

Chemotherapy

first line - yes or no

when – early versus delayed

2nd line – yes or no

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What is mesothelioma?

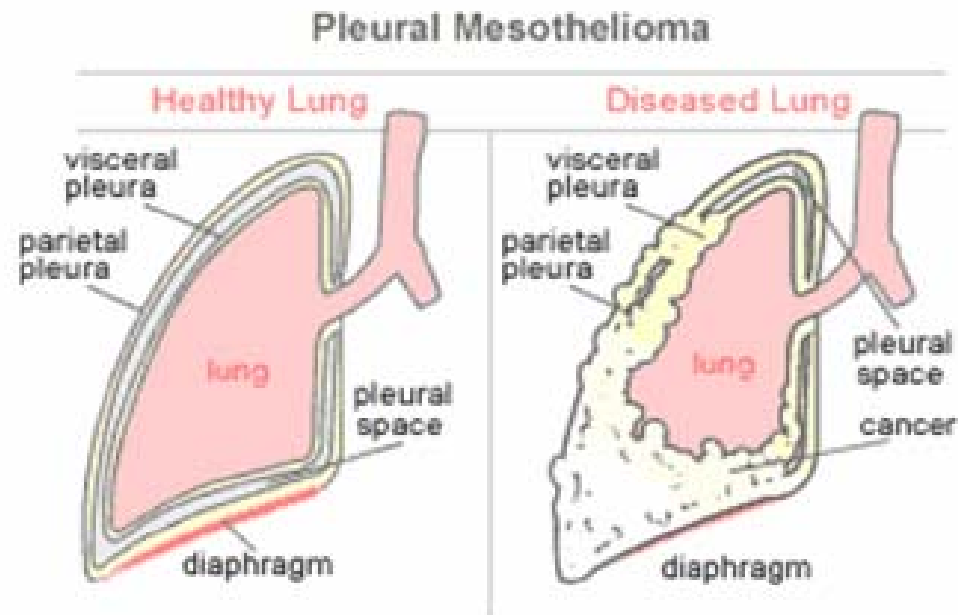


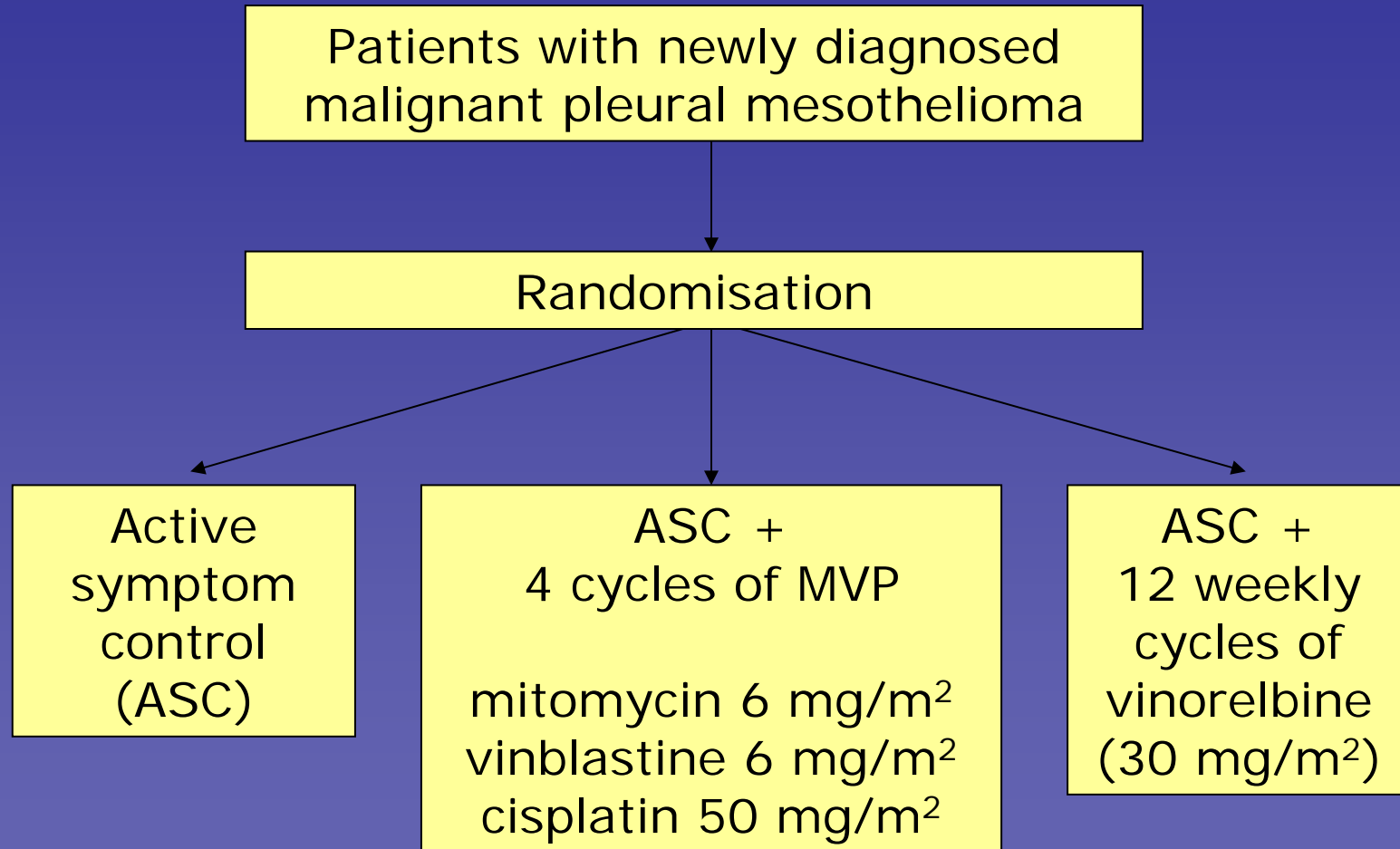


Figure 3

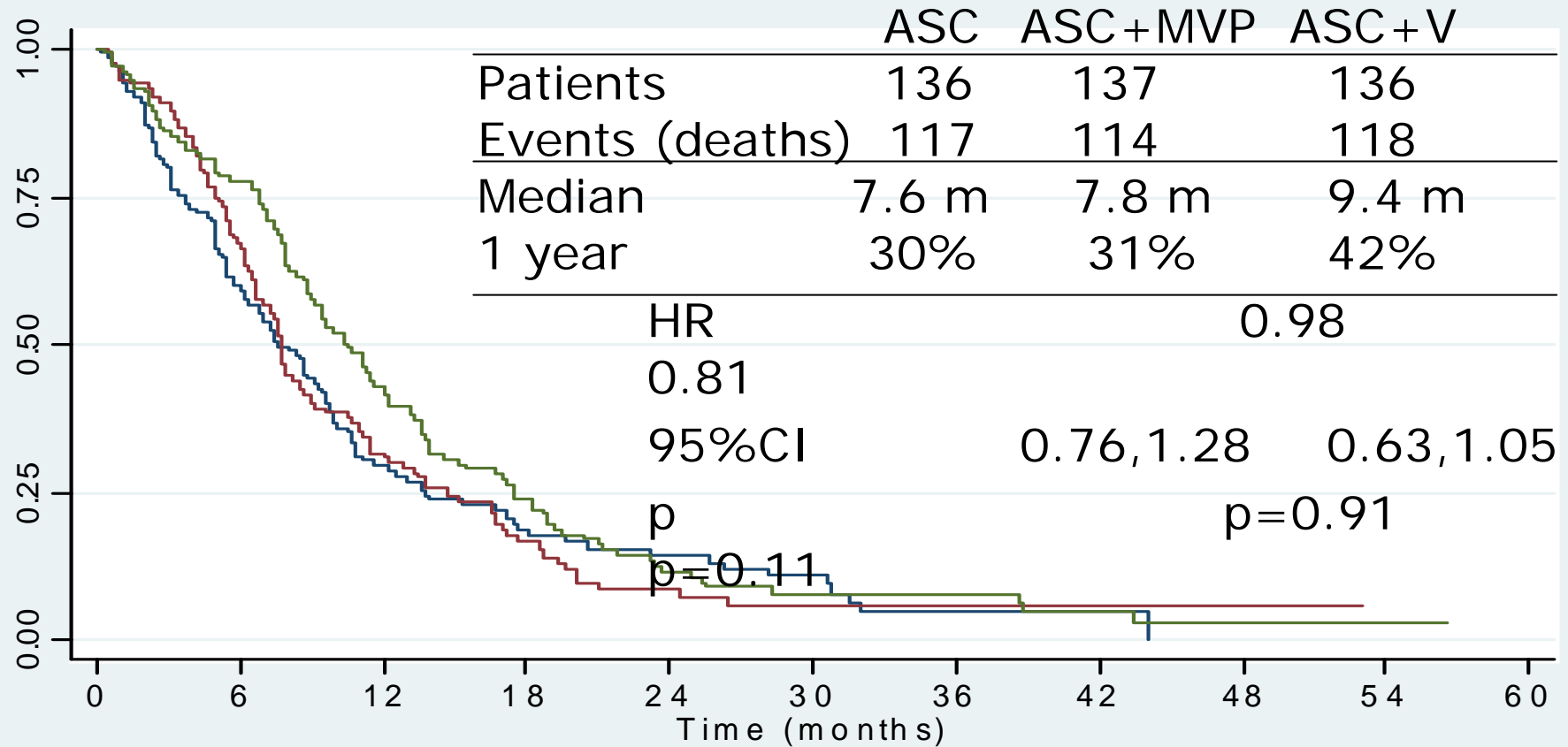
Why would you have chemotherapy?

- Prolong life
- Decrease symptoms
- Maintain QOL
- Toxicity must be acceptable

