ASCO 2013: Lung Cancer Highlights

Paul Germonpré

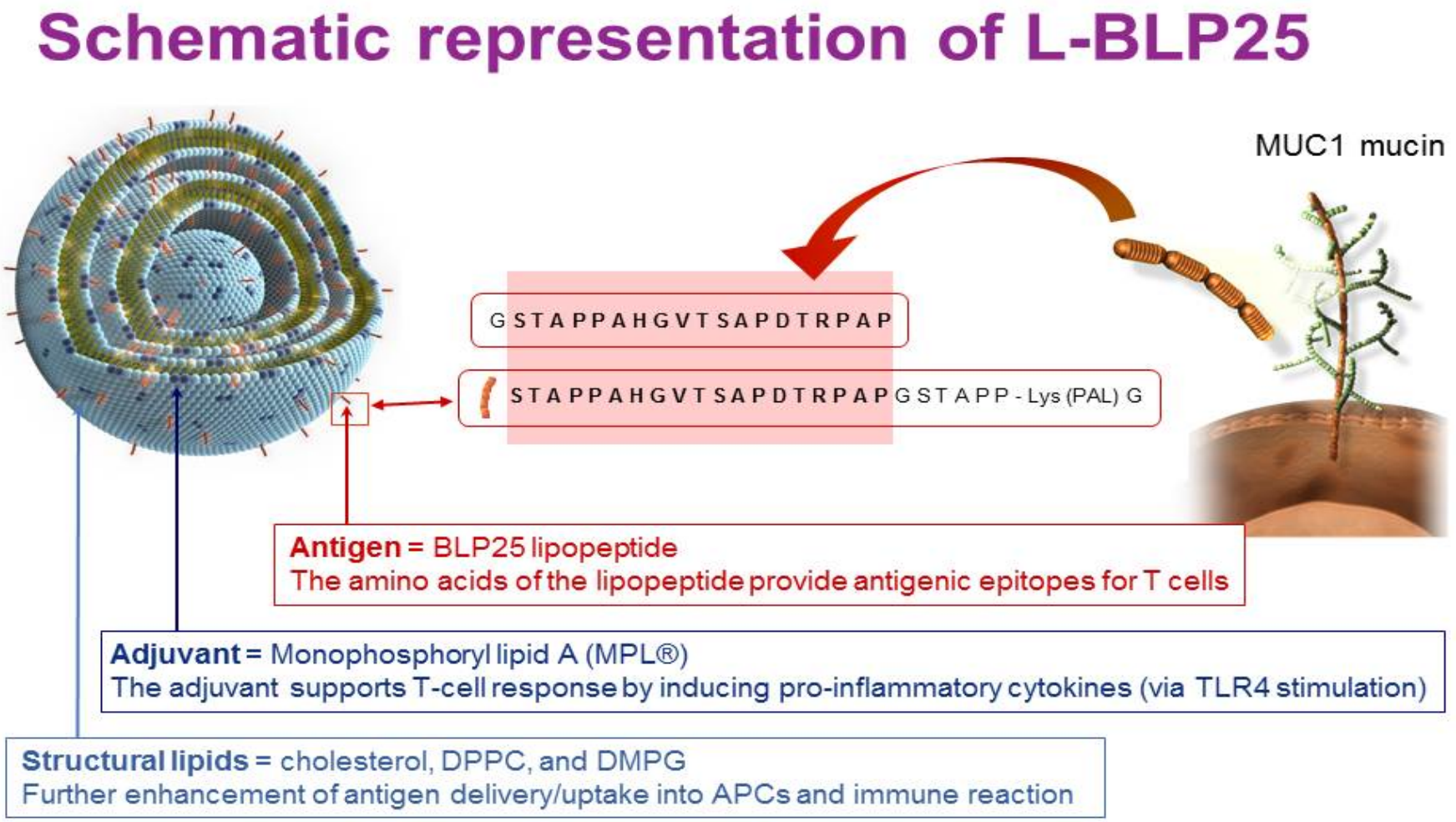
ASCO 2013: Lung Cancer Highlights

- How to improve outcome in stage III NSCLC?
- Customized chemotherapy for NSCLC
- Maintenance treatment for advanced non-squamous NSCLC
- Targeted treatments

How to improve outcome in stage III NSCLC?

- Vaccination?
- More irradiation?
- Adding surgery to radiotherapy?
- Adding radiotherapy to surgery?

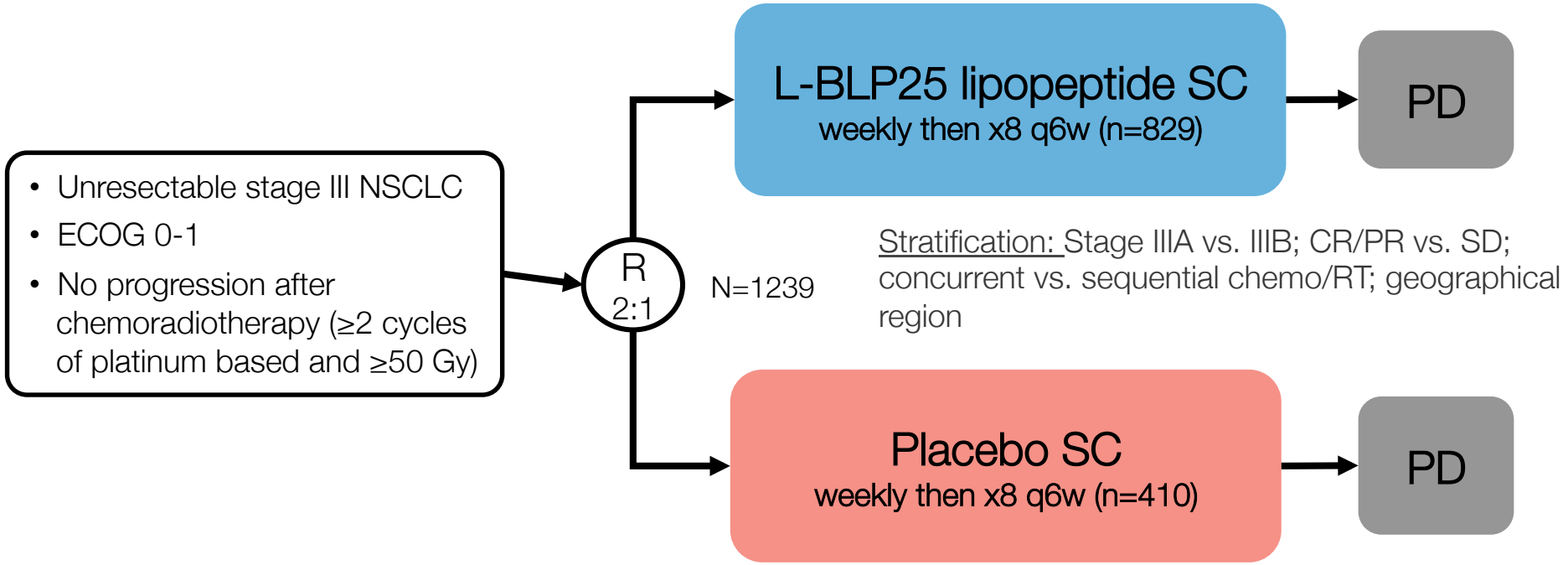
START trial: phase III study of L-BLP25 immunotherapy for unresectable stage III NSCLC



Butts et al. J Clin Oncol 31, 2013 (suppl; abstr 7500)

START trial: phase III study of L-BLP25 immunotherapy for unresectable stage III NSCLC

Objective: to evaluate the MUC1 antigen-specific cancer immunotherapy (L-BLP25) in patients with stage III NSCLC who had not progressed after primary chemoradiotherapy

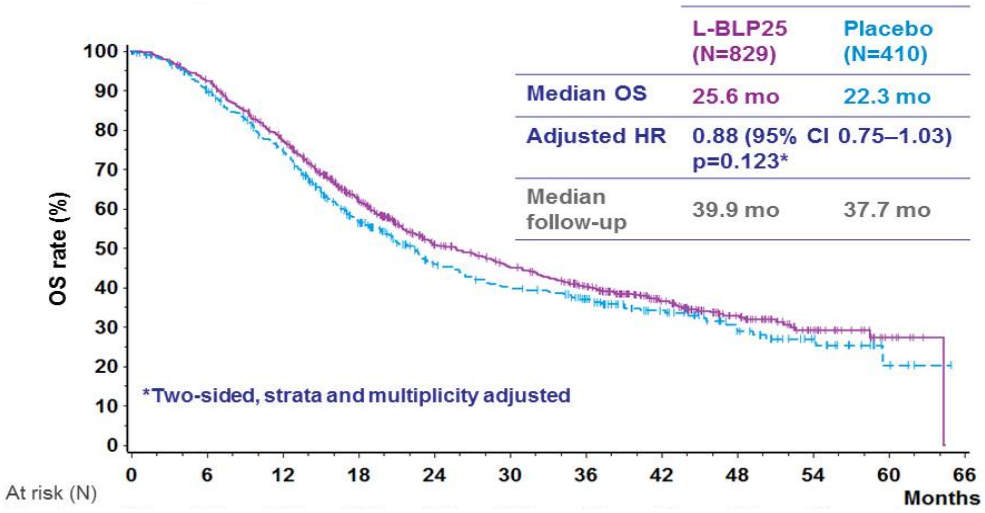


Primary endpoint: Overall survival

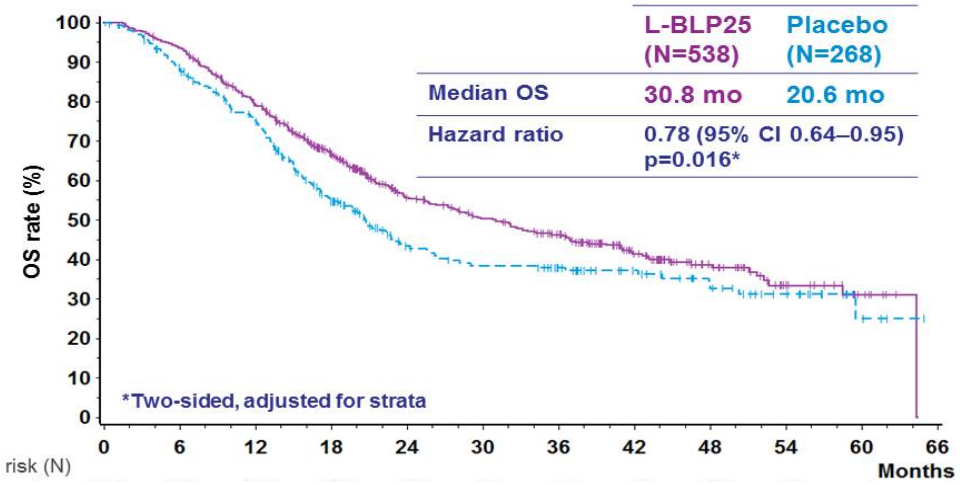
Butts et al. J Clin Oncol 31. 2013 (suppl: abstr 7500)

START trial: phase III study of L-BLP25 immunotherapy for unresectable stage III NSCLC

Overall survival in all patients



Overall survival in concurrent CRT subgroup

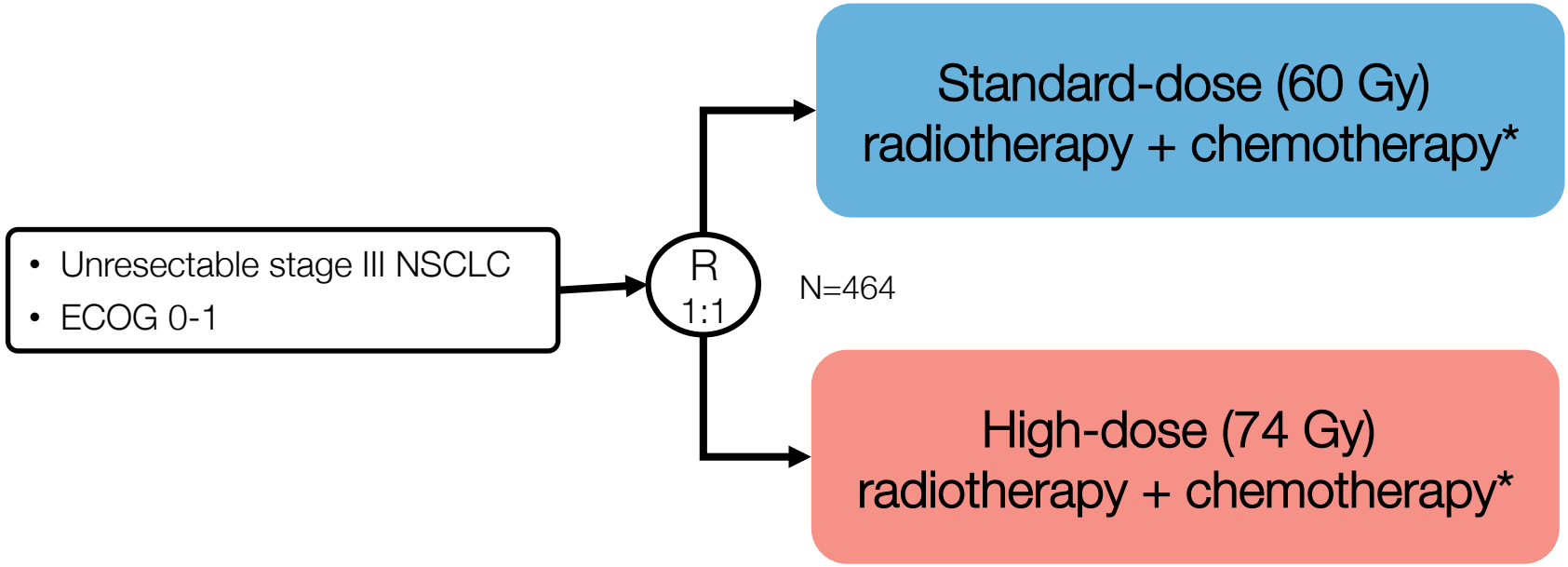


Median overall survival	L-BLP25	Placebo	HR (95% CI)	p value
All patients	25.6 m	22.3 m	0.88 (0.75–1.03)	0.123
Concurrent chemo/RT	30.8 m	20.6 m	0.78 (0.64–0.95)	0.016
Sequential chemo/RT	19.4 m	24.6 m	1.12 (0.87-1.44)	0.38

Butts et al. J Clin Oncol 31, 2013 (suppl; abstr 7500)

Standard-dose (60Gy) *vs* high-dose (74Gy) chemoradiotherapy for stage III NSCLC

Objective: to evaluate OS with high-dose vs. standard-dose conformal radiation therapy with concurrent chemotherapy in patients with stage III NSCLC



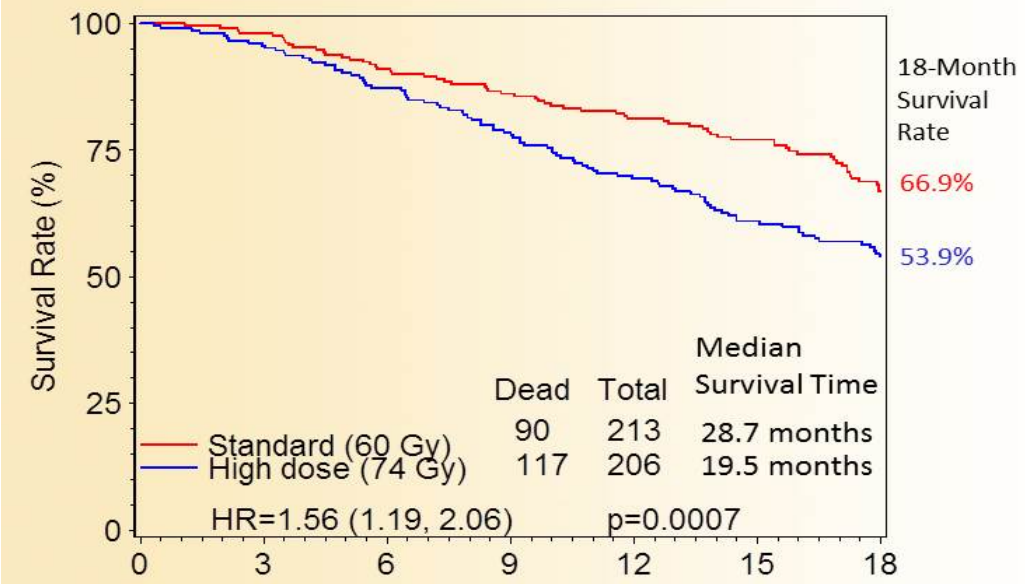
Primary endpoint: Overall survival

* Carboplatin + Paclitaxel ± Cetuximab

Bradley et al. J Clin Oncol 31, 2013 (suppl; abstr 7501)

