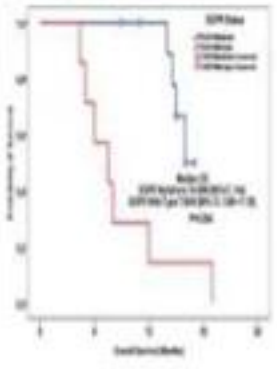
- Intracranial tumor response(Follow up to 15-09-2013)

	CR(%)	PR(%)	SD(%)	PD(%)	ORR(%)	mPFS (mo)	OS (mo)
N=20	5 (25.0)	11 (55.0)	3 (15.0)	1 (5.0)	16 (80.0)	7.0	15.0
95%CI					(60.8~99.2)	4.9~13.1	12.8~17.2

- Progression free



Overall survival



MO07.11, Lee; M0O7.12, Yun

Brain Metastases

- The most common tumor in the brain is NSCLC.
- Major issue in terms of morbidity and mortality.
- Optimal management, timing of therapy etc remain unclear.
- Major site of relapse.
- Current questions:
  - Role of radiosensitizers
  - Value of current systemic therapies

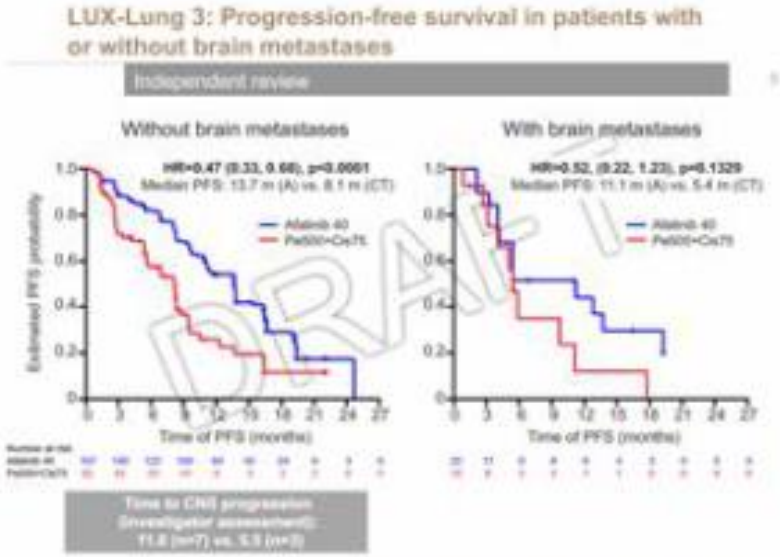
Clinical data of concurrent EGFR TKI with WBRT

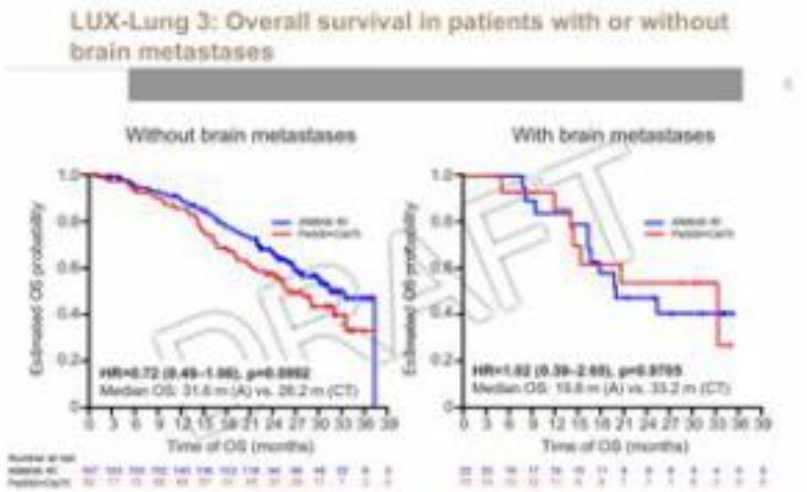
Author	Study	EGFR TKI	Treatment	N	WBRT (dose/ fraction)	RR	TTP	OS	Toxicity
Lind (2009)	Phase I	Erlotinib Cohort 1: 100mg (n=4) Cohort 2: 150mg (n=7)	Erlotinib for 1 week → Concurrent RT → Maintenance	11	30 Gy (10 Fx)	45% 5 PR 2 SD	141 days	133 days	No G3 in cohort 1 1 G3 rash, 1 G3 fatigue in cohort 2
Ma (2009)	Phase II	Gefitinib 250mg/d	Gefitinib 250mg/d With concurrent WBRT	21	40Gy	81%	10m	13m	Rash, diarrhea mostly Grade
Pesce (2012)	Randomized phase II	Gefitinib Vs. Tamoxifen	Gefitinib 250m/d With concurrent WBRT Vs TMZ 75mg/m2 for 20 days	59 (G:16) (T:43)	30 Gy			4.9 M G:6.3M T: 4.9M	No toxicity
Welsh (2013)	Phase II	Erlotinib 150mg	Erlotinib for 1 week → Concurrent RT → Maintenance	40	35 Gy 2.5Gy/day	86%	PFS for CNS 8.2 M EGFR WT:6.2m EGFR M+: 12.3 m	11.8 M EGFR wild : 5.3m (n=8) EGFR mutant : 19.1m (n=8)	4 G3 rash No increased neurotoxicity

