Decision-Making for Patients with Localized and Locally Advanced NSCLC

Leora Horn MD Msc
Associate Professor of Medicine
Ingram Associate Professor of Cancer Research
Vanderbilt Ingram Cancer Center
Nashville, TN

Disclosures

Advisory Committee	Celgene Corporation, Genentech BioOncology, Lilly, Merck
Consulting Agreements	Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Xcovery
Other Remunerated Activities	EMD Serono Inc

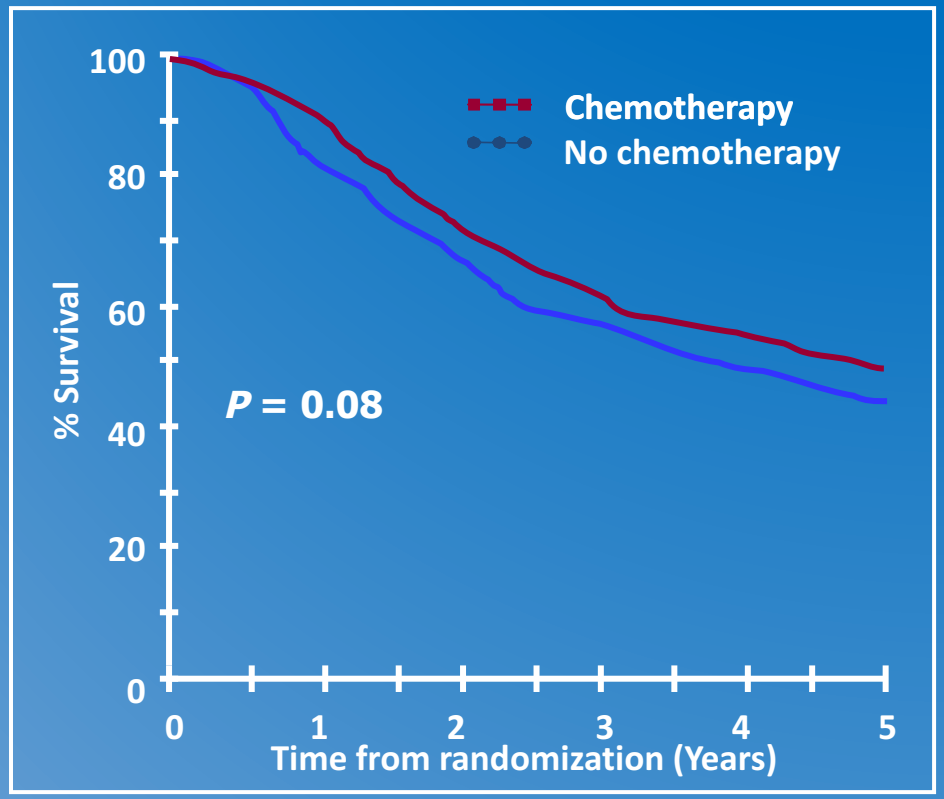
Recurrence Patterns in NSCLC

Stage	Number of Studies/Patients	Local (%)	Distant (%)
I	11/3288	32	68
II	9/599	26	74
IIIA	7/969	20	80

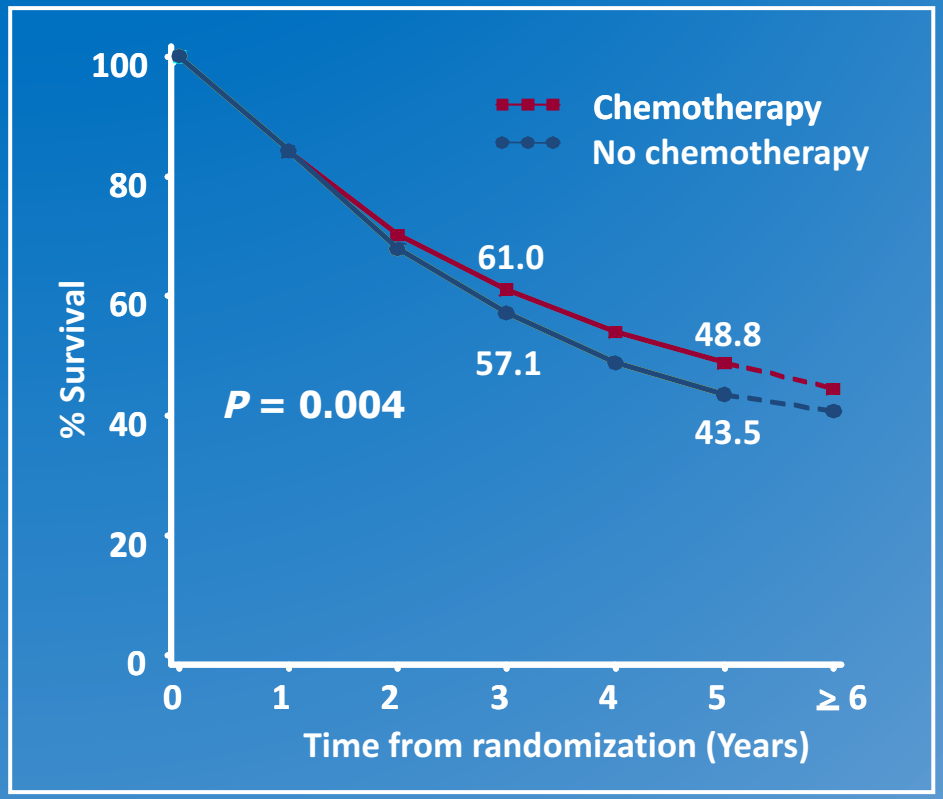
The majority of patients with early stage disease will have recurrence at a distant site