Standard-dose (60Gy) *vs* high-dose (74Gy) chemoradiotherapy for stage III NSCLC

Overall survival

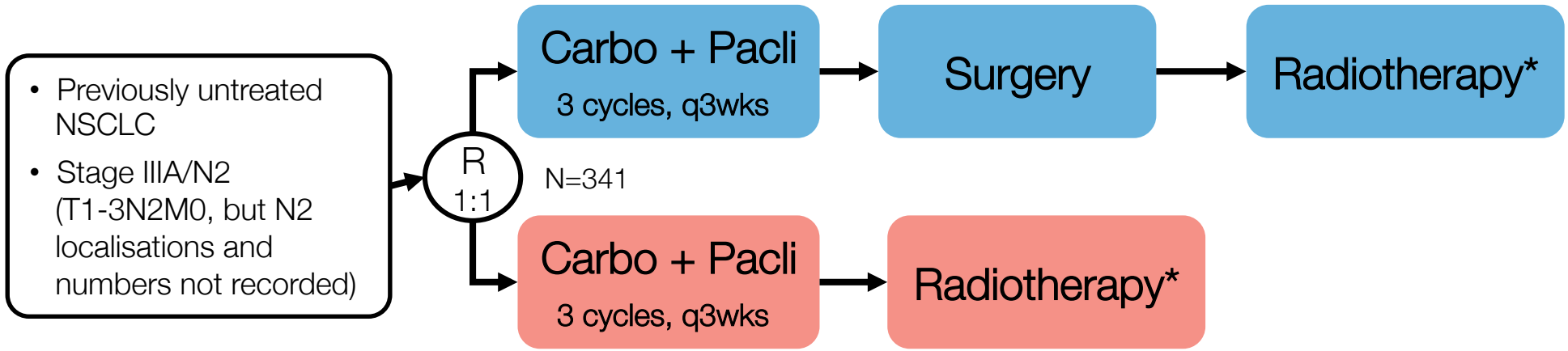


	Standard dose	High dose	HR	p value
OS, months	28.7	19.5	1.56	0.0007
Failure/total	67%	77%	1.3	0.0116
Local	31%	39%	1.37	0.0319
Distant	46%	50%	1.15	0.1576

Bradley et al. J Clin Oncol 31, 2013 (suppl; abstr 7501)

Role of surgery in T1-3N2M0 NSCLC (Nordic Thoracic Oncology Group trial)

Objective: to investigate effect on OS of the addition of surgery among patients with stage III/ N2 NSCLC treated with chemotherapy and radiotherapy



Primary endpoint: overall survival

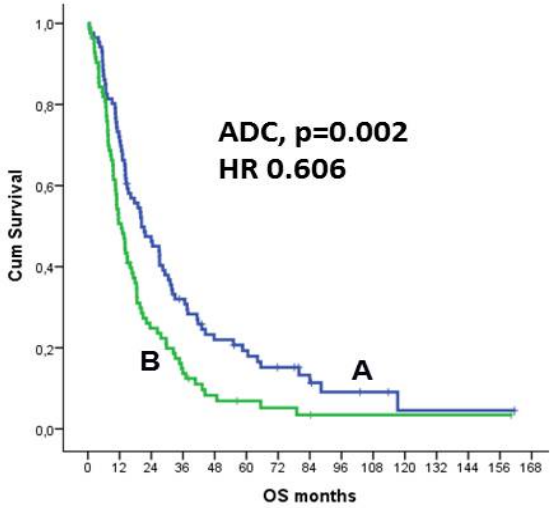
* RT was given 4 weeks after surgery or immediately after chemotherapy and included either 2 Gy x 30 fractions (60 Gy) or 1.7 Gy bid for 18 days (61.2 Gy)

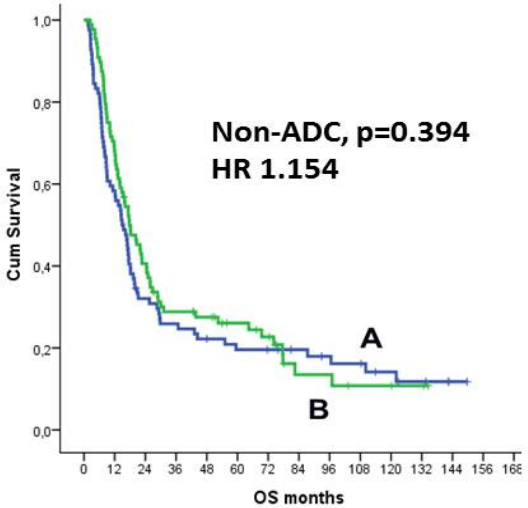
Sørensen et al. J Clin Oncol 31. 2013 (suppl: abstr 7504)

Role of surgery in T1-3N2M0 NSCLC (Nordic Thoracic Oncology Group trial)

Median overall survival	n	Surgery *	No surgery	HR	p
All patients	341	17.3 m	14.9 m	0.866	0.218
AdenoCA subgroup	169	20.3 m	12.7 m	0.606	0.002
Non-adenoCA subgroup	172	14.9 m	17.7 m	1.154	0.394
T1N2	61	31.7 m	18.4 m	0.472	0.009
T2N2	205	15.4 m	14.9 m	-	0.767
T3N2	75	13.4 m	12.5 m	-	0.930

* Surgery was possible in 78% of pts (complete resection in 71%)





Sørensen et al. J Clin Oncol 31, 2013 (suppl; abstr 7504)

Role of surgery in T1-3N2M0 NSCLC (Nordic Thoracic Oncology Group trial)

Median overall survival	n	Surgery *	No surgery	HR	p
All patients	341	17.3 m	14.9 m	0.866	0.218
AdenoCA subgroup	169	20.3 m	12.7 m	0.606	0.002
Non-adenoCA subgroup	172	14.9 m	17.7 m	1.154	0.394
T1N2	61	31.7 m	18.4 m	0.472	0.009
T2N2	205	15.4 m	14.9 m	-	0.767
T3N2	75	13.4 m	12.5 m	-	0.930

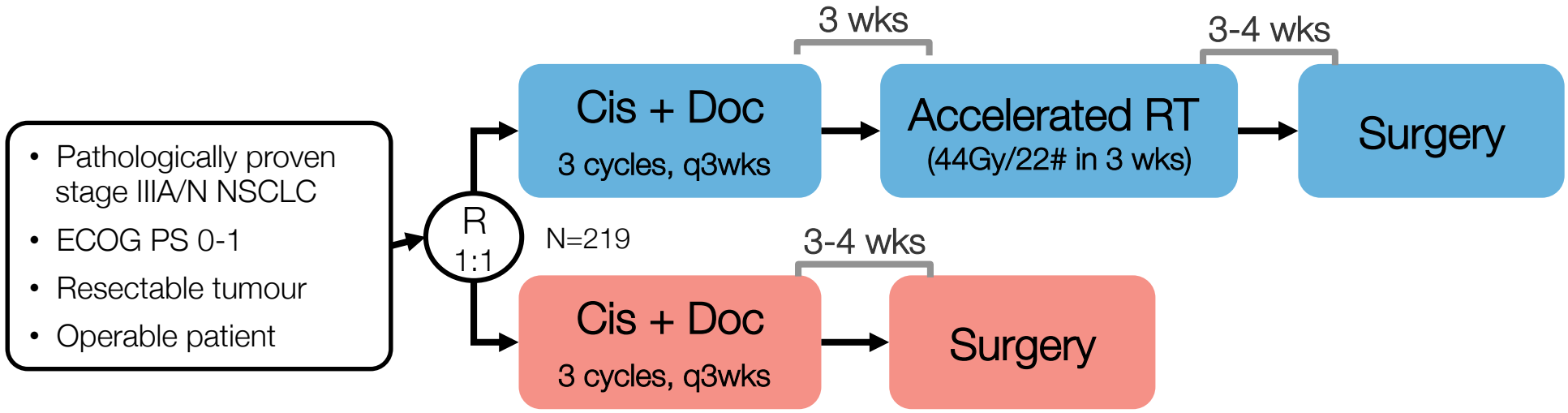
* Surgery was possible in 78% of pts (complete resection in 71%)

- Overall the addition of surgery to “chemoradiation with curative intent” does not improve survival
- In the adenocarcinoma subgroup (esp. T1N2 tumors) the survival in the trimodality arm was better compared to the bimodality

Sørensen et al. J Clin Oncol 31, 2013 (suppl; abstr 7504)

Role of preoperative RT in stage IIIA/N2 NSCLC (SAKK 16/00)

Objective: to investigate effect on OS of the addition of preoperative radiotherapy among patients with stage III/N2 NSCLC treated with induction chemotherapy followed by surgery

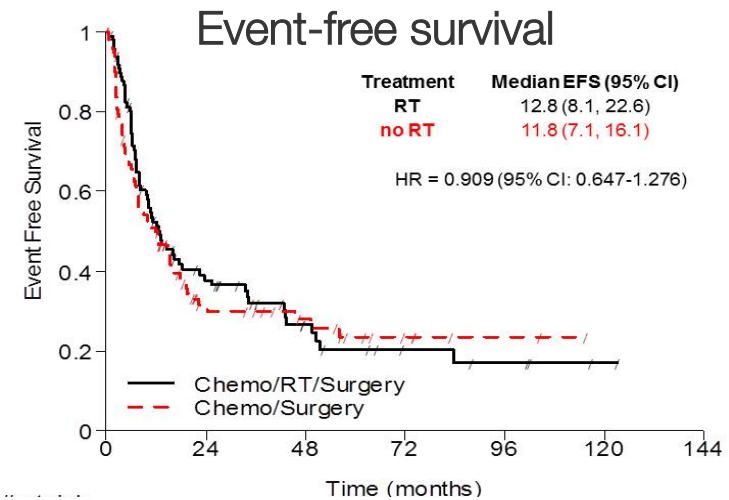


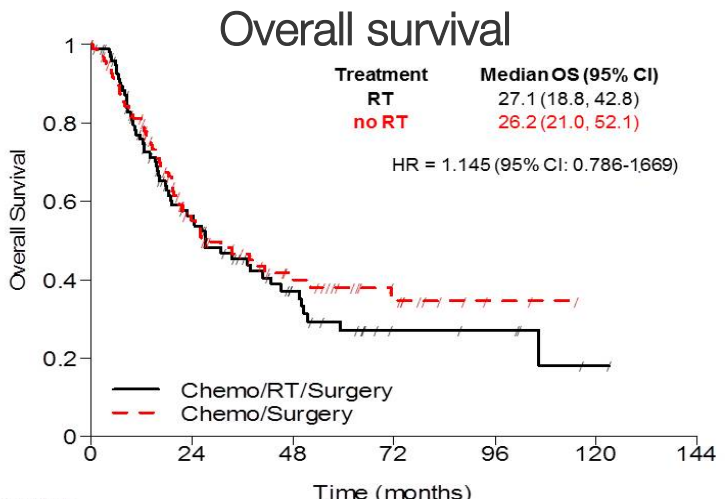
Primary endpoint: Event-free survival

At 3rd interim analysis the futility boundary was crossed → trial stopped

Pless et al. J Clin Oncol 31. 2013 (suppl: abstr 7503)

Role of preoperative RT in stage IIIA/N2 NSCLC (SAKK 16/00)





	CT+RT+S	CT+S	HR (95% CI)
Resected pts	82%	81%	
R0-resection	90%	80%*	
Median EFS	12.8 m	11.8 m	0.91 (0.65–1.28)
Median OS	27.1 m	26.2 m	1.15 (0.79–1.67)

- Radiotherapy did not improve EFS or OS, nor did it reduce the local failure rate
- However, OS rates are high with a median of 27 months

* R1-R2 resections received PORT

Pless et al. J Clin Oncol 31. 2013 (suppl: abstr 7503)

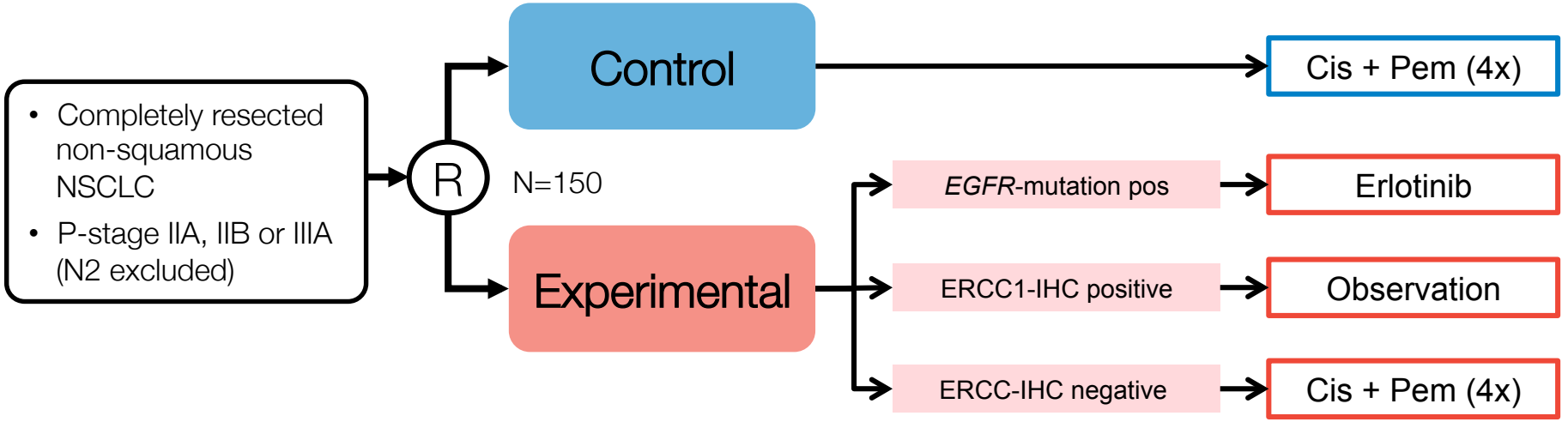
How to improve outcome in stage III NSCLC?

- Vaccination? Not yet
- More irradiation? No
- Adding surgery to radiotherapy? No
- Adding radiotherapy to surgery? No

Customized chemotherapy for NSCLC

- ERCC1-IHC
- RRM1 and ERCC1 protein expression
- BRCA1 and RAP80 mRNA expression

Phase II trial of customized adjuvant chemotherapy in resected NSCLC (TASTE trial)

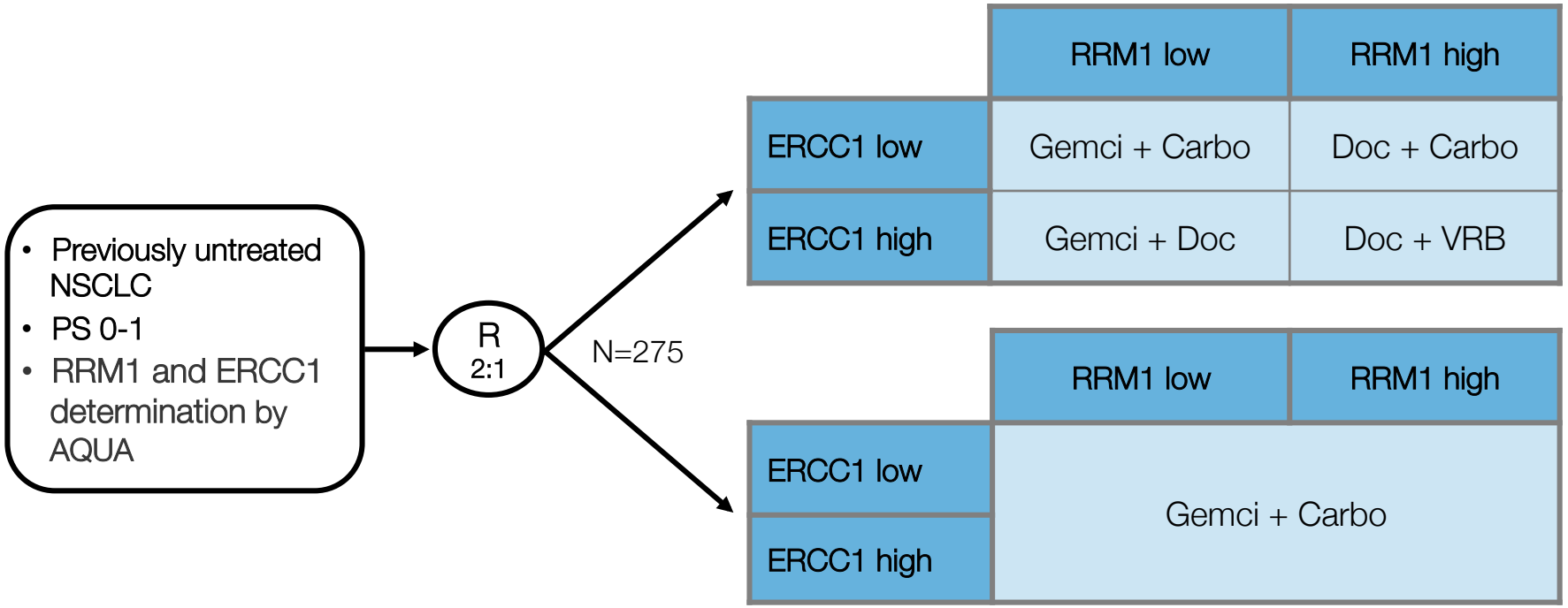


- Key results
  - ERCC1 was positive in 38 patients (19 in each arm), EGFR mutation was identified in 10 patients (3 in control arm, 7 in customised arm)
  - Feasibility was demonstrated with all patients starting therapy within 2 months of surgery
- Key conclusions
  - Although the feasibility of a national biology-driven trial in the adjuvant setting study was demonstrated the study was cancelled due to the unexpected unreliability of the ERCC1 IHC read-out