Lind et al, Int J Radiation Oncol Biol Phy 2009;74:1391-6
Welsh et al J Clin Oncol 2013;31:895-902

EGFR TKI (Afatanib) and CNS Metastases

- Retrospective analysis of the value of chemotherapy or afatanib in patients treated on the LUX-lung 3 study.

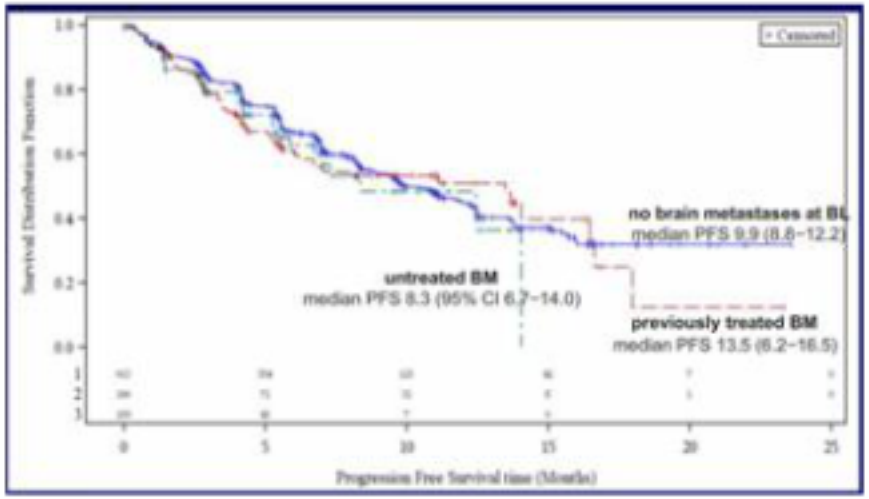




MO07.13, Schuler

Clinical Experience with crizotinib in patients with advanced ALK-rearranged NSCLC and brain metastases (PROFILE 1005, 1007)

- Retrospective study to evaluate the activity of crizotinib in CNS.



- No difference in outcomes.
- CNS remains the dominant site of acquired resistance with the development of new lesions, regardless of whether patients presented with CNS disease

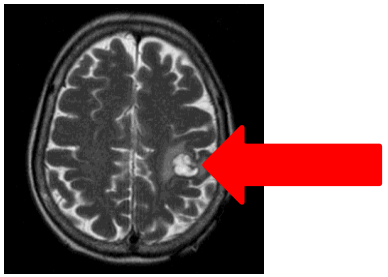
Costa,

Crizotinib in patients with advanced ALK-positive NSCLC and brain metastases

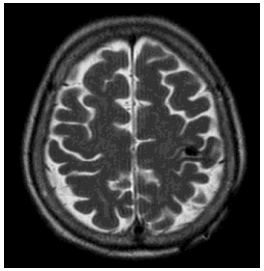
- Retrospective analysis of patients with (n=275) or without (n=613) brain metastases from PROFILE 1005 and PROFILE 1007
- Clinical outcomes:
  - Intracranial DCR at 12 weeks: ~60%
  - Intracranial CRs: 11/275 (4%)
  - Intracranial target lesion ORR (patients with ≥1 brain metastasis; 10/40): 25%
  - Systemic ORR (all patients with brain metastases at baseline): 49%
- Among patients with no detectable brain metastases at baseline:
  - 9% developed symptomatic brain metastases after starting crizotinib treatment