Mountain Chest 1997

LACE and BMJ Meta-analysis



Trend towards OS benefit

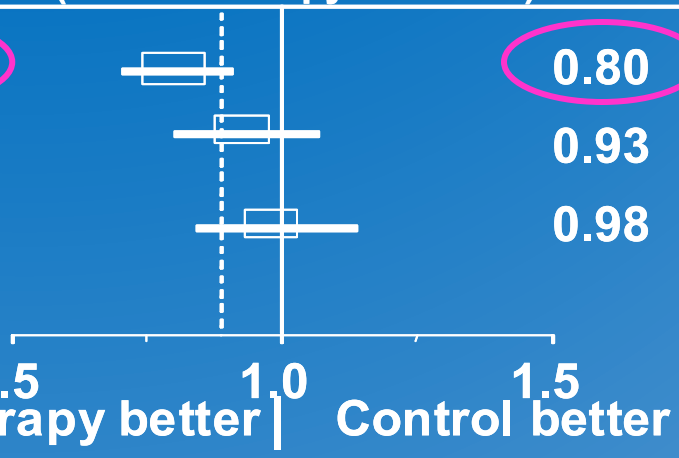


5% benefit in OS

Non-small Cell Lung Cancer Collaborative Group. *BMJ* 1995;311:899-909
Pignon et al. *Journal of Clinical Oncology* 26, no. 21 (July 2008);3552-9.

Chemotherapy Effect & Associated Drugs

Category	No. Deaths / No. Entered	HR	[95% CI]
Cisplatin + vinorelbine	929 / 1888	0.80	[0.70;0.91]
Cisplatin + 1 other drug	741 / 1373	0.93	[0.80;1.07]
Cisplatin + 2 other drugs	686 / 1323	0.98	[0.84;1.14]

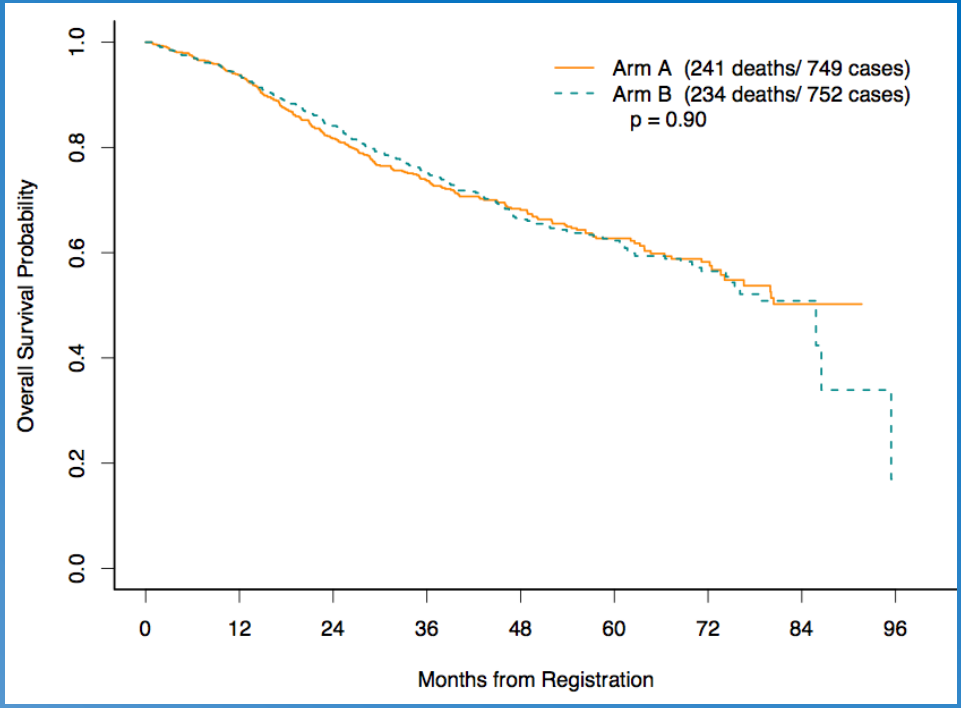


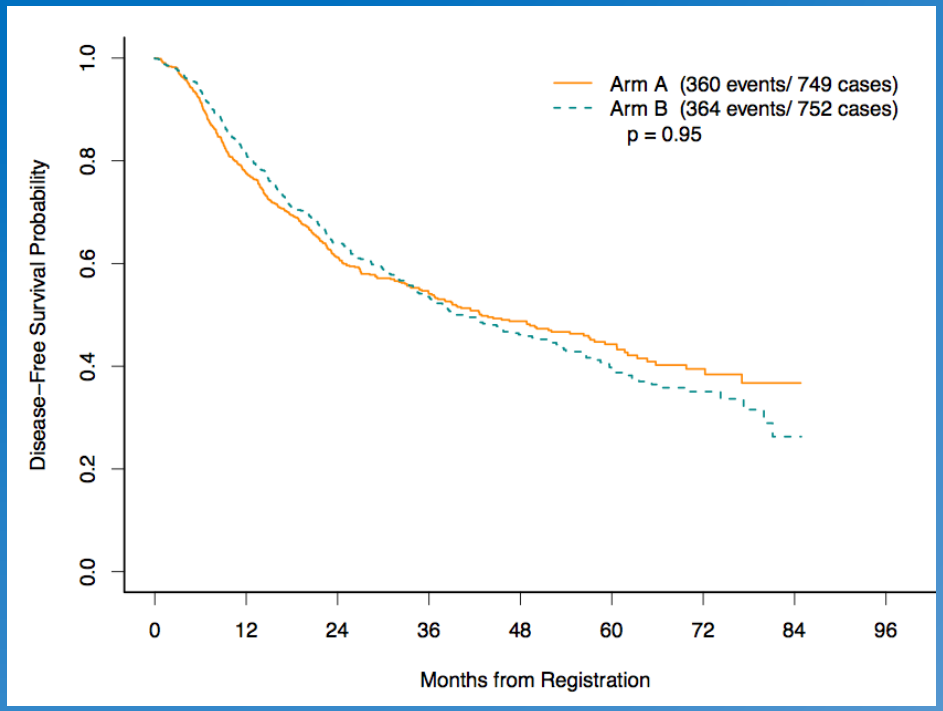
Test for heterogeneity: p = 0.104

The effect of cisplatin+vinorelbine was marginally better than the effect of other drug combinations, this is significant when the other combinations are pooled (*p* = 0.04, post-hoc analysis)

Pignon et al. *Journal of Clinical Oncology* 26, no. 21 (July 2008) 3552-9.