Soria et al. J Clin Oncol 31, 2013 (suppl; abstr 7505)

Phase III trial of molecular analysis-directed chemotherapy for advanced NSCLC

Objective: to investigate feasibility of using ERCC1 and RRM1 as predictive markers for response to platinum agents and gemcitabine in patients with advanced NSCLC

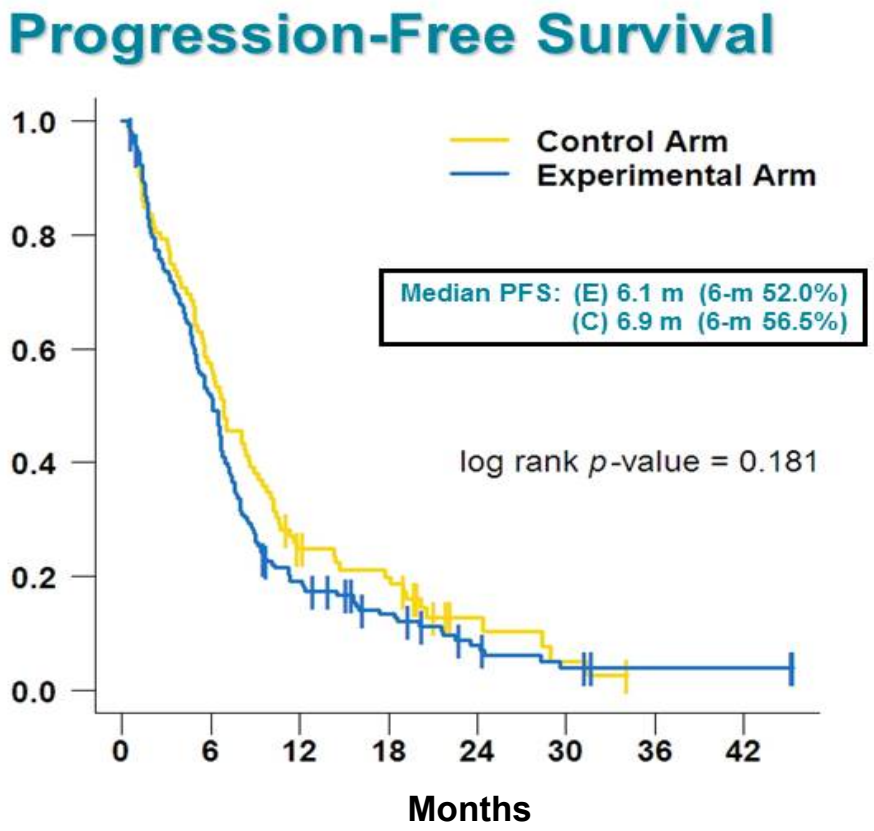


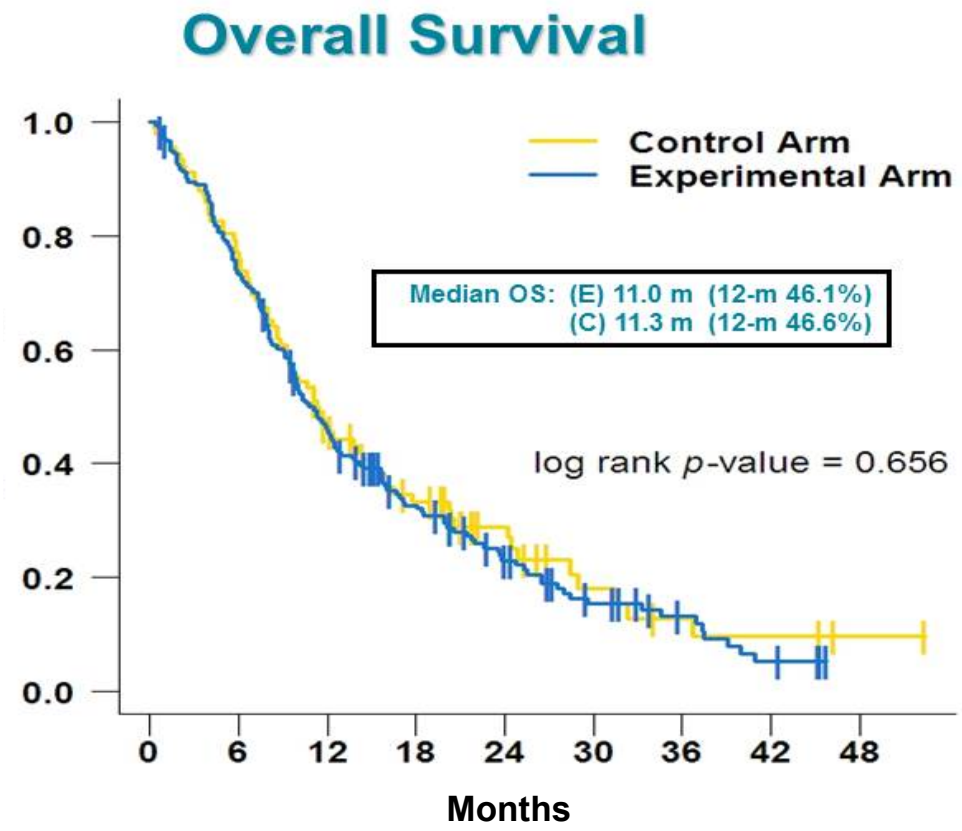
Primary endpoint: PFS

NB: up to 6 cycles of chemo; no maintenance; no bevacizumab

Bepler et al. J Clin Oncol 31, 2013 (suppl; abstr 8001)

Phase III trial of molecular analysis-directed chemotherapy for advanced NSCLC



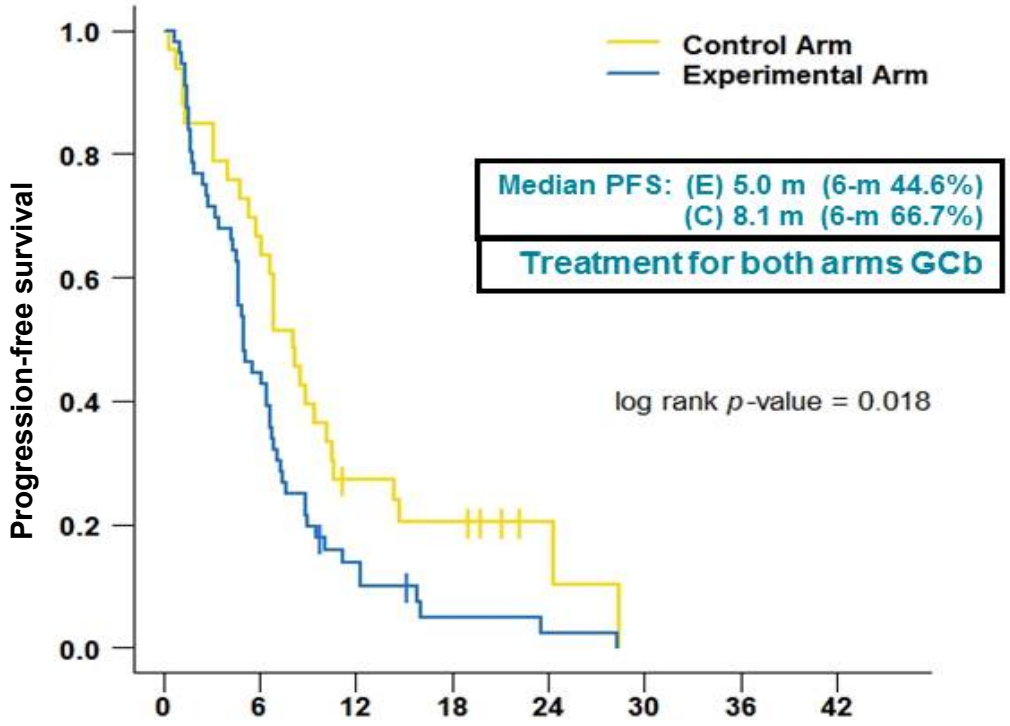


Treatment assignment based on molecular analyses was feasible in 98% of tumour specimens of NSCLC, but did not result in improved survival.

Bepler et al. J Clin Oncol 31, 2013 (suppl; abstr 8001)

Phase III trial of molecular analysis-directed chemotherapy for advanced NSCLC

PFS in subgroup of RRM1-low and ERCC1 low tumors

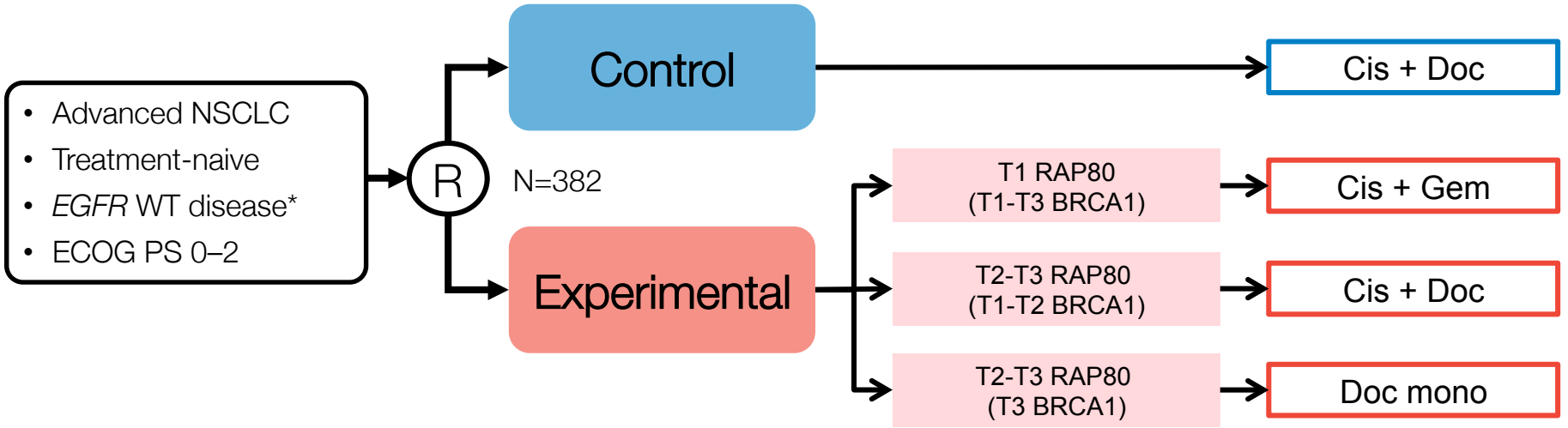


Beware of unknown and confounding imbalances between treatment arms, even in case of treatment selection based on molecular profiling.

Bepler et al. J Clin Oncol 31, 2013 (suppl; abstr 8001)

Phase III of chemotherapy customization based on BRCA1-RAP80 expression (BREC)

Objective: to investigate feasibility of using BRCA1 and RAP80 mRNA expression as predictive markers for response to platinum and taxane chemotherapy in patients with advanced NSCLC

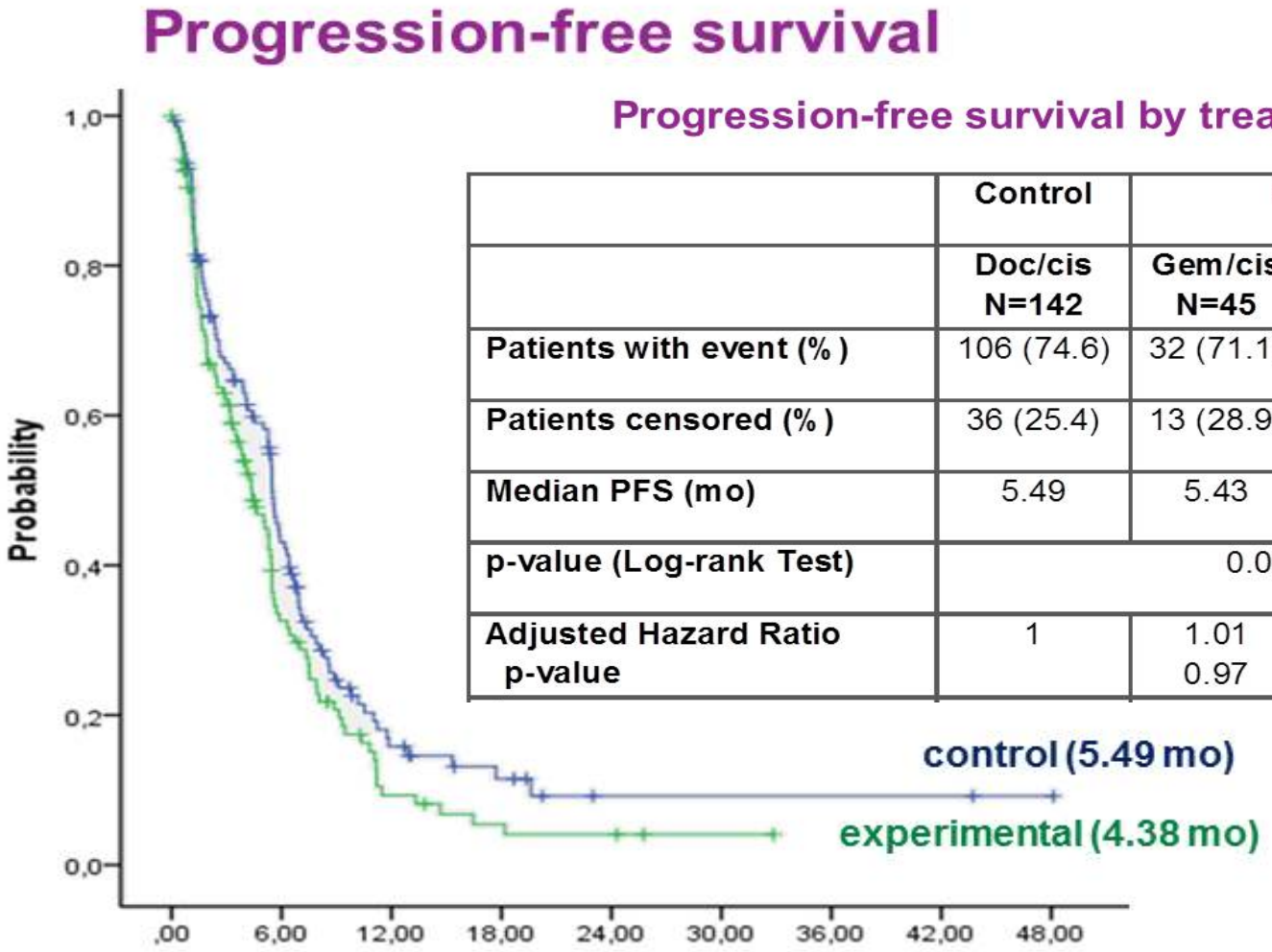


Primary endpoint: PFS

Planned interim-analysis on 279 pts

Moran et al. J Clin Oncol 31, 2013 (suppl; abstr LBA8002)

Phase III of chemotherapy customization based on BRCA1-RAP80 expression (BREC)



Progression-free survival by treatment arm

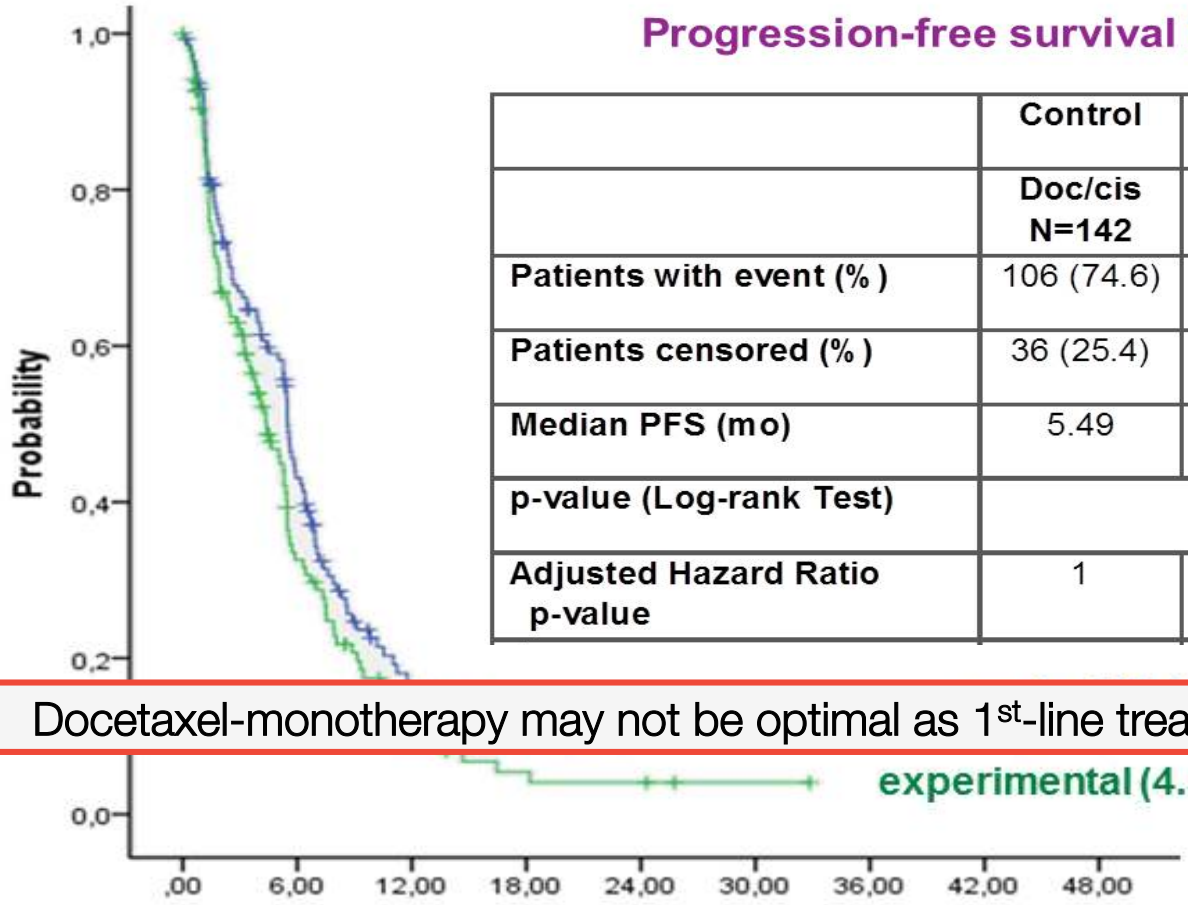
	Control	Experimental		
	Doc/cis N=142	Gem/cis N=45	Doc/cis N=49	Doc N=43
Patients with event (%)	106 (74.6)	32 (71.1)	40 (81.6)	37 (86)
Patients censored (%)	36 (25.4)	13 (28.9)	9 (18.4)	6 (14)
Median PFS (mo)	5.49	5.43	5.49	2.50
p-value (Log-rank Test)	0.003			
Adjusted Hazard Ratio p-value	1	1.01 0.97	1.05 0.83	2.65 0.0001