Intracranial CR with crizotinib

Before treatment



After 6 weeks of treatment



Courtesy of J-Y Han, National Cancer Center, Goyang, South Korea

Mini oral presentation by Dr Costa at WCLC 2013:
Programme number: MO07.02
Targeted therapies II, Bayside Auditorium B
Monday October 28th; 4:15 pm–5:45 pm

DCR, disease control rate

L. Crinò, et al. Presented at ECCO-ESMO 2013; Abstract 3413

Comments

- No advantage to adding EGFR TKI to radiotherapy.
- Not surprisingly, the drugs treat CNS metastases.
- Interestingly, the CNS remains a major site for progression.

Adjuvant Chemotherapy in 2013
State of the art

- Standard : Cisplatin based chemotherapy
- Standard : Stage II-IIIA
- Option : IB (>4 cm recommended)
- Option : carboplatin
- Criteria
  - <75 yrs
  - <2 months after surgery
  - PS 0-1
  - No post-operative complications
- No established role for targeted therapies (erlotinib, gefitinib, bevacizumab) !

Class	Agent	Biomarkers	Robustness
Cytotoxic drugs	Cisplatin	**ERCC1** **RRM1** **BRCA1**	**+** **+**
	Gemcitabine	**RRM1**	**+**
	Pemetrexed	**FPGS** **TS**	**-** **+**
	Paclitaxel	**MAPtau** **Beta-tubulin III**	**+** **+**
Targeted therapies	Erlotinib	**EGFR mutation** **FISH EGFR** **K-Ras wt** **RASSF1A / 9pLOH**	**+++** **+** **+** **+**
	Bevacizumab	**circulating VEGF**	**-**
	PF-02341066	**EML4-ALK**	**+++**

A phase 2 study of the GI-4000 KRAS vaccine following curative therapy in patients with stage I-III lung adenocarcinoma harboring *KRAS* G12C, G12D, G12V or G12R mutation

- K-ras is the most common mutation in nonsquamous carcinoma.
- Immunotherapeutic directed against the most common abnormalities.
- Feasible, favorable outcome compared to matched controls.

Comparison to Matched Controls

Characteristic	GI 4000 (N=24)	Matched Group (N=64)
Male sex	7 (29%)	21 (33%)
Age at diagnosis – Median yrs	63	66
Pathological Stage		
I	12	42
II	5	2
III	7	20
Recurrence free survival per year		
1	86%	85%
2	68%	71%
3	60%	69%
Overall survival per year		
1	100%	93%
2	100%	88%
3	92%	83%
Hazard ratio for survival (p-value)	0.58 (0.29)*	

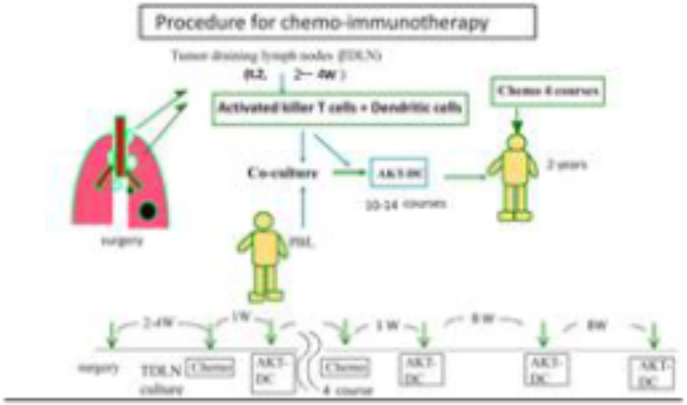
*adjusted for age, sex, KRAS genotype and stage