E1505 Overall Survival and DFS





OS hazard ratio (ChB:Ch): 0.99 95% CI: (0.82-1.19); *p* = 0.90

Med OS Arm A Chemo NR

Med OS Arm B +Bev 85.8 (74.9-NA) mo

DFS hazard ratio (ChB:Ch): 0.99 95% CI: (0.86-1.15); *p* = 0.95

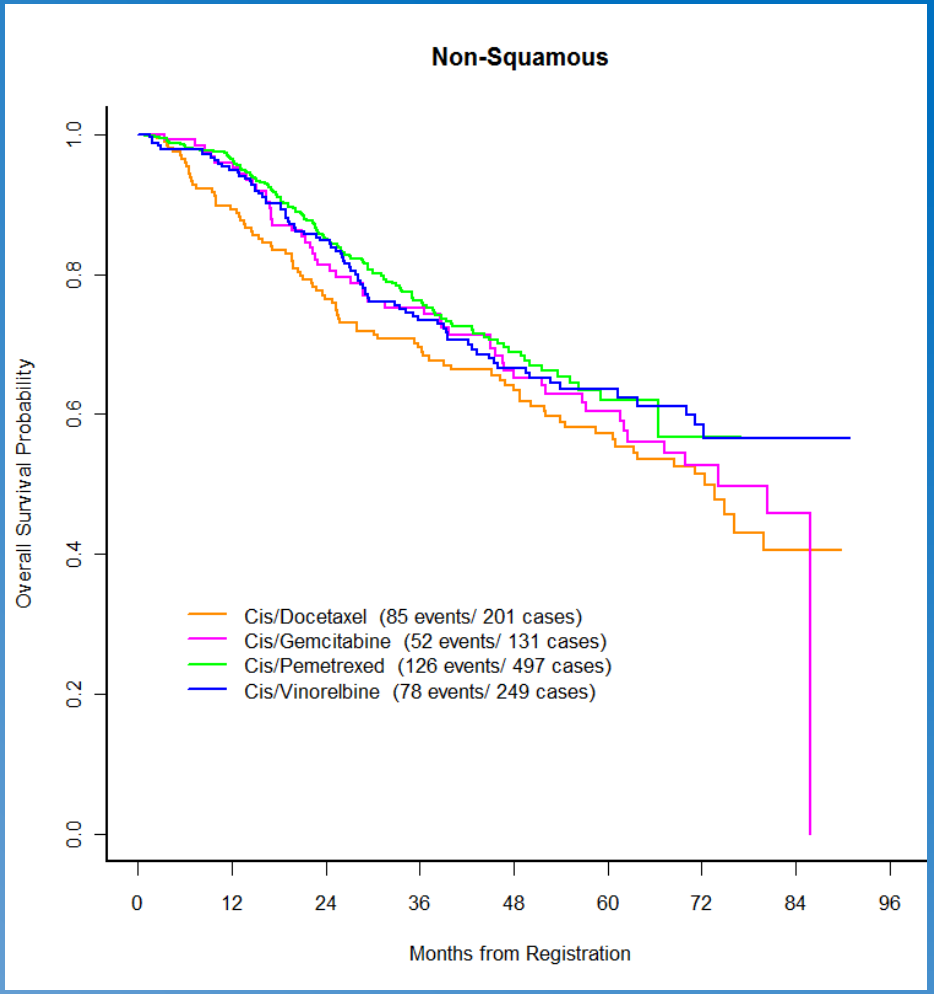
Med DFS ArmA Chemo 42.9 (95% CI 36.7-57.0) mo

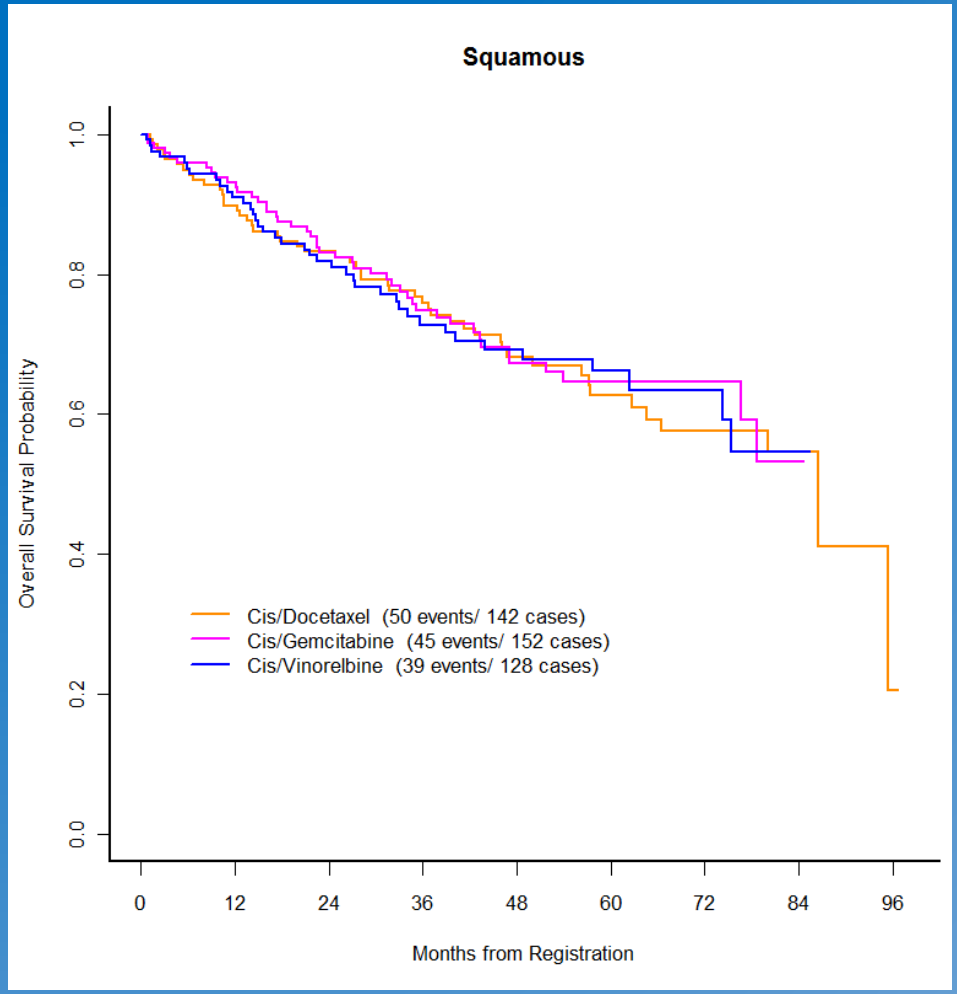
Med DFS ArmB +Bev 40.6 (95% CI 35.5-49.5) mo