HR 1.35 (*P* .03)

Moran et al. J Clin Oncol 31, 2013 (suppl; abstr LBA8002)

Phase III of chemotherapy customization based on BRCA1-RAP80 expression (BREC)

Progression-free survival



Progression-free survival by treatment arm

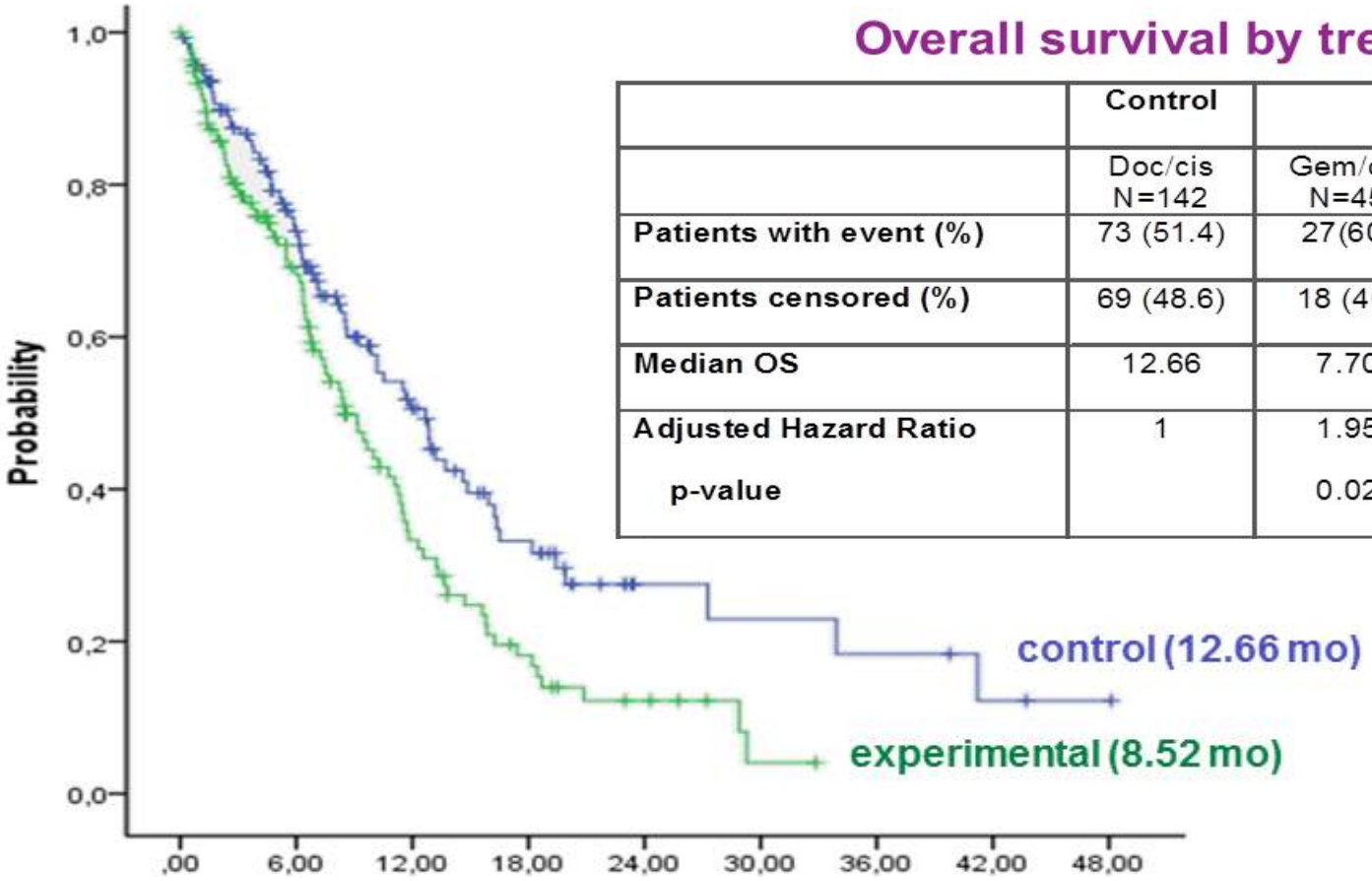
	Control	Experimental		
	Doc/cis N=142	Gem/cis N=45	Doc/cis N=49	Doc N=43
Patients with event (%)	106 (74.6)	32 (71.1)	40 (81.6)	37 (86)
Patients censored (%)	36 (25.4)	13 (28.9)	9 (18.4)	6 (14)
Median PFS (mo)	5.49	5.43	5.49	2.50
p-value (Log-rank Test)	0.003			
Adjusted Hazard Ratio p-value	1	1.01 0.97	1.05 0.83	2.65 0.0001

Docetaxel-monotherapy may not be optimal as 1st-line treatment in PS 0-1 pts (!)

Moran et al. J Clin Oncol 31, 2013 (suppl; abstr LBA8002)

Phase III of chemotherapy customization based on BRCA1-RAP80 expression (BREC)

Overall survival by treatment arm



Overall survival by treatment arm

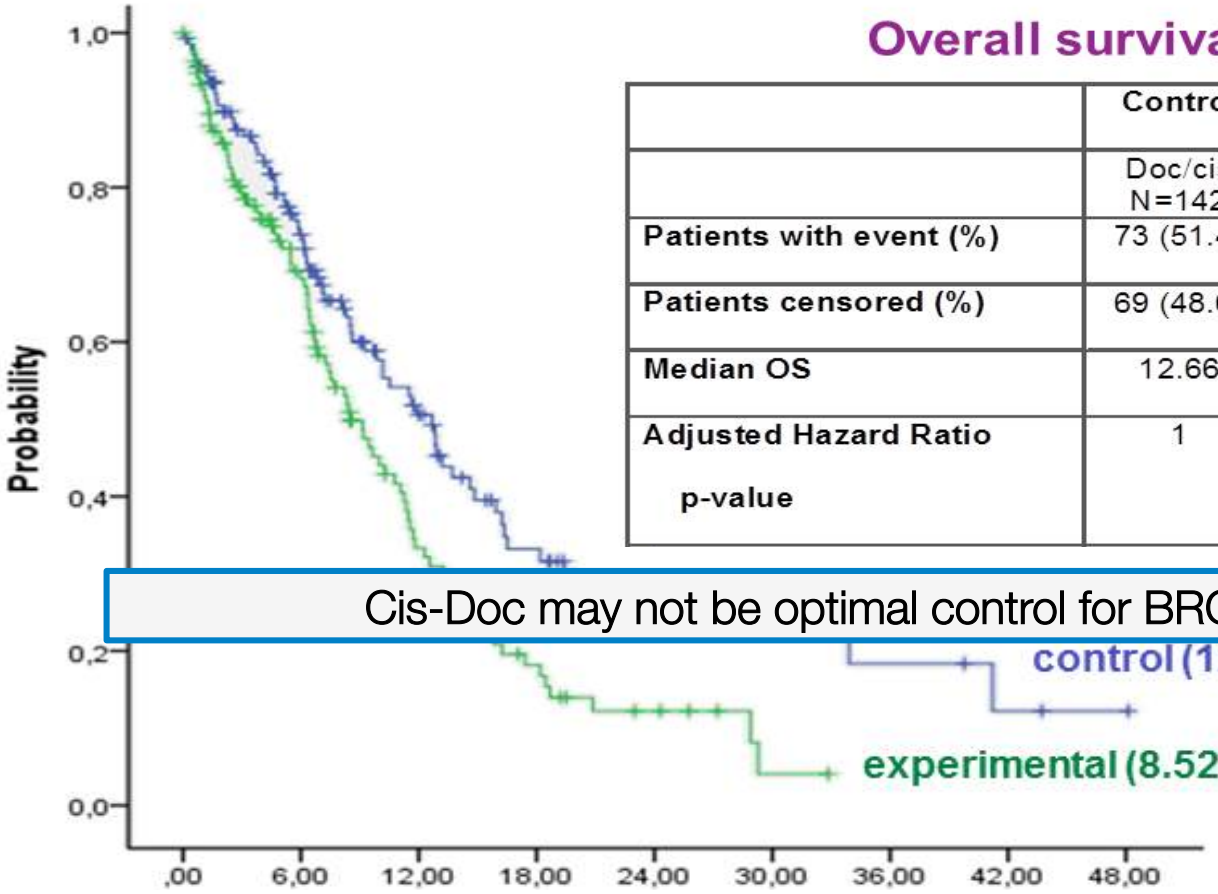
	Control	Experimental		
	Doc/cis N=142	Gem/cis N=45	Doc/cis N=49	Doc N=43
Patients with event (%)	73 (51.4)	27(60)	30(61.2)	32(74.4)
Patients censored (%)	69 (48.6)	18 (40)	19(38.8)	11(25.6)
Median OS	12.66	7.70	11.25	7.24
Adjusted Hazard Ratio	1	1.95	1.31	2.54
p-value		0.02	0.28	0.001

HR 1.85 (*P* <.0001)

Moran et al. J Clin Oncol 31, 2013 (suppl; abstr LBA8002)

Phase III of chemotherapy customization based on BRCA1-RAP80 expression (BREC)

Overall survival by treatment arm



Overall survival by treatment arm

	Control	Experimental		
	Doc/cis N=142	Gem/cis N=45	Doc/cis N=49	Doc N=43
Patients with event (%)	73 (51.4)	27(60)	30(61.2)	32(74.4)
Patients censored (%)	69 (48.6)	18 (40)	19(38.8)	11(25.6)
Median OS	12.66	7.70	11.25	7.24
Adjusted Hazard Ratio	1	1.95	1.31	2.54
p-value		0.02	0.28	0.001

Cis-Doc may not be optimal control for BRCA1customization (?)

Moran et al. J Clin Oncol 31, 2013 (suppl; abstr LBA8002)

Customized chemotherapy for NSCLC

- Phase III trials of chemo-customization are feasible, but have not yet resulted in improved outcomes.
- A patient with NSCLC is more than the molecular profile of the tumour!!!

Maintenance treatment for advanced non-squamous NSCLC

- Paclitaxel or Pemetrexed as platinum partner?
- Pemetrexed and/or bevacizumab maintenance?

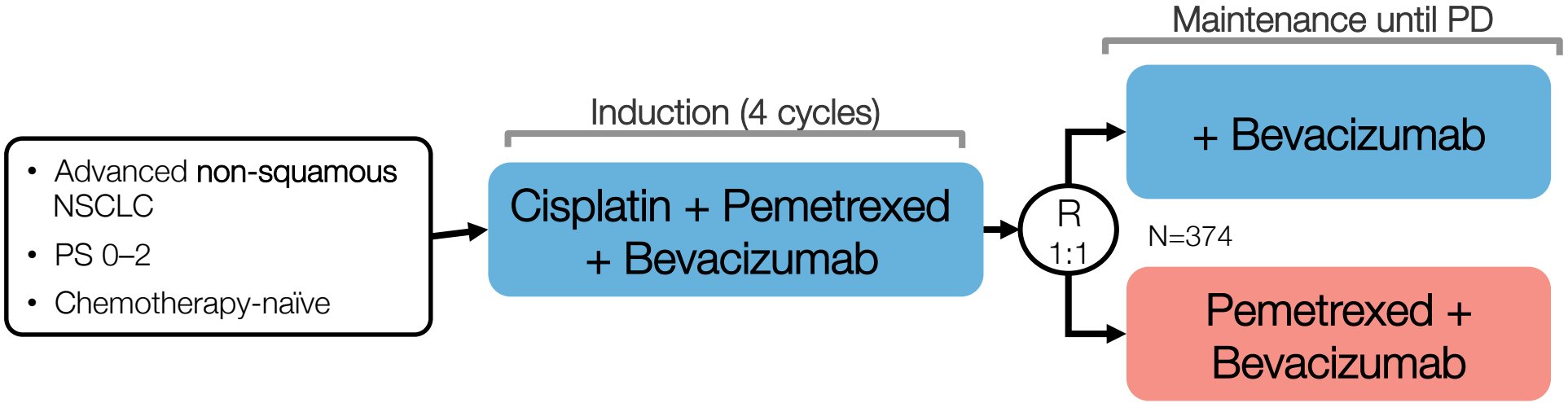
Maintenance in non-squamous NSCLC

		Median PFS (m)	HR	Median OS (m)	HR
ECOG	CarboPacli → Placebo *vs* CarboPacliBev→Bev	4.5 *vs* 6.2	0.66 *	10.3 *vs* 12.3	0.79 *
Avail	CisGemci → Placebo *vs* CisGemciBev→Bev	6.1 *vs* 6,5	0.82 *	13.1 *vs* 13.4	1.03
Paramount	CisPem→ Placebo *vs* CisPem→Pem	5.6 *vs* 6.9	0.59 *	14.0 *vs* 16.9	0.78 *

* *P* <0.005

Avaperl trial: 2 different maintenance regimens
(Cis+Pem+Bev followed by Pem+Bev *vs* Bev)

Objective: to evaluate effect on survival of maintenance treatment with bevacizumab +pemetrexed compared with bevacizumab in advanced non-squamous NSCLC.