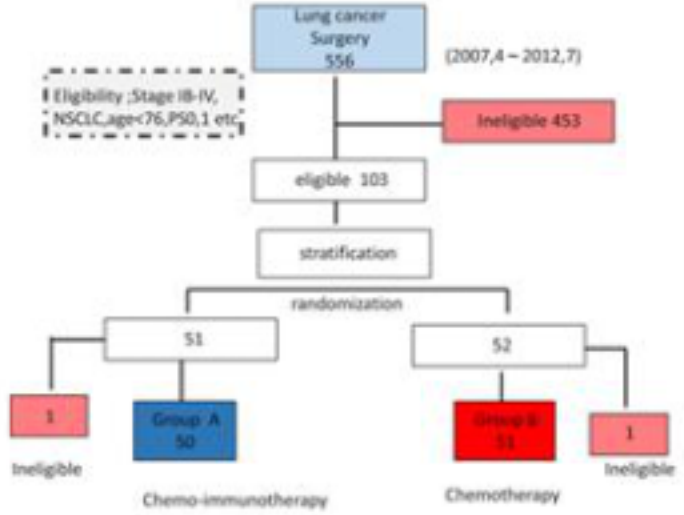
MO08.04 Chaft

MO08.04: Adjuvant GI-4000 KRAS vaccine

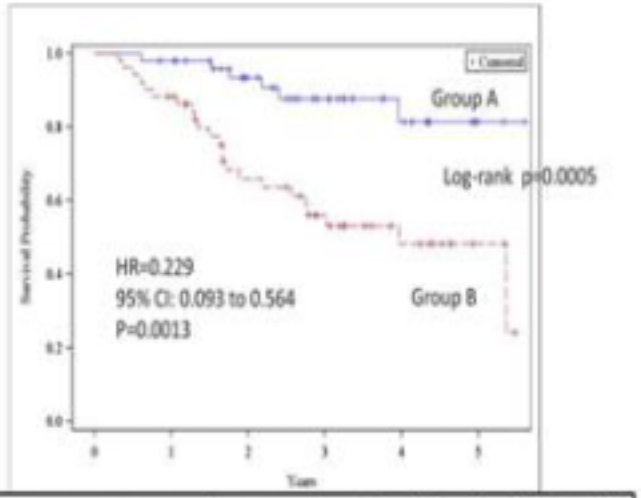
- Phase 2 feasibility and immunogenicity study
- Population: 24 pts with a KRAS mutation
- P Stage I-III
- 50% developed a new (9/13) or increased (3/6) immune response
- HR for survival : p = .58

Randomized controlled phase III trial of adjuvant chemo-immunotherapy with activated killer T cells and dendritic cells in patients with resected primary lung cancer





Kaplan-Meier estimates of overall survival for group A and B.

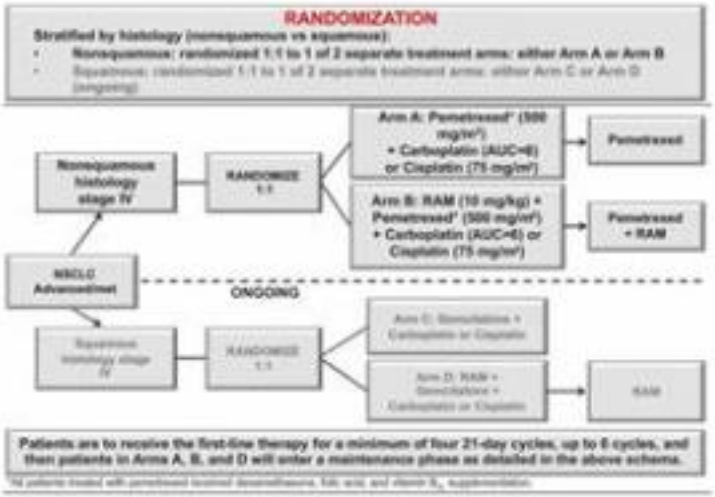


Group	n	Event	Censored	% Censored	Median (months)
A	50	6	44	88.00	30.72
B	51	23	28	54.90	34.23
Total	101	29	72	71.29	32.20

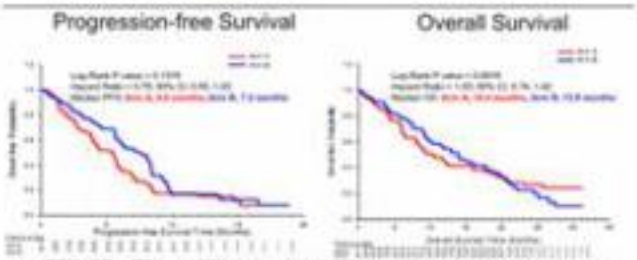
MO08.07 Kimura

Phase II randomized, open-label study of ramucirumab (IMC-1121B) in combination with first line platinum based chemotherapy: Results from non-squamous patients Doebele et al.