OS= overall survival, DFS = disease free survival: median f/up 50.3 months; 475 deaths

Abstr 8507 Presented by: H. Wakelee ASCO 2016

Pooled OS Chemo Analysis (all patients regardless of treatment arm)





Non-squamous: Logrank *p* = 0.18

Squamous: Logrank *p* = 0 .99

Pignon et al. *Journal of Clinical Oncology* 26, no. 21 (July 2008) 3552-9.

Chemotherapy Group Comparisons: Vinorelbine as reference*

NonSquamous	OS-HR	95% CI	*P*-value	DFS-HR	95% CI	*P*-value
Docetaxel	1.3	0.96-1.77	0.09	1.18	0.91-1.51	0.21
Gemcitabine	1.14	0.81-1.63	0.45	1.17	0.88-1.57	0.27
Pemetrexed	0.97	0.73-1.29	0.83	1.09	0.88-1.36	0.43
	Logrank p = 0.18 (OS)			Logrank p = 0.58 (DFS)		

Squamous	OS-HR	95% CI	*P*-value	DFS-HR	95% CI	*P*-value
Docetaxel	1.02	0.67-1.55	0.94	0.90	0.63-1.29	0.55
Gemcitabine	0.98	0.64-1.51	0.93	0.93	0.65-1.33	0.68
	Logrank p = 0.99 (OS)			Logrank p = 0.83 (DFS)		

No difference in median # cycles by chemotherapy group

* No adjustments for multiple comparisons

Abstr 8507 Presented by: H. Wakelee ASCO 2016

Toxicity

Toxicity Gr 3-5	Squamous (n = 422)			Non-Squamous (n = 1078)			
	V-127	D-140	G-149	V-241	D-199	G-132	P-485
	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Anemia	12	3	15	12	3	7	4
Febrile neutropenia	**9**	6	1	**15**	7	2	0
Neutrophil count decreased	**54**	39	41	**58**	40	44	12
Platelet count decreased	3	2	**23**	3	2	**12**	1
Fatigue	15	17	12	15	13	9	9
Diarrhea	6	9	1	5	10	2	1
Nausea	8	15	11	11	11	5	8
Vomiting	6	12	5	6	7	3	5
Dehydration	12	12	7	10	11	2	3
Hypertension	17	14	19	17	12	18	25
Thromboembolic event	6	2	5	6	4	9	3
WORST DEGREE	85	80	82	83	74	83	**64**

4% anaphylaxis in docetaxel arm

Reporting all attributions:
With bevacizumab significantly increased:

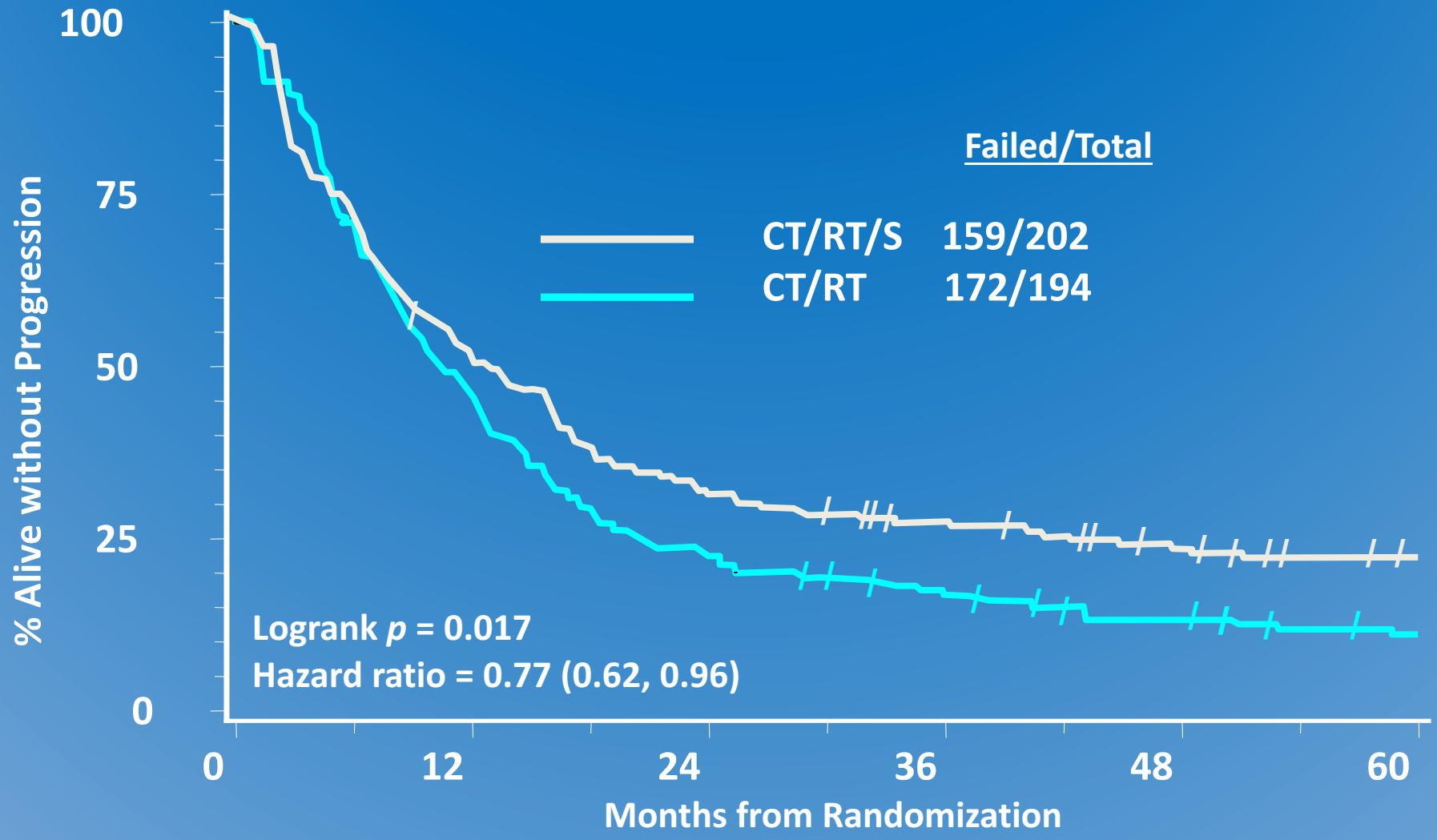
- Neutropenia and Hypertension
- Overall worst grade 3-5, but no significant difference observed in grade 5 AEs