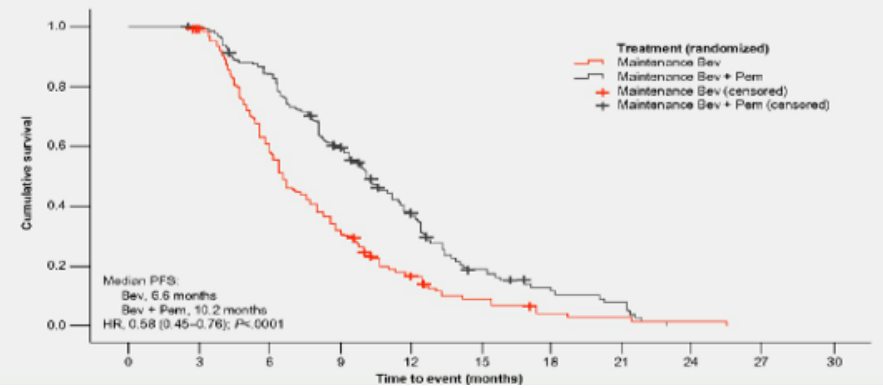


Primary endpoint: PFS

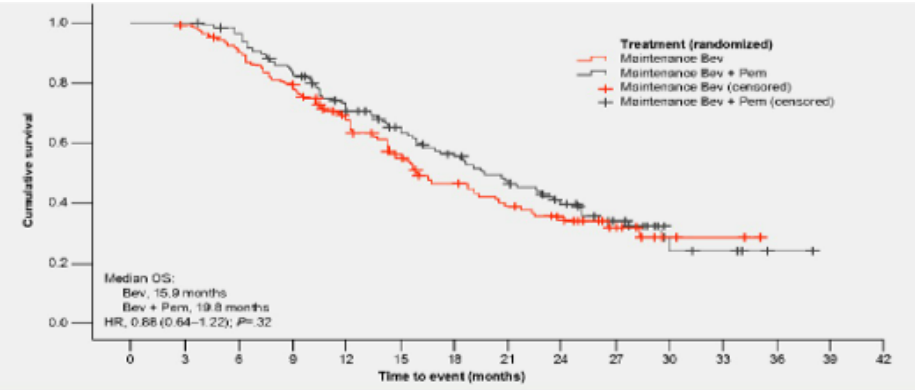
Rittmeyer et al. J Clin Oncol 31. 2013 (suppl: abstr 8014)

AvaperI trial: 2 different maintenance regimens
(Cis+Pem+Bev followed by Pem+Bev *vs* Bev)

PFS from induction treatment



OS from induction treatment



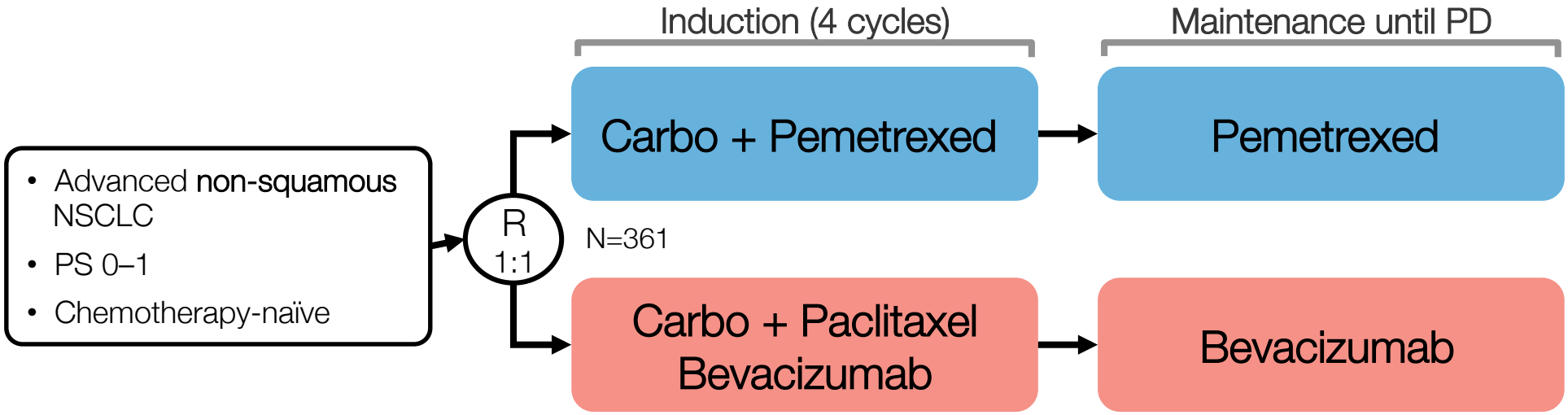
	Bev	Pem + Bev	HR	p
Median PFS				
from randomisation	3.7 m	7.4 m	0.57	<0.0001
from induction	6.6 m	10.2 m	0.58	<0.0001
Median OS				
from randomisation	13.2 m	17.1 m	0.87	0.29
from induction	15.9 m	19.8 m	0.88	0.32

- Maintenance with Pem+Bev results in superior PFS compared to Bev alone
- No improvement in OS demonstrated

Rittmeyer et al. J Clin Oncol 31. 2013 (suppl: abstr 8014)

Pronounce trial: 2 different maintenance regimens
(Carbo+Pem→Pem *vs* Carbo+Pacli+Bev→Bev)

Objective: phase III superiority trial in advanced non-squamous NSCLC (with subgroup analysis of elderly pts).

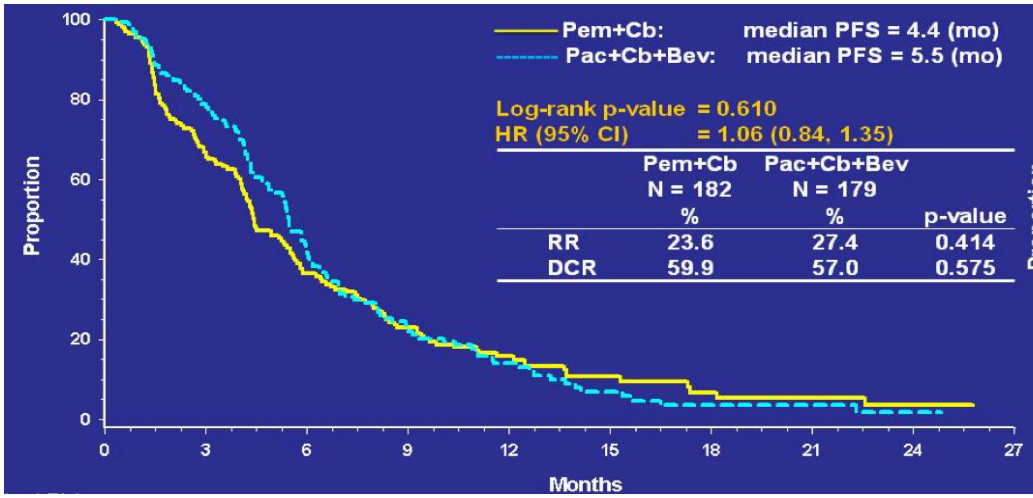


Primary endpoint: PFS without grade 4 AE
Secondary endpoint: PFS, OS, ORR, safety

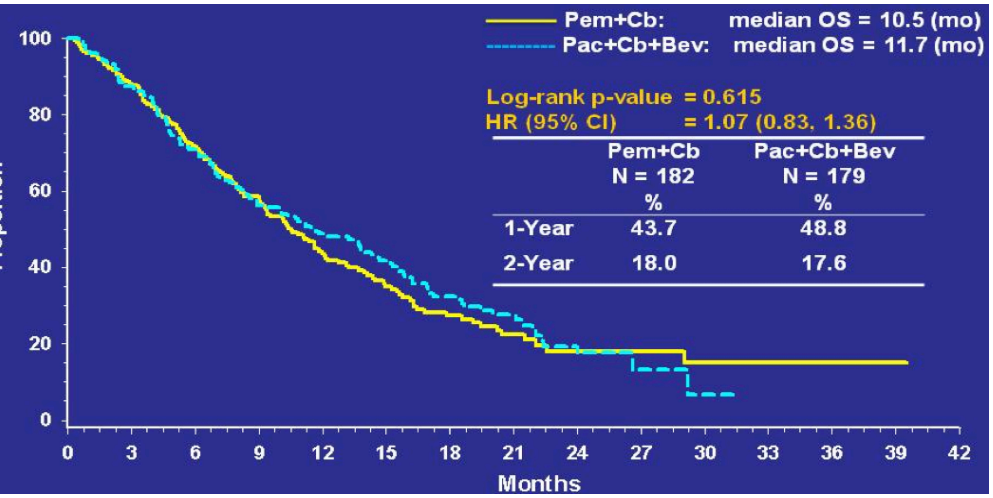
Zinner et al. J Clin Oncol 31. 2013 (suppl: abstr LBA8003)

Pronounce trial: 2 different maintenance regimens
(Carbo+Pem→Pem *vs* Carbo+Pacli+Bev→Bev)

Progression-free survival



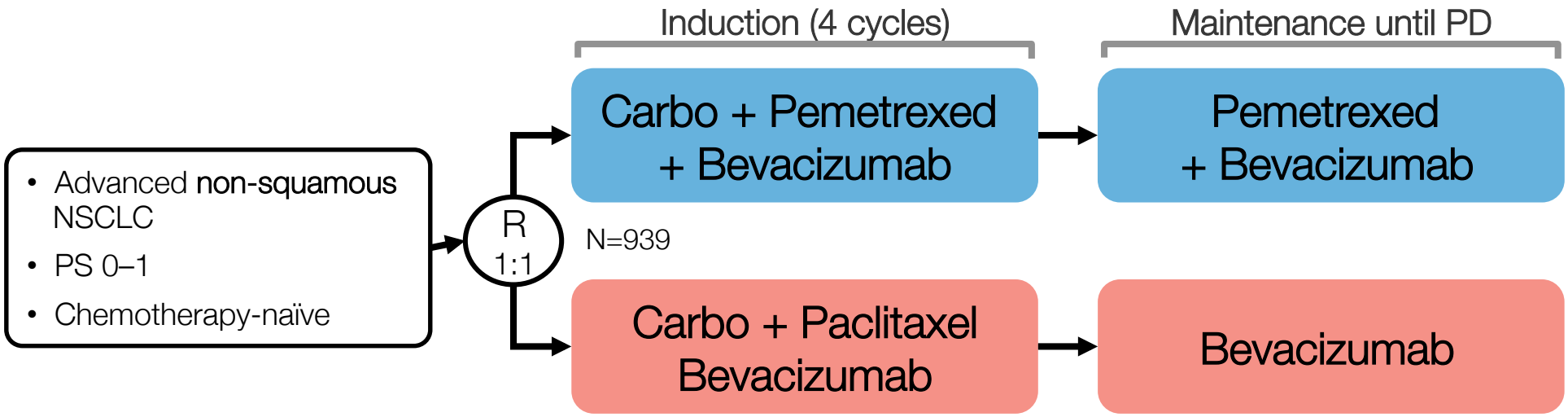
Overall survival



- The primary endpoint (G4PFS) was not met (3.9m *vs* 2.9m; HR 0,85, P 0,176)
- There were no differences for any of the secondary endpoints (PFS, OS, RR)
- There were no unexpected toxicities and both regimens demonstrated tolerability
- Carbo+Pem→Pem is not superior to Carbo+Pacli+Bev→Bev

Zinner et al. J Clin Oncol 31. 2013 (suppl: abstr LBA8003)

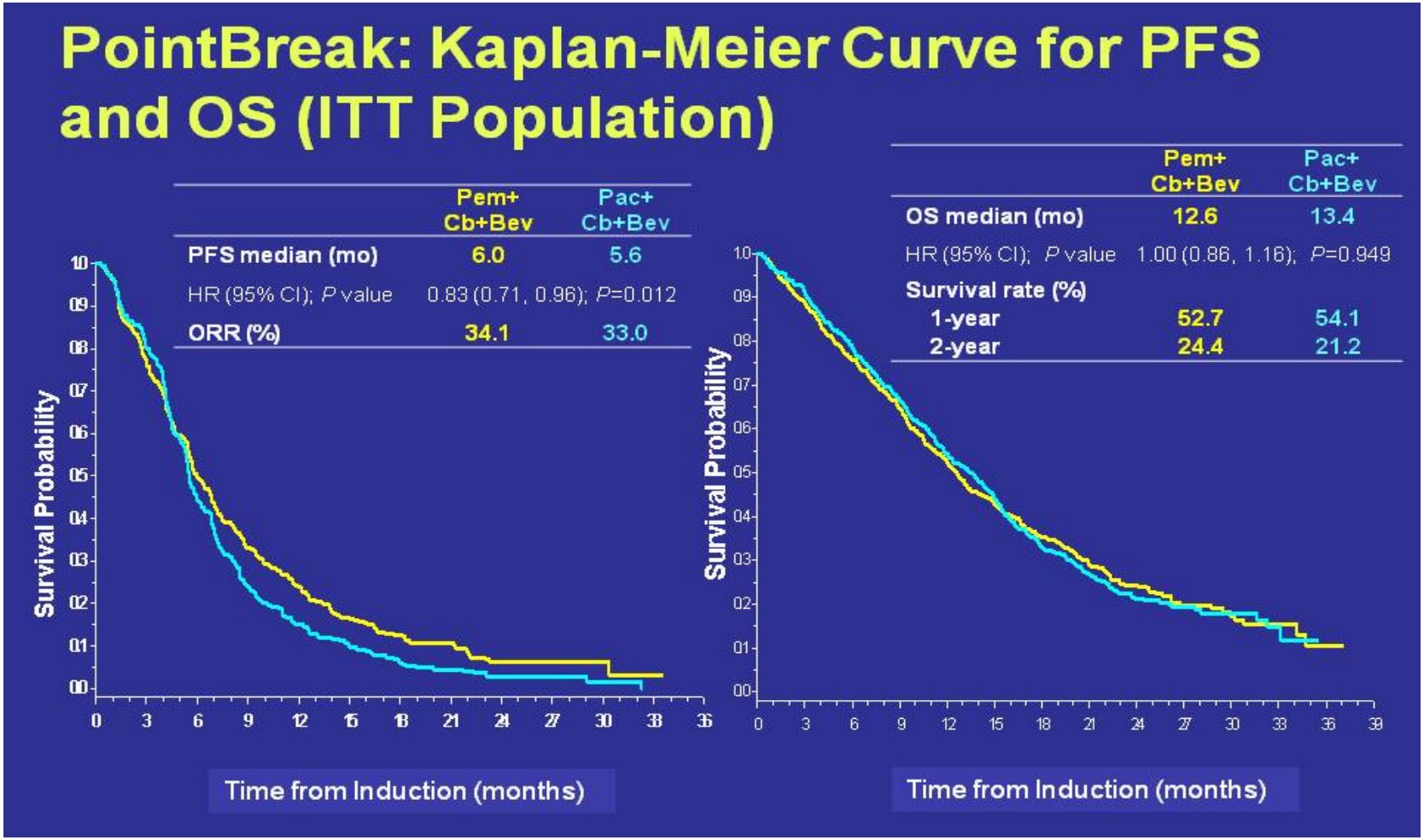
PointBreak trial: 2 different maintenance regimens
(Carbo+Pem+Bev→Pem+Bev *vs* Carbo+Pacli+Bev→Bev)



Primary endpoint: OS
Secondary endpoint: PFS, TTP, ORR, PRO, safety
Exploratory analyses: OS and PFS ~age subgroups

Socinski et al. J Clin Oncol 31, 2013 (suppl; abstr 8004)

PointBreak trial: 2 different maintenance regimens
(Carbo+Pem+Bev→Pem+Bev *vs* Carbo+Pacli+Bev→Bev)



Socinski et al. J Clin Oncol 31, 2013 (suppl; abstr 8004)

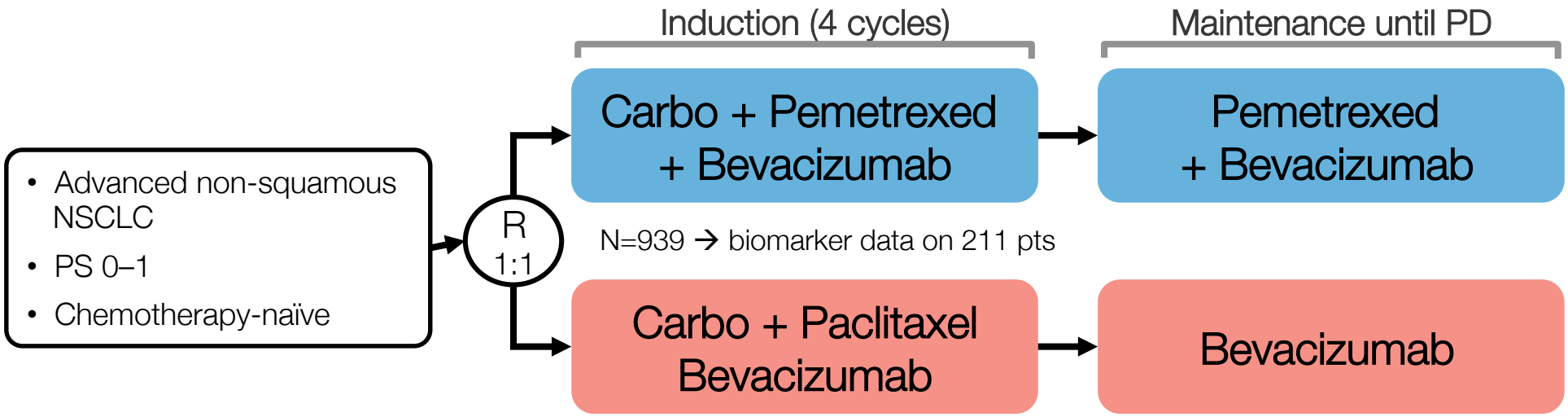
Maintenance in non-squamous NSCLC: lack of consistency?

		Median PFS (m)	HR	Median OS (m)	HR
ECOG	CarboPacli → Placebo *vs* CarboPacliBev→Bev	4.5 *vs* 6.2	0.66 *	10.3 *vs* 12.3	0.79 *
Avail	CisGemci → Placebo *vs* CisGemciBev→Bev	6.1 *vs* 6,5	0.82 *	13.1 *vs* 13.4	1.03
Paramount	CisPem→ Placebo *vs* CisPem→Pem	5.6 *vs* 6.9	0.59 *	14.0 *vs* 16.9	0.78 *
Avaperl	CisPemBev→Bev *vs* CisPemBev→PemBev	6.6 *vs* 10.2	0.58 *	15.9 *vs* 19.8	0.88
Pronounce	Carbo+Pem→Pem *vs* Carbo+Pacli+Bev→Bev	4.4 *vs* 5.5	1.06	10.5 *vs* 11.7	1.07
Pointbreak	Carbo+Pem+Bev→Pem+Bev *vs* Carbo+Pacli+Bev→Bev	6.0 *vs* 5.6	0.83 *	12.6 *vs* 13.4	1.00

* $P < 0.005$

Translational research analysis of PointBreak trial in patients with nonsquamous NSCLC

Objective: to investigate the correlation of biomarkers with OS, PFS and RR in the PointBreak study.