- Ram is a fully human monoclonal antibody (IgG1) vs. VEGFR2.
- Success in gastric cancer, but failed in phase III breast cancer study (press release 9.26.2013)



Efficacy Results



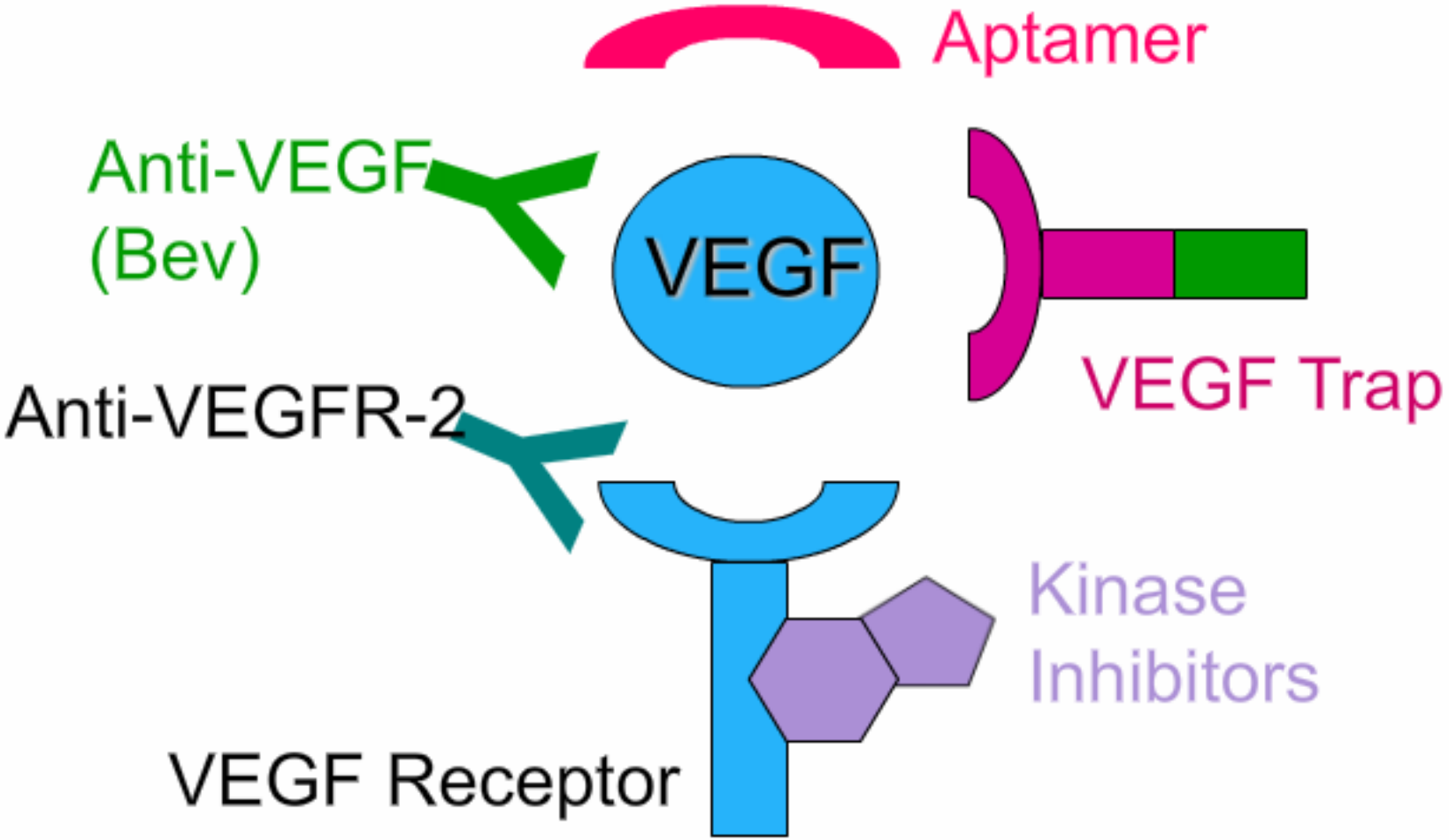
- ORR (CR + PR) was 38% in Arm A and 49%, including one complete response, in Arm B (p=0.180).
- Disease control rate was 70% in Arm A and 86% in Arm B (p=0.032).