For Chemotherapy Analysis:

- Known toxicity profiles of agents observed
- Vinorelbine > Neutropenia/ Febrile Neutropenia
- Gemcitabine > Thrombocytopenia
- Non-Squamous: Pemetrexed was associated with less total grade 3-5 toxicity than other chemotherapy groups ($p < 0.001$)

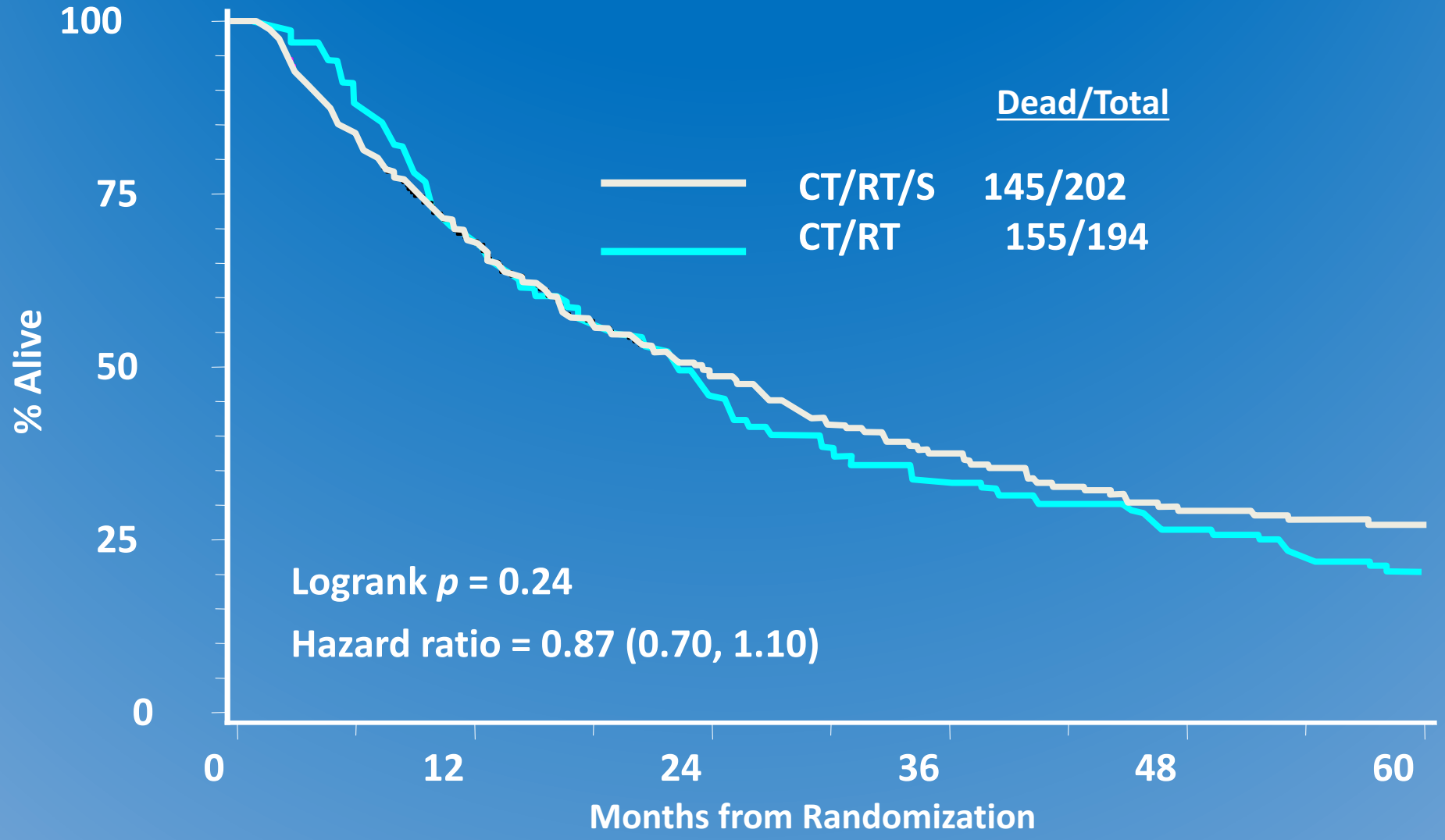
Abstr 8507 Presented by: H. Wakelee ASCO 2016