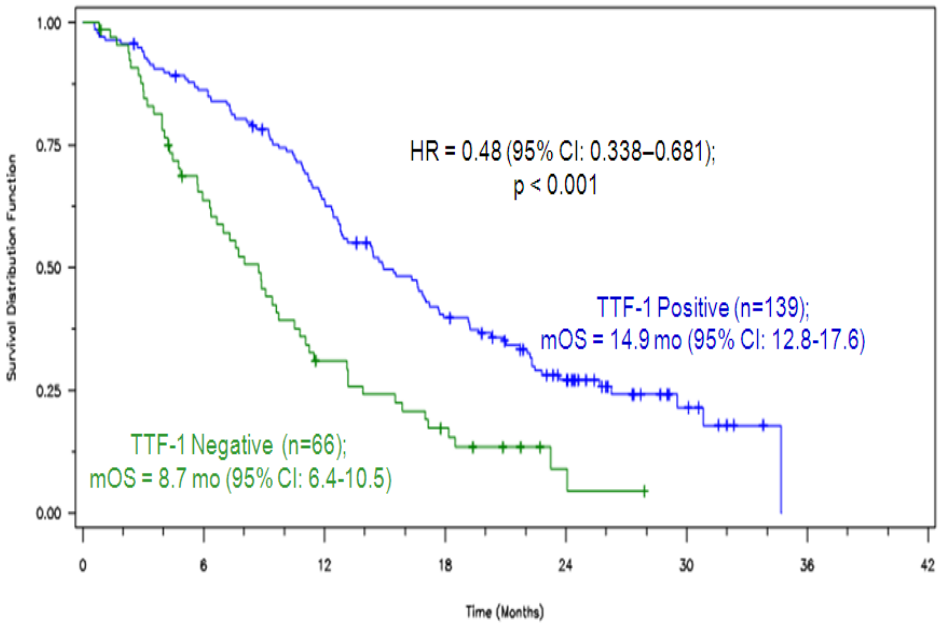
Specimens assessed using IHC (TS, TTF-1 and FR) and EGFR mutation status

Evaluable biomarker data for at least one assay were available for 211 patients

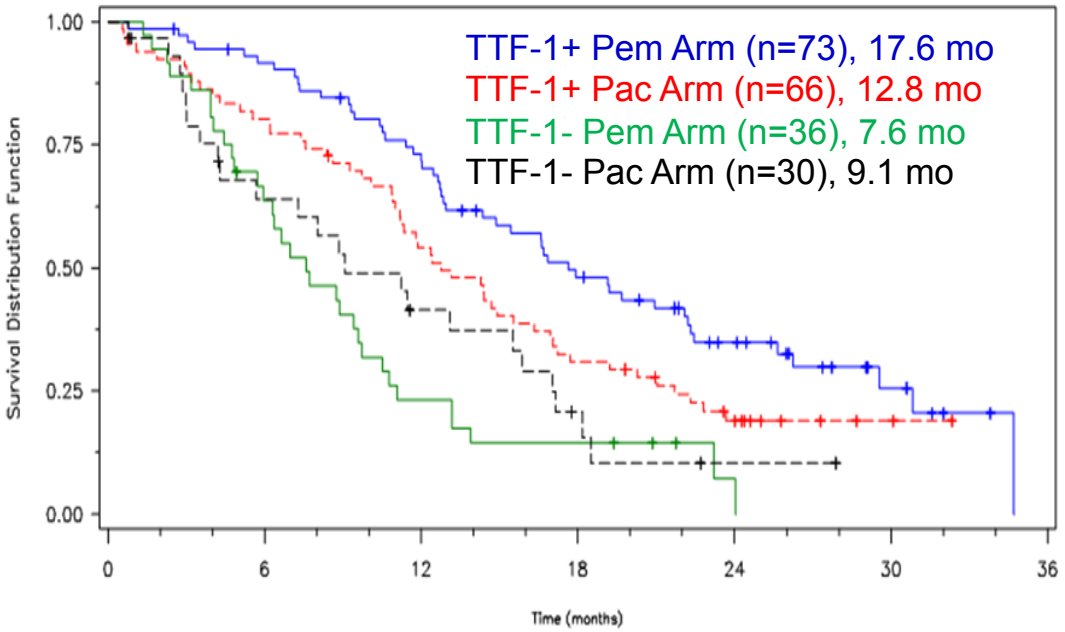
TS: thymidylate synthase; TTF-1 thyroid transcription factor-1; FR: folate receptor-

Translational research analysis of PointBreak trial in patients with nonsquamous NSCLC

Overall survival in all patients



Overall survivall ~ treatment arm



- None of the protein markers (measured by IHC using a positive/negative cut point) demonstrated a significant treatment by marker interaction for OS → presumably underpowered!!
- TTF-1 expression is prognostic in non-squamous tumors treated with chemotherapy
- TTF-1 expression shows a correlation (p 0.08) with PFS and OS following pemetrexed (predictive marker??)

Garon et al. J Clin Oncol 31, 2013 (suppl; abstr 8086)

Maintenance treatment for advanced non-squamous NSCLC

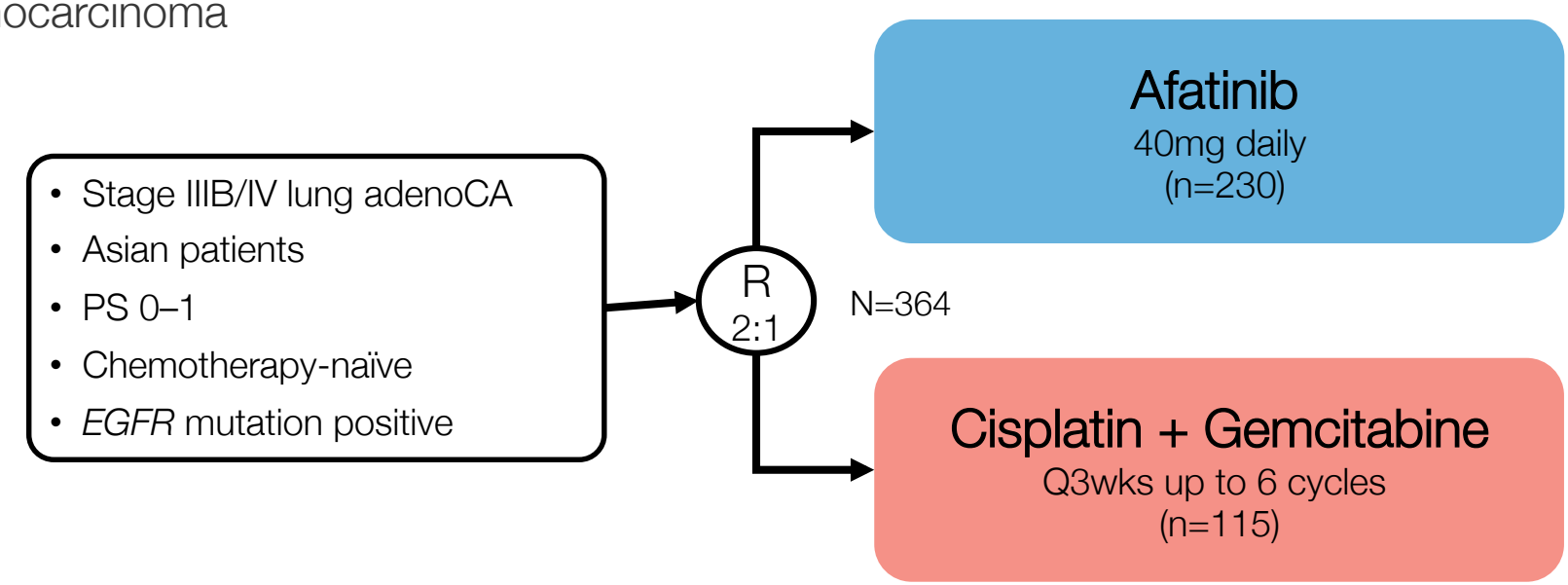
- Pemetrexed as preferred platinum partner in TTF-1 positive NSCLC
- Maintenance?

Targeted treatments for NSCLC

- EGFR-TKI
- Immunotherapy
- New targets

LUX-Lung 6: afatinib *vs* cisplatin + gemcitabine as 1st-line treatment for *EGFR*-mutation^{+} NSCLC

Objective: to compare the efficacy and safety of first-line treatment with afatinib versus gemcitabine+cisplatin in Asian patients with EGFR mutation-positive stage IIIB/IV lung adenocarcinoma

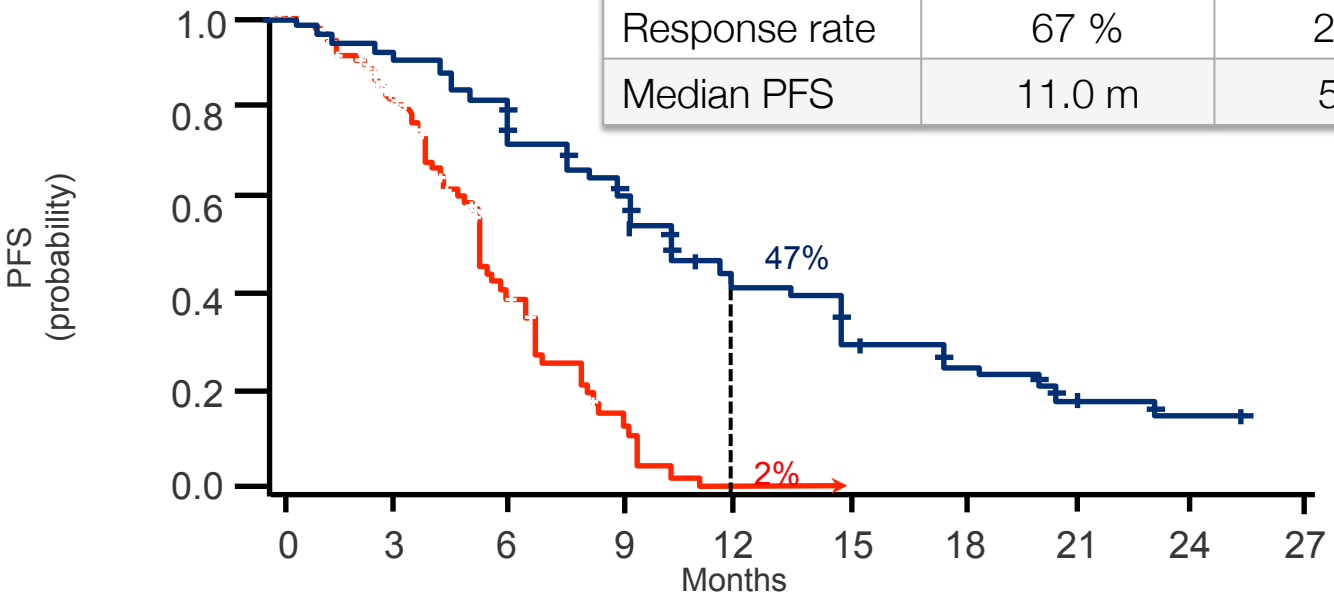


Primary endpoint: PFS

Wu et al. J Clin Oncol 31. 2013 (suppl: abstr 8016)

LUX-Lung 6: afatinib *vs* cisplatin + gemcitabine as 1st-line treatment for *EGFR*-mutation$^+$ NSCLC

	Afatinib	Cis-Gemci	
Response rate	67 %	23 %	p<0.0001
Median PFS	11.0 m	5.6 m	HR 0.28 (p<0.0001)



- In EGFR mutation-positive Asian patients, afatinib significantly prolonged PFS and was associated with significant improvements in ORR, DCR and better symptom control and quality of life compared with gemcitabine+cisplatin
- AEs were as expected in both arms, with a more favourable safety profile with afatinib

Wu et al. J Clin Oncol 31. 2013 (suppl: abstr 8016)

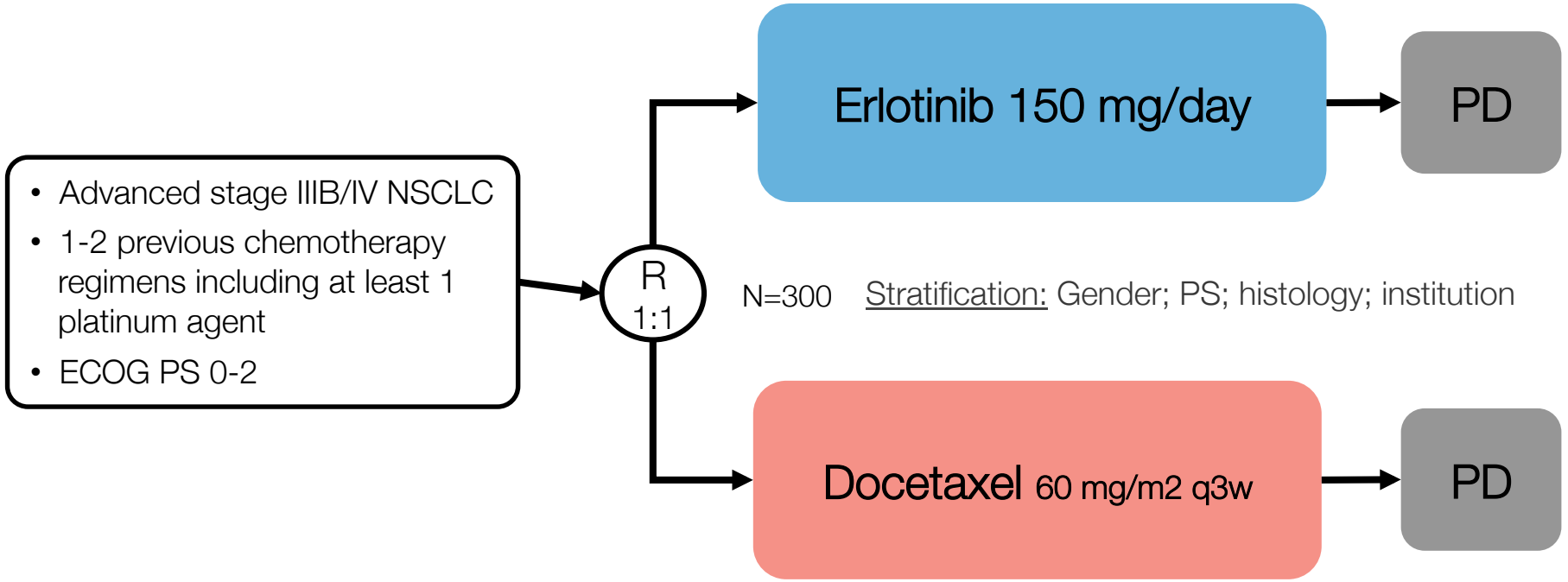
Phase III trials of 1st line EGFR-TKI *vs* chemo in *EGFR* mutation positive NSCLC

Trial	N	Ethnicity	EGFR-TKI	Chemotherapy
IPASS (subgroup)	261	asian	Gefitinib	Cis + Doc (6x)
WJTOG3405	172	asian	Gefitinib	Cis + Doc (6x)
NEJ002	228	asian	Gefitinib	Carbo + Pacli (6x)
OPTIMAL	165	asian	Erlotinib	Carbo + Gemci (4x)
EURTAC	174	caucasian	Erlotinib	Cis/Carbo + Doc/Gemci (4x)
LUX-Lung 3	345	mixed	Afatinib	Cis + Pem (6x)
LUX-Lung 6	364	asian	Afatinib	Cis + Gemci (6x)

Trial	*EGFR* mutations	RR (%)	PFS (m)	HR PFS
IPASS (subgroup)	19Del/L858R + other (8%)	71 *vs* 47	9.6 *vs* 6.3	0.48
WJTOG3405	19Del/L858R	62 *vs* 32	9.2 *vs* 6.3	0.49
NEJ002	19Del/L858R + other (6%)	74 *vs* 31	10.8 *vs* 5.4	0.30
OPTIMAL	19Del/L858R	83 *vs* 36	14.7 *vs* 4.6	0.16
EURTAC	19Del/L858R	58 *vs* 15	9.7 *vs* 5.2	0.37
Lux-Lung 3	19Del/L858R + other (11%)	56 *vs* 23	11.1 *vs* 6.9	0.58
Lux-Lung 6	19Del/L858R + other (11%)	67 *vs* 23	11.0 *vs* 5.6	0.28

DELTA trial: phase III study of erlotinib versus docetaxel as 2nd or 3rd line therapy

Objective: to evaluate erlotinib versus docetaxel in Japanese patients with NSCLC previously treated with ≥1 chemotherapy

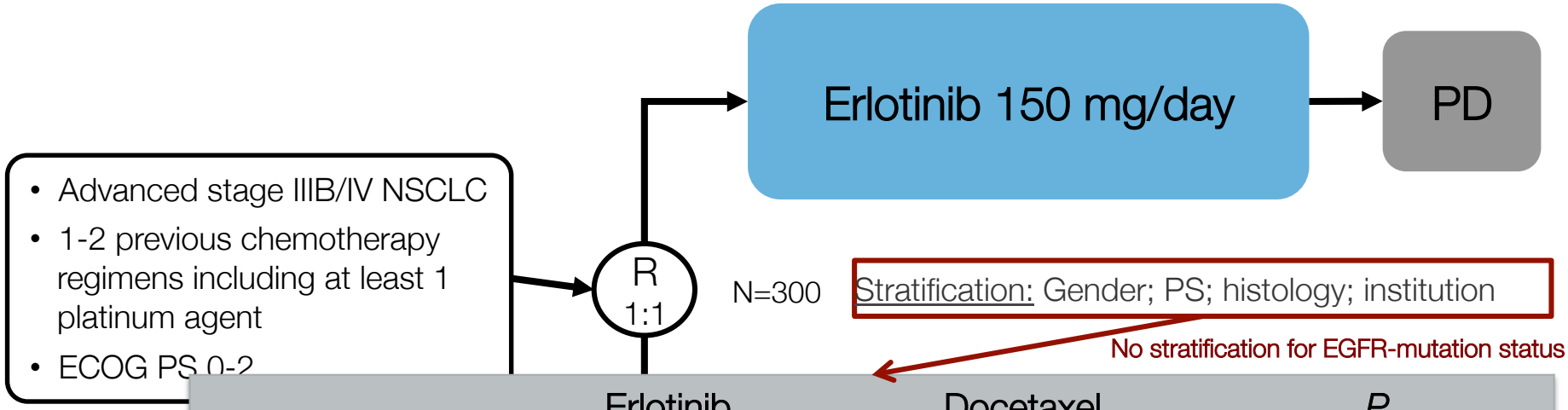


Primary endpoint: Progression-free survival

Okano et al. J Clin Oncol 31, 2013 (suppl; abstr 8006)