Arm A: Pemetrexed + Carboplatin or Cisplatin
Arm B: RAM + Pemetrexed + Carboplatin or Cisplatin

Drug-related Adverse Events Reported in >15% of Patients in Either Arm

	Arm A (N=49), n, (%)		Arm B (N=67), n, (%)			
					Related to Ramucirumab	
Adverse Event	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3
Patients with ≥1 TEAE	53 (91.3)	35 (56.5)	67 (100)	47 (70.1)	54 (80.6)	34 (50.7)
Fatigue	41 (59.4)	12 (17.4)	41 (61.2)	8 (11.9)	34 (50.7)	6 (9.0)
Nausea	35 (50.7)	3 (4.3)	34 (50.7)	6 (9.0)	22 (32.8)	4 (6.0)
Anemia	36 (52.2)	12 (17.4)	29 (43.3)	8 (11.9)	13 (19.4)	3 (4.5)
Neutropenia	16 (23.2)	13 (18.8)	24 (35.8)	14 (20.9)	8 (11.9)	5 (7.5)
Thrombocytopenia	17 (24.6)	14 (20.3)	23 (34.3)	17 (25.4)	5 (7.5)	4 (6.0)
Decreased appetite	17 (24.6)	1 (1.4)	20 (29.9)	2 (3.0)	17 (25.4)	2 (3.0)
Vomiting	21 (30.4)	1 (1.4)	19 (28.4)	4 (6.0)	13 (19.4)	3 (4.5)
Diarrhea	16 (23.2)	1 (1.4)	12 (17.9)	1 (1.5)	4 (6.0)	0 (0.0)
Dysgeusia	5 (7.2)	0 (0.0)	12 (17.9)	0 (0.0)	7 (10.4)	0 (0.0)
Hypertension	2 (2.9)	1 (1.4)	12 (17.9)	6 (9.0)	12 (17.9)	6 (9.0)
Epistaxis	3 (4.3)	0 (0.0)	11 (16.4)	0 (0.0)	9 (13.4)	0 (0.0)
Constipation	14 (20.3)	0 (0.0)	9 (13.4)	0 (0.0)	6 (9.0)	0 (0.0)