Intergroup 0139/RTOG 9309
Progression-Free Survival by Treatment Arms



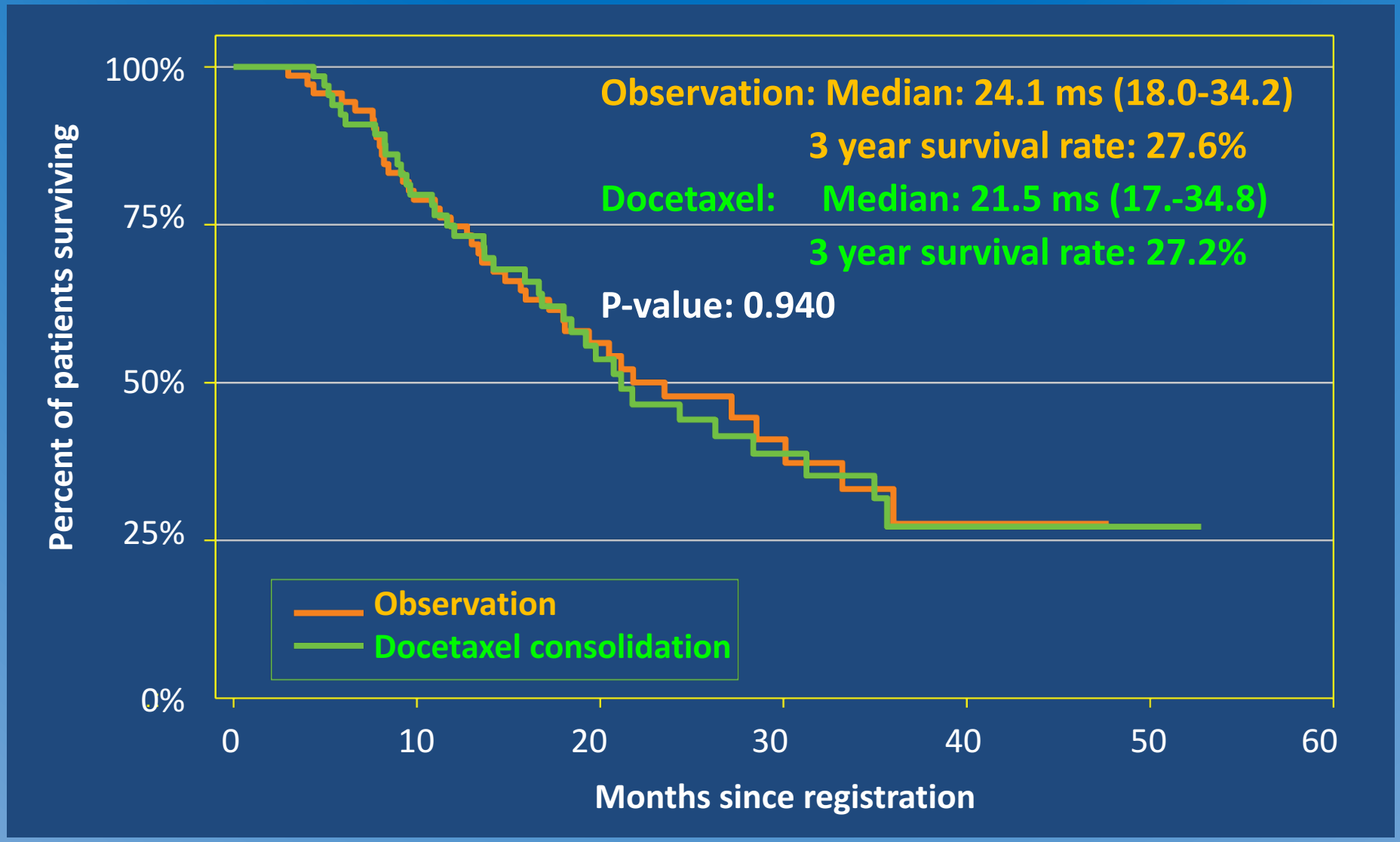
Albain et al. PASCO 2005

Intergroup 0139/RTOG 9309
Overall Survival by Treatment Arms

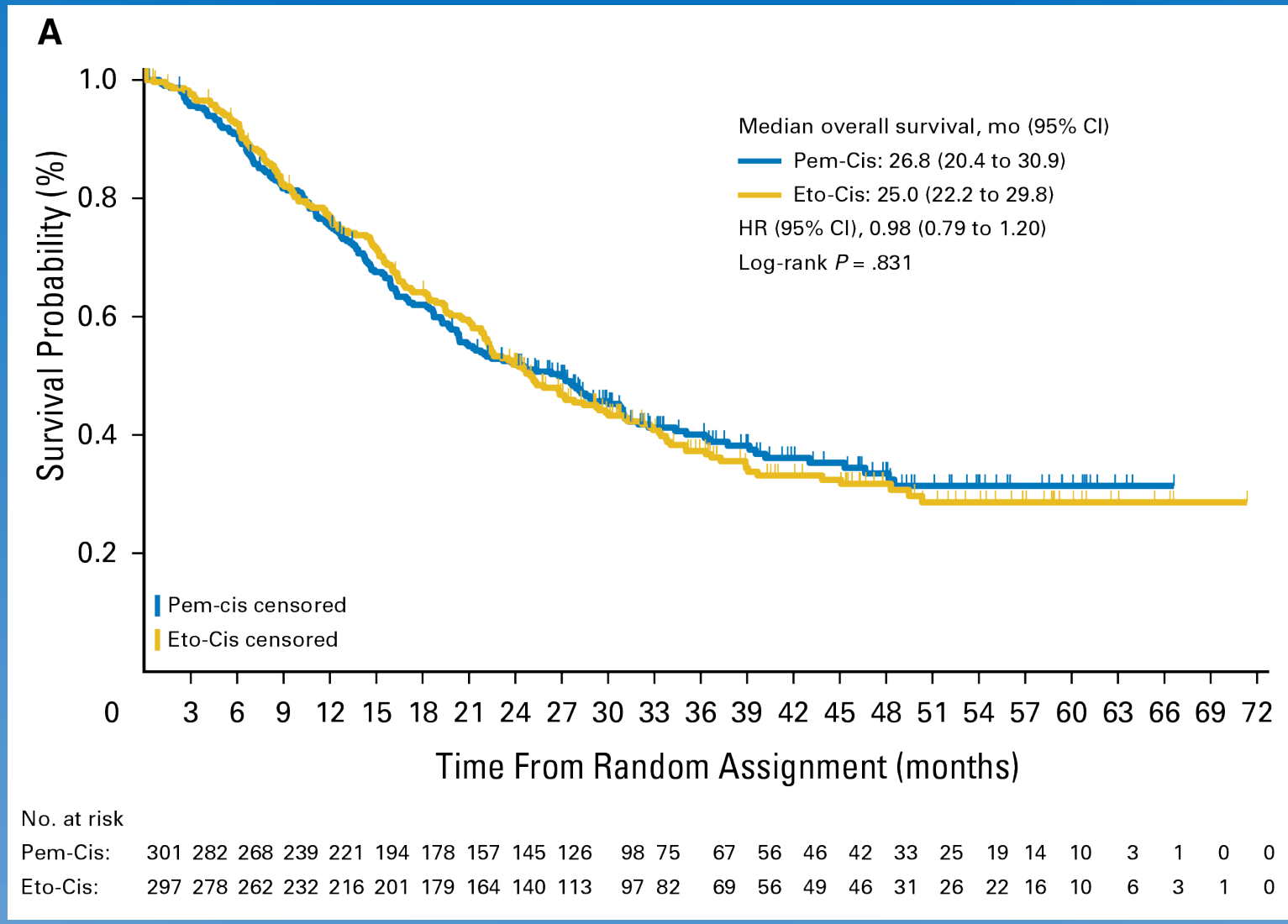


Albain et al. PASCO 2005

HOG Trial: No Different in Overall Survival Cisplatin/Etoposide +/- docetaxel



PROCLAIM: No Difference in OS by Treatment Arm Cisplatin/Pemetrexed vs. Cisplatin/Etoposide



S. Senan et al. Journal of Clinical Oncology 34, no. 9

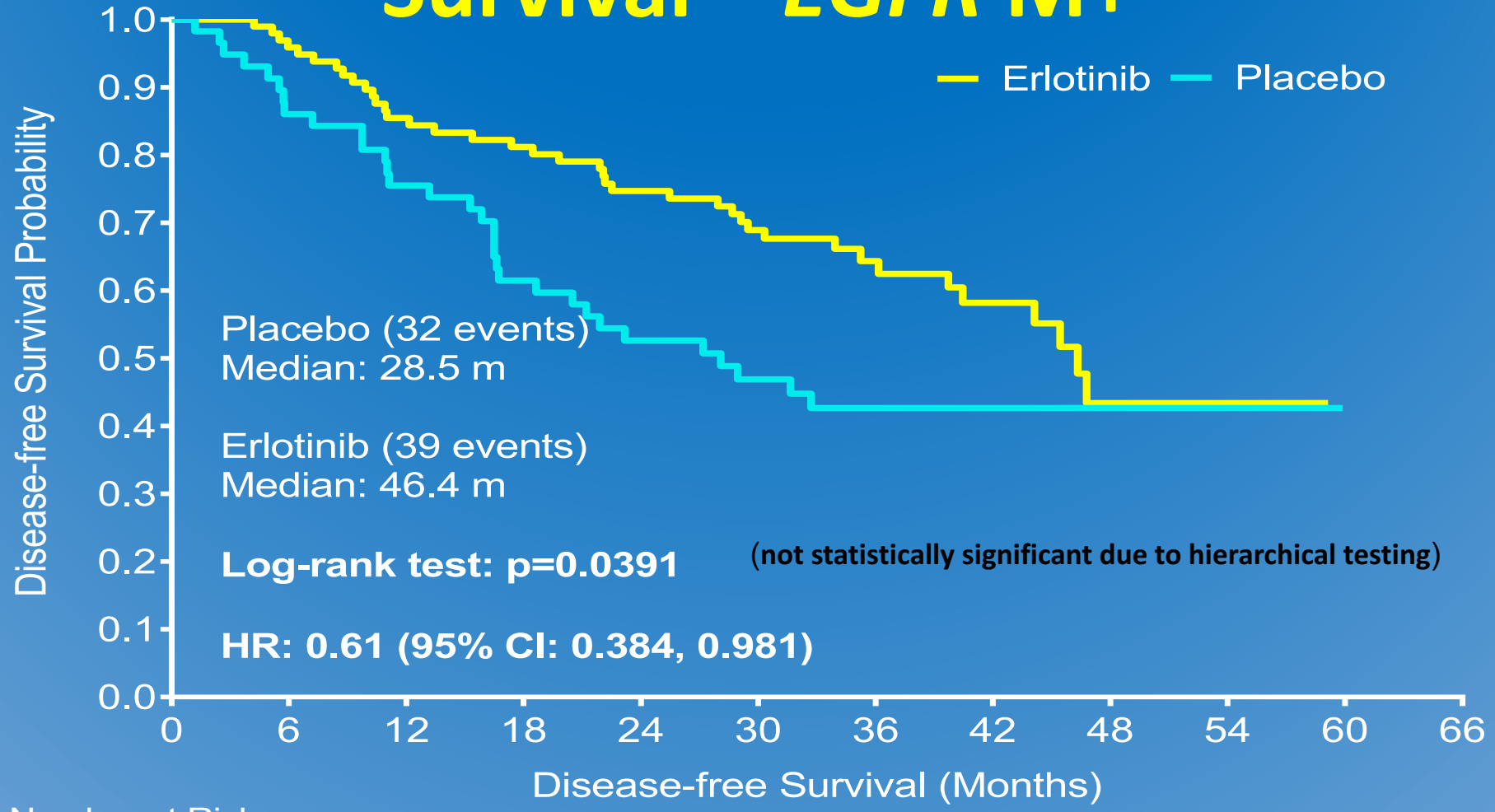
Press Release

Durvalumab met a primary endpoint of statistically-significant and clinically-meaningful progression-free survival (PFS) in 'all-comer' patients with locally-advanced, unresectable (Stage III) non-small cell lung cancer in a planned interim analysis.

Overall Survival is not reported
Goal is Cure!

AZ Press Release May 12, 2017

RADIANT: Disease-free Survival – *EGFR* M+

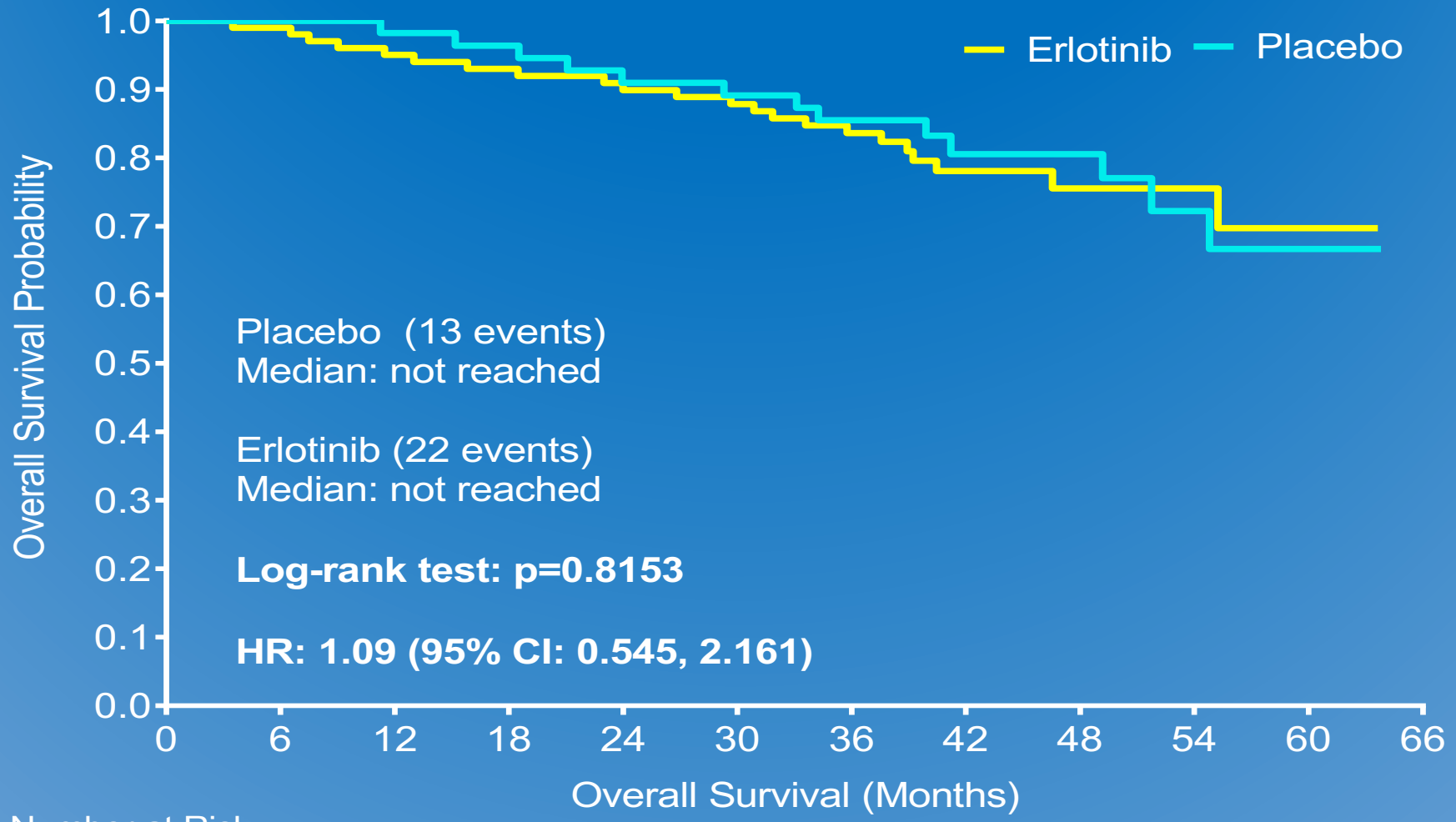


Number at Risk

Placebo	59	49	43	35	30	23	15	12	10	5	0	0
Erlotinib	102	94	80	76	68	56	35	22	10	3	0	0

Kelly et al., ASCO 2015

RADIANT: Overall Survival – *EGFR* M+



Number at Risk

Placebo	59	57	56	53	51	50	41	30	24	14	5	0
Erlotinib	102	100	94	91	88	86	75	43	26	15	7	0

Kelly et al., ASCO 2015

Press Release

- Adjuvant gefitinib reduced the risk of disease recurrence by 40% versus standard chemotherapy in patients with stage I-IIIA EGFR-positive non-small cell lung cancer, according to findings from the phase III trial.
- At a median follow-up of 36.5 months, the median disease-free survival was 28.7 months with gefitinib versus 18.0 months with a regimen of vinorelbine plus cisplatin (HR, 0.60; 95% CI, 0.42-0.87; p = 0.005)

Overall Survival is not reported
Goal is Cure!

Wu et al 2017 ASCO Annual Meeting