DELTA trial: phase III study of erlotinib versus docetaxel as 2nd or 3rd line therapy

Objective: to evaluate erlotinib versus docetaxel in Japanese patients with NSCLC previously treated with ≥1 chemotherapy

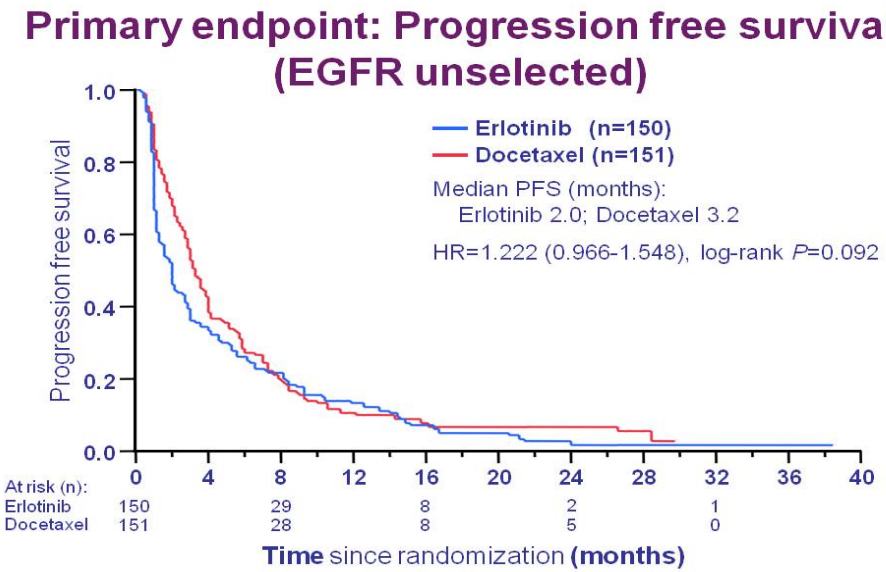


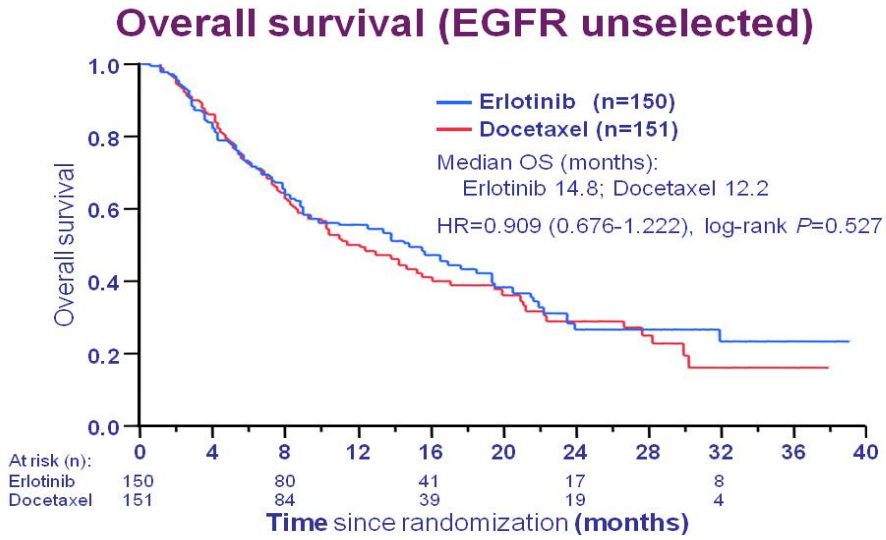
	Erlotinib	Docetaxel	*P*
EGFR wild type	73 %	60 %	0.117
EGFR mutation +	15 %	21 %	
Not examined	12 %	19 %	

No stratification or information regarding the prior lines of treatment

Okano et al. J Clin Oncol 31. 2013 (suppl: abstr 8006)

DELTA trial: phase III study of erlotinib versus docetaxel as 2nd or 3rd line therapy



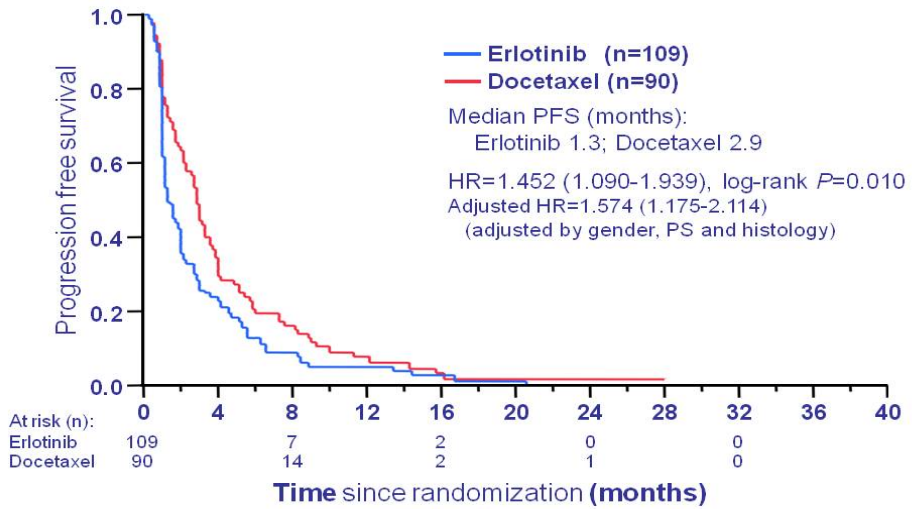


	Erlotinib	Docetaxel	HR	p value
Median PFS				
EGFR unselected	2.0 m	3.2 m	1.222	0.092
EGFR wild type	1.3 m	2.9 m	1.452	0.010
EGFR mutant	9.3 m	7.0 m	0.963	0.906
Median OS				
EGFR unselected	14.8 m	12.2 m	0.909	0.527
EGFR wild type	9.0 m	10.1 m	0.979	0.907
EGFR mutant	Not reached	27.8 m	0.425	0.128

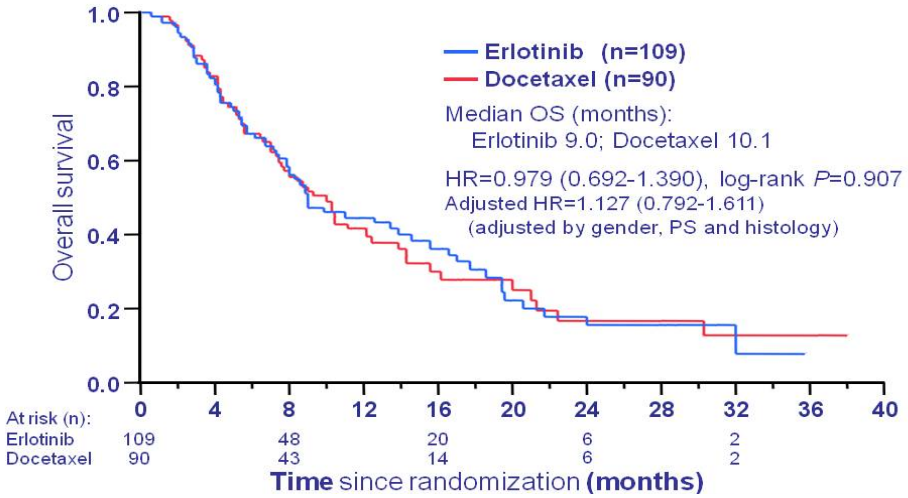
Okano et al. J Clin Oncol 31, 2013 (suppl; abstr 8006)

DELTA trial: phase III study of erlotinib versus docetaxel as 2nd or 3rd line therapy

Progression free survival (EGFR wild type)



Overall survival (EGFR wild type)

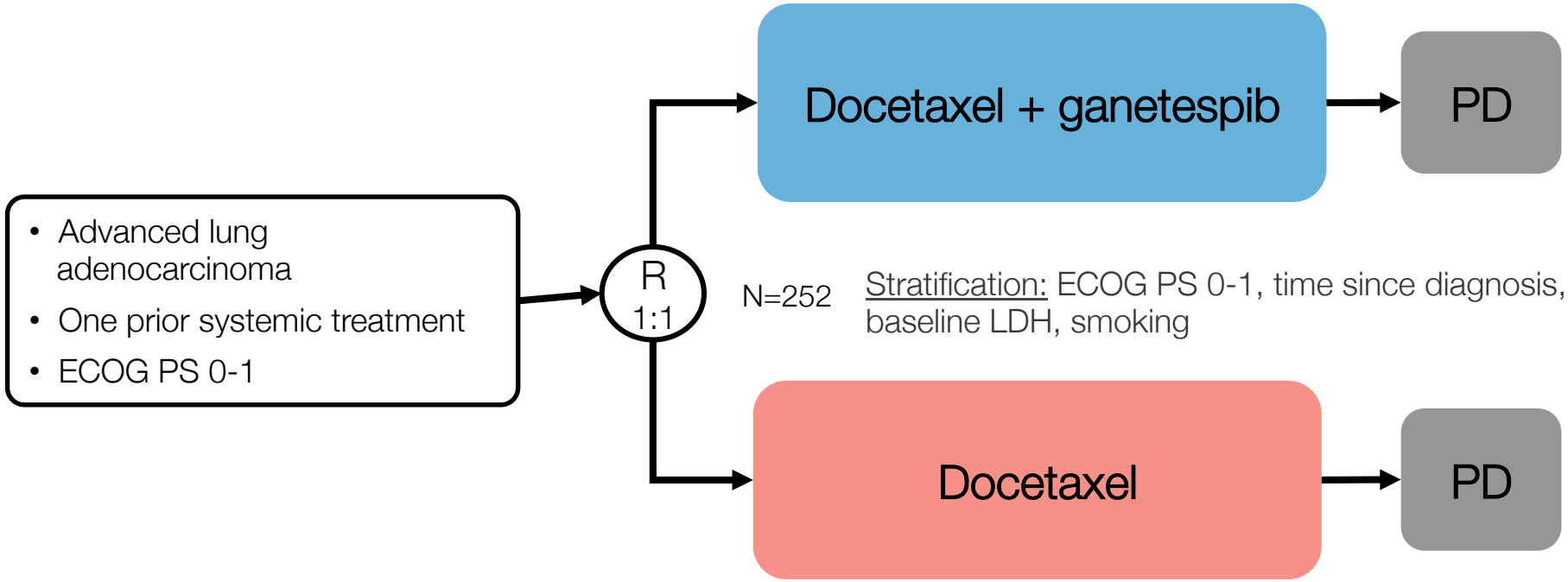


- Relatively small trial with potential imbalances between treatment arms
- Erlotinib failed to show better PFS over docetaxel as 2nd or 3rd-line therapy in EGFR-unselected NSCLC
- While PFS was significantly longer in docetaxel than erlotinib in EGFR wild-type tumours, the difference did not translate into OS in this pragmatic trial

Okano et al. J Clin Oncol 31, 2013 (suppl; abstr 8006)

Galaxy-1: docetaxel ± ganetespib (HSP-90 inhibitor) as 2nd-line for lung adenocarcinoma

Objective: to investigate safety and efficacy of the second generation heat shock protein-90 inhibitor, ganetespib, in patients with advanced lung adenocarcinoma

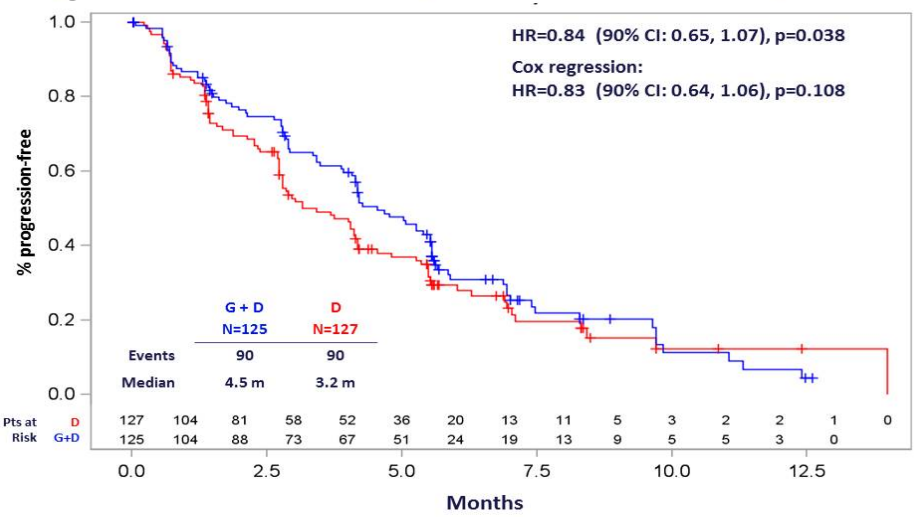


Primary endpoint: Progression-free survival in patients with elevated LDH or KRAS+ tumours

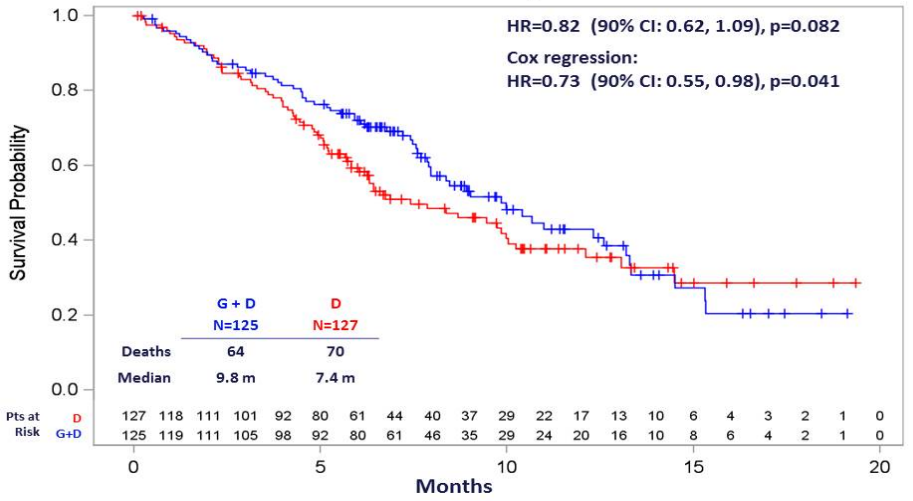
Ramalingam et al. J Clin Oncol 31, 2013 (suppl; abstr CRA8007)

Galaxy-1: docetaxel ± ganetespib (HSP-90 inhibitor) as 2nd-line for lung adenocarcinoma

Progression-free survival in all adenocarcinoma



Overall survivall in all adenocarcinoma



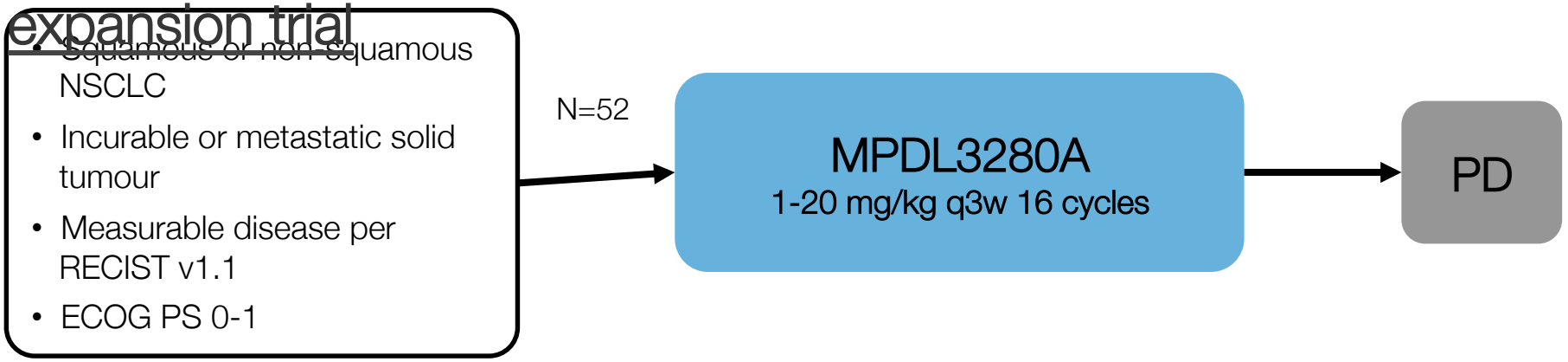
- Ganetespib in combination with docetaxel improved OS and PFS compared with docetaxel alone
- Survival benefits were most pronounced among patients who were enrolled more than 6 months after diagnosis of advanced NSCLC
- Phase III trial in patients with advanced disease >6 months is ongoing (GALAXY-2)

Ramalingam et al. J Clin Oncol 31, 2013 (suppl; abstr CRA8007)

MPDL3280A, an engineered PD-L1 antibody, locally advanced or metastatic NSCLC

Objective: to determine recommended Phase II dose of the human engineered* monoclonal PD-L1 antibody, MPDL3208A, in patients with various tumours including squamous or non-squamous NSCLC

Open-label, Phase Ia dose expansion trial



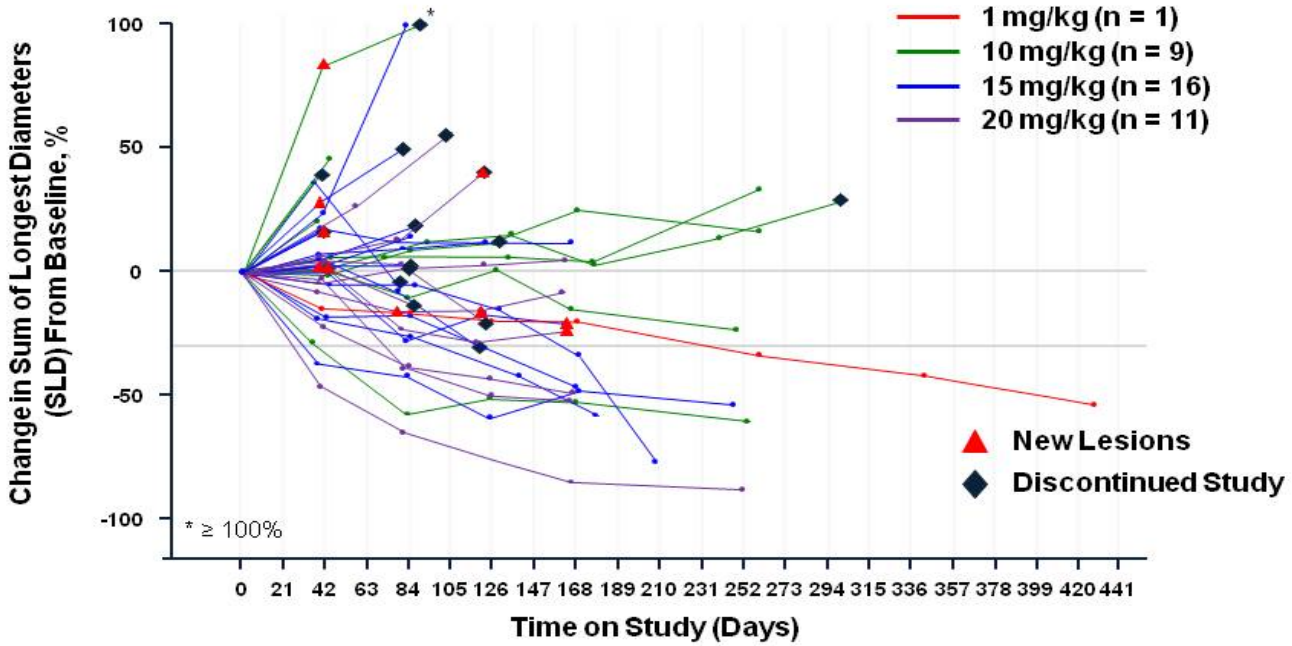
Primary endpoints: safety and ORR

* Engineered specifically to avoid killing of activated T-cells

Spigel et al. J Clin Oncol 31, 2013 (suppl; abstr 8008)

MPDL3280A, an engineered PD-L1 antibody, locally advanced or metastatic NSCLC

Tumor burden over time (NSCLC patients)



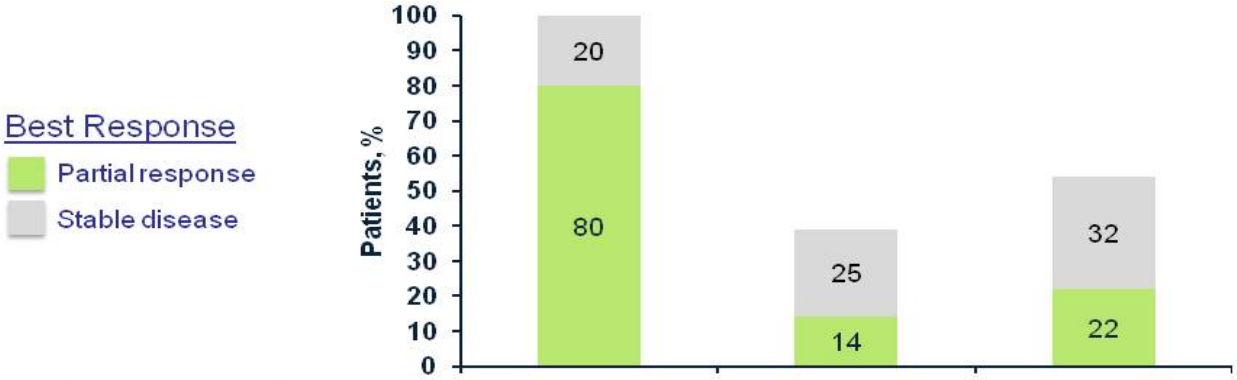
Patients first dosed at 1-20 mg/kg prior to Aug 1, 2012 with at least 1 post-baseline evaluable tumor assessment; data cutoff Feb 1, 2013.

Spigel et al. J Clin Oncol 31, 2013 (suppl; abstr 8008)

MPDL3280A, an engineered PD-L1 antibody, locally advanced or metastatic NSCLC

RECIST 1.1 Response Rate (ORR), % (n/n)			
	PD-L1 Positive	PD-L1 Negative	All*
Overall population (N = 140)	36% (13/36)	13% (9/67)	21% (29/140)
NSCLC (n = 41)	**80% (4/5)**	**14% (4/28)**	**22% (9/41)**
Squamous (n = 9)	100% (2/2)	17% (1/6)	33% (3/9)
Non-squamous (n = 31)	67% (2/3)	14% (3/22)	19% (6/31)

1 patient had an undetermined histology status.



*8 patients had unknown tumor PD-L1 status: 1 squamous patient, 6 non-squamous patients.
Patients first dosed at 1-20 mg/kg prior to Aug 1, 2012; data cutoff Feb 1, 2013.

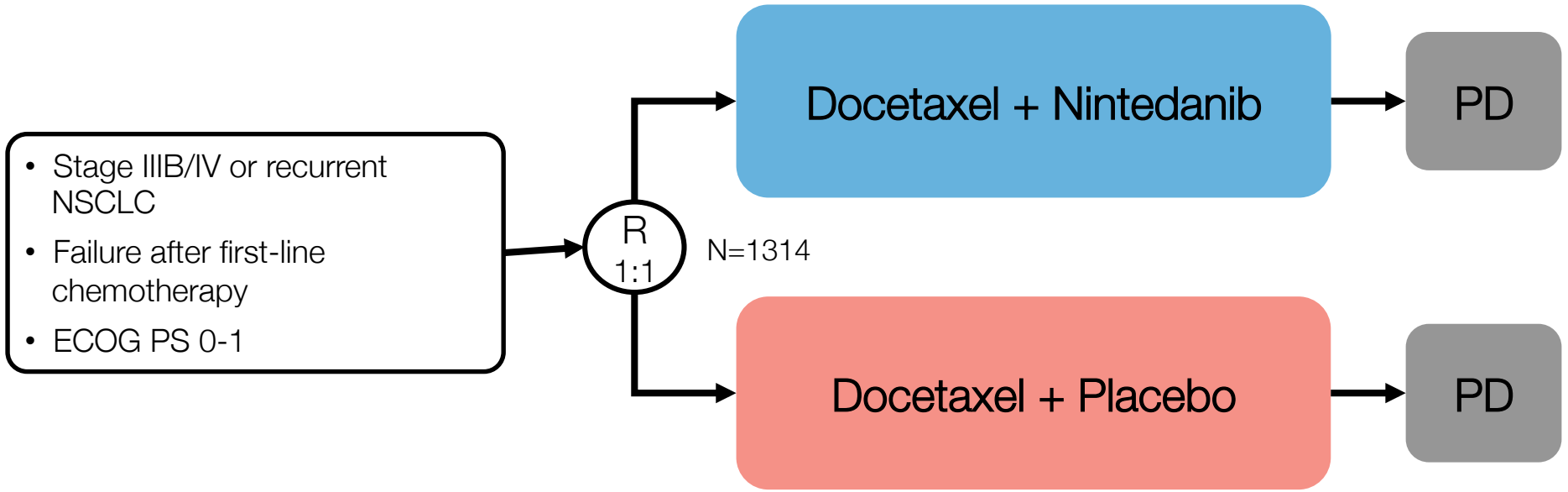
- Treatment with MPDL3280A was well tolerated (no grade 3-5 pneumonitis-related events or treatment-related deaths), and no dose-limiting toxicities up to 20 mg/kg
- Responses are ongoing in all responders in both squamous and non-squamous NSCLC
- PD-L1 tumour status correlated with higher response to MPDL3280A

Spigel et al. J Clin Oncol 31, 2013 (suppl; abstr 8008)

LUME Lung-1 trial: docetaxel ± nintedanib in NSCLC progressing after 1st-line chemotherapy

Nintedanib : oral angiokinase inhibitor targeting VEGFR 1–3, FGFR 1–3, and PDGFR α/β as well as RET

Objective: to evaluate nintedanib plus docetaxel in patients with stage IIIB/IV or recurrent NSCLC progressing after first-line chemotherapy



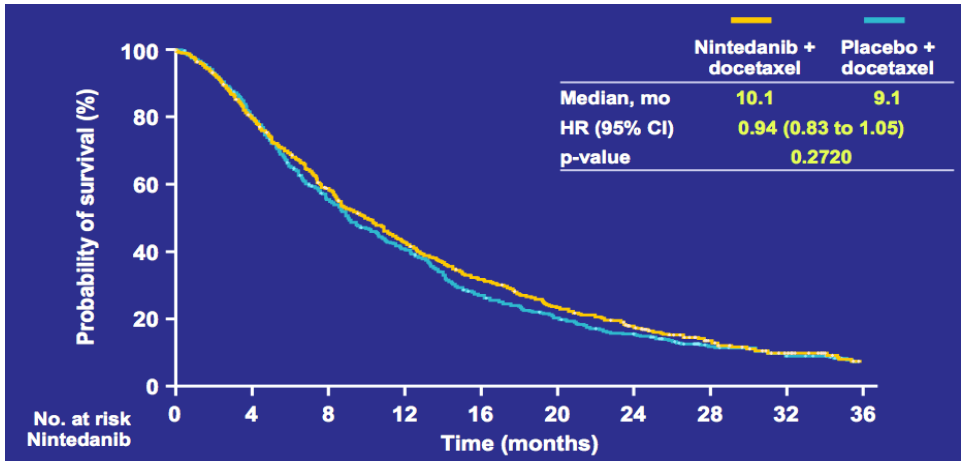
Primary endpoint: PFS

Secondary endpoints: OS in the total population & OS in adenocarcinoma

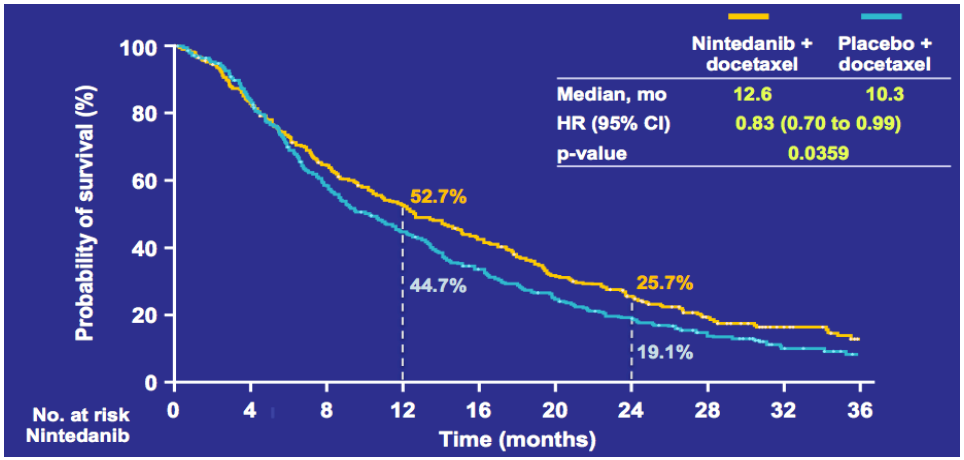
Reck et al. J Clin Oncol 31. 2013 (suppl: abstr LBA8011)

LUME Lung-1 trial: docetaxel ± nintedanib in NSCLC progressing after 1st-line chemotherapy

Overall survivall in all patients



Overall survivall in adenocarcinoma

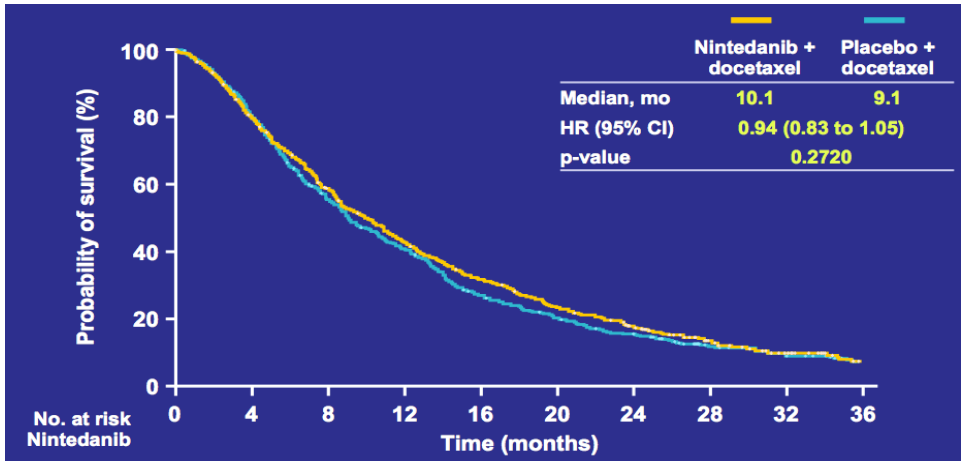


	Nintedanib+ docetaxel	Placebo+ docetaxel	HR	p value
Median PFS				
All patients	3.4 m	2.7 m	0.79	0.0019
Adenocarcinoma	4.0 m	2.8 m	0.77	0.0153
SCC	2.2 m	2.6 m	0.77	0.0200
Median OS				
All patients	10.1 m	9.1 m	0.94	0.2720
Adenocarcinoma	12.6 m	10.3 m	0.83	0.0359
SCC	8.6 m	8.7 m	1.01	0.8907

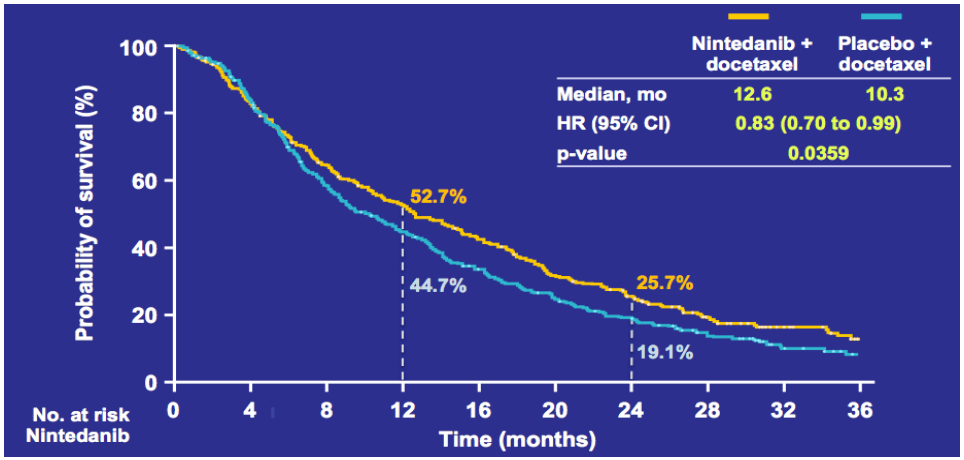
Reck et al. J Clin Oncol 31. 2013 (suppl: abstr LBA8011)

LUME Lung-1 trial: docetaxel ± nintedanib in NSCLC progressing after 1st-line chemotherapy

Overall survivall in all patients



Overall survivall in adenocarcinoma



- LUME-Lung 1 met its primary endpoint: nintedanib in combination with docetaxel significantly prolonged PFS for all patients regardless of histology
- A significant improvement in OS was demonstrated in patients with adenocarcinoma
- Nintedanib plus docetaxel had a manageable safety profile with no unexpected safety findings

Reck et al. J Clin Oncol 31. 2013 (suppl: abstr LBA8011)

Targeted treatments for NSCLC

- EGFR-TKI: nothing new
- Immunotherapy: promising, but …needs confirmation
- New targets: promising, but …needs confirmation