Targeting the VEGF Pathway



E1505: Phase III Adjuvant Chemotherapy +/- Bevacizumab

Resected IB≥4cm–IIIA

No planned XRT

N = 1500

R

Chemotherapy* x 4 cycles

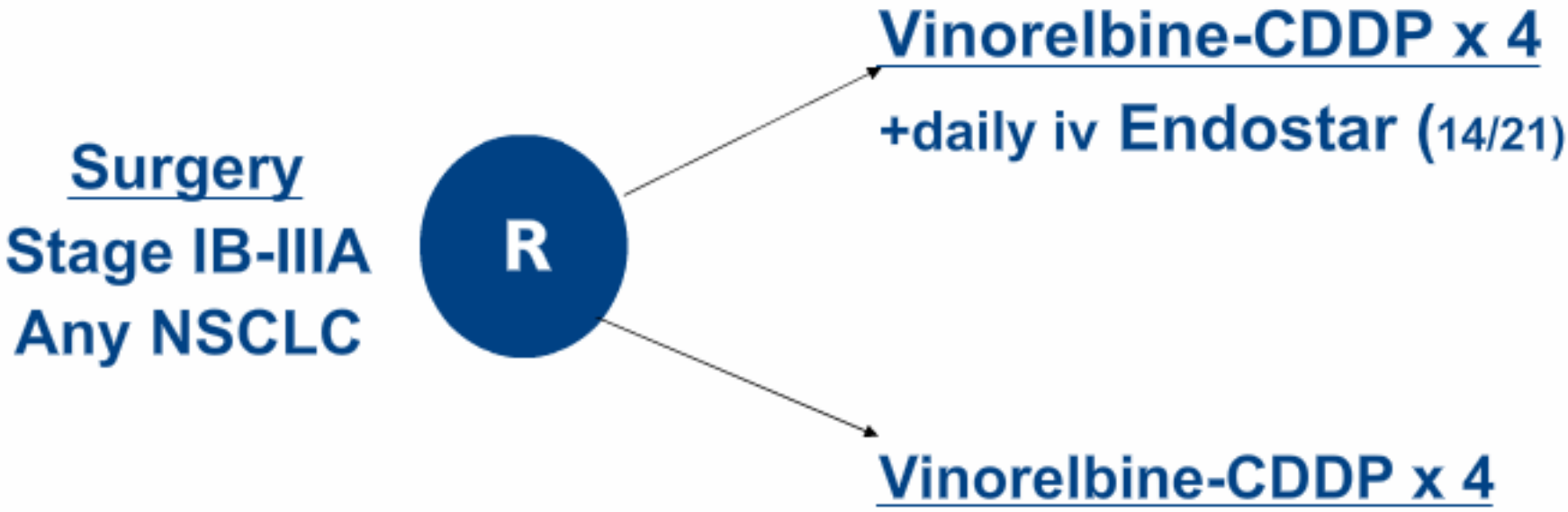
Chemotherapy* x 4 cycles + bevacizumab x 1 year

*Specified regimens

- Cisplatin and docetaxel
- Cisplatin and vinorelbine
- Cisplatin and gemcitabine

Primary endpoint: overall survival

MO08.05: Adjuvant Endostar (A recombinant human endostatin) in resected NSCLC

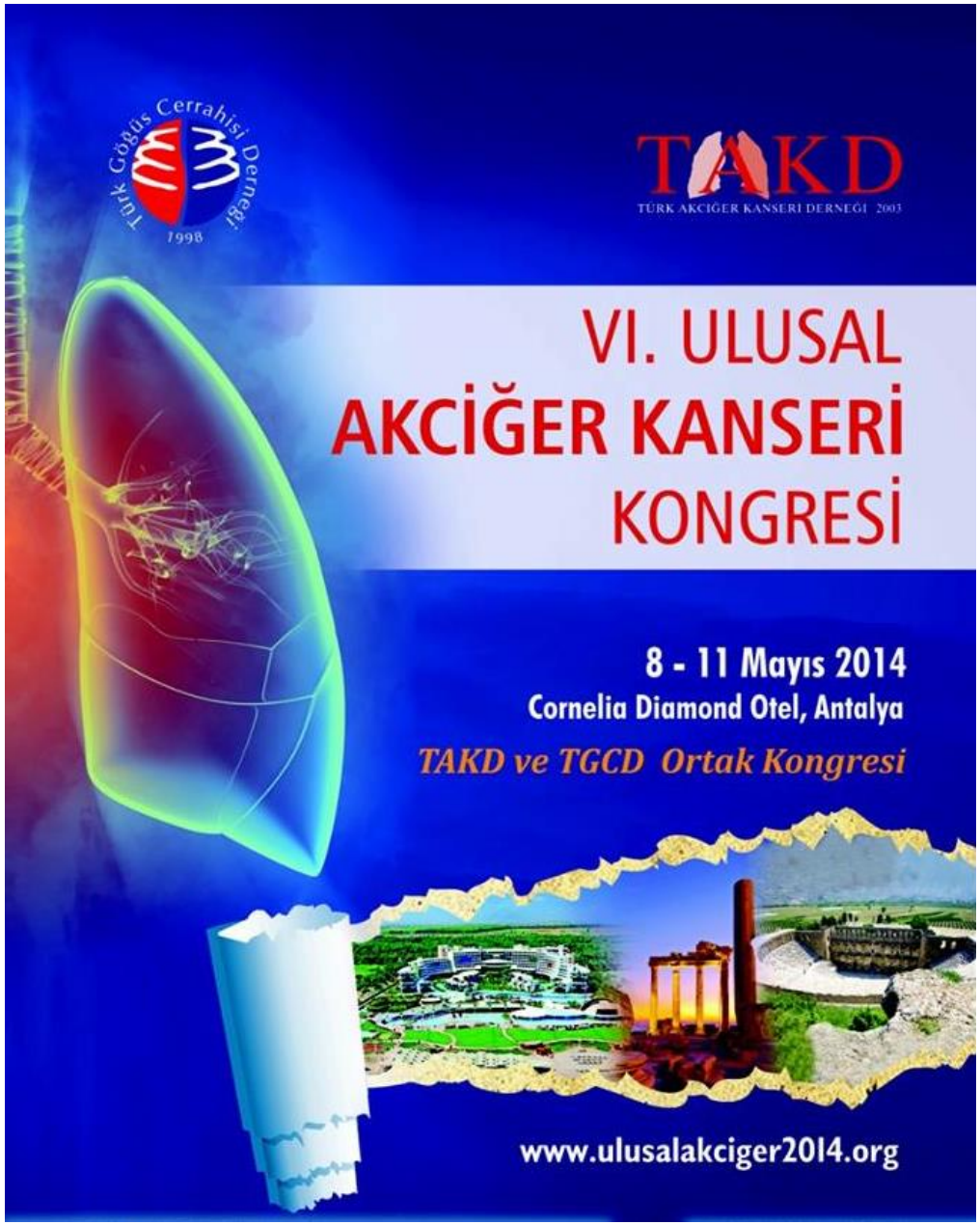


Phase II/III randomized study
Stratified by gender, stage, histology

Objective: DFS

Adjuvant Chemotherapy in 2013
Conclusion / Challenges

- **Customized therapy**
  - Micrometastatic disease different from stage IV?
  - Role of –omics ?
- **Unvalidated agents in the metastatic setting**
  - Reluctance from community
- **Alternative approaches**
  - Effect on tumor ? Host ?
  - Local treatment
- **Pattern of relapse**
  - Customize the follow-up ?



Gelişmeleri izlemek için 8-11 Mayıs 2014 KONGREMİZE BEKLİYORUZ

Predictors of trimodality therapy use and overall survival in patients with stage III non-small cell lung cancer (NSCLC) in the National Cancer Database

Mary Jo Fidler, MD[1], Michael J. Liptay, MD[2], Philip Bonomi, MD[1], David J. Sher, MD, MPH[3]

Rush University Medical Center, Chicago, IL
(1) Department of Medical Oncology
(2) Department of Cardiothoracic Surgery
(3) Department of Radiation Oncology

RESULTS

- Three and 5-year overall survival probabilities were 17% and 9.6%, respectively
- Number of surgeries decreased from earliest to most recent cohort (9.9% vs 7.2% p<0.0001)
  - Frequency of pneumonectomy decreased, 24% of surgeries (earliest) vs. 14% (most recent cohort) p<0.0001
- On univariable analysis, TMT was associated with a significant survival advantage (median 26 vs 12 months, p < 0.0001)
- On multivariable regression, TMT was persistently associated with improved survival (HR 0.49), also maintained after propensity matching (HR 0.49)
  - In subset Cox regression in patients treated between 2003-2005, in which there was a comorbidity variable, TMT was still significant (HR 0.52)
  - Survival advantage also seen after pneumonectomy

RUSH UNIVERSITY MEDICAL CENTER

CONCLUSIONS 1

- *In this large national database, TMT was associated with a significant survival benefit*
- *TMT was associated with superior survival in multivariate analyses, in a sensitivity analysis in a cohort with co-morbidity scores, and after propensity matching*
- *TMT remains a valid treatment paradigm for locally advanced non-small cell lung cancer*

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CONCLUSIONS 2

- *TMT was not commonly implemented across CoC-accredited programs.*
- *Measures often associated with higher socioeconomic status were statistically significant predictors of TMT.*
- *The academic nature and volume of the facility strongly influenced TMT, suggesting more aggressive practice patterns in university-based, high-volume institutions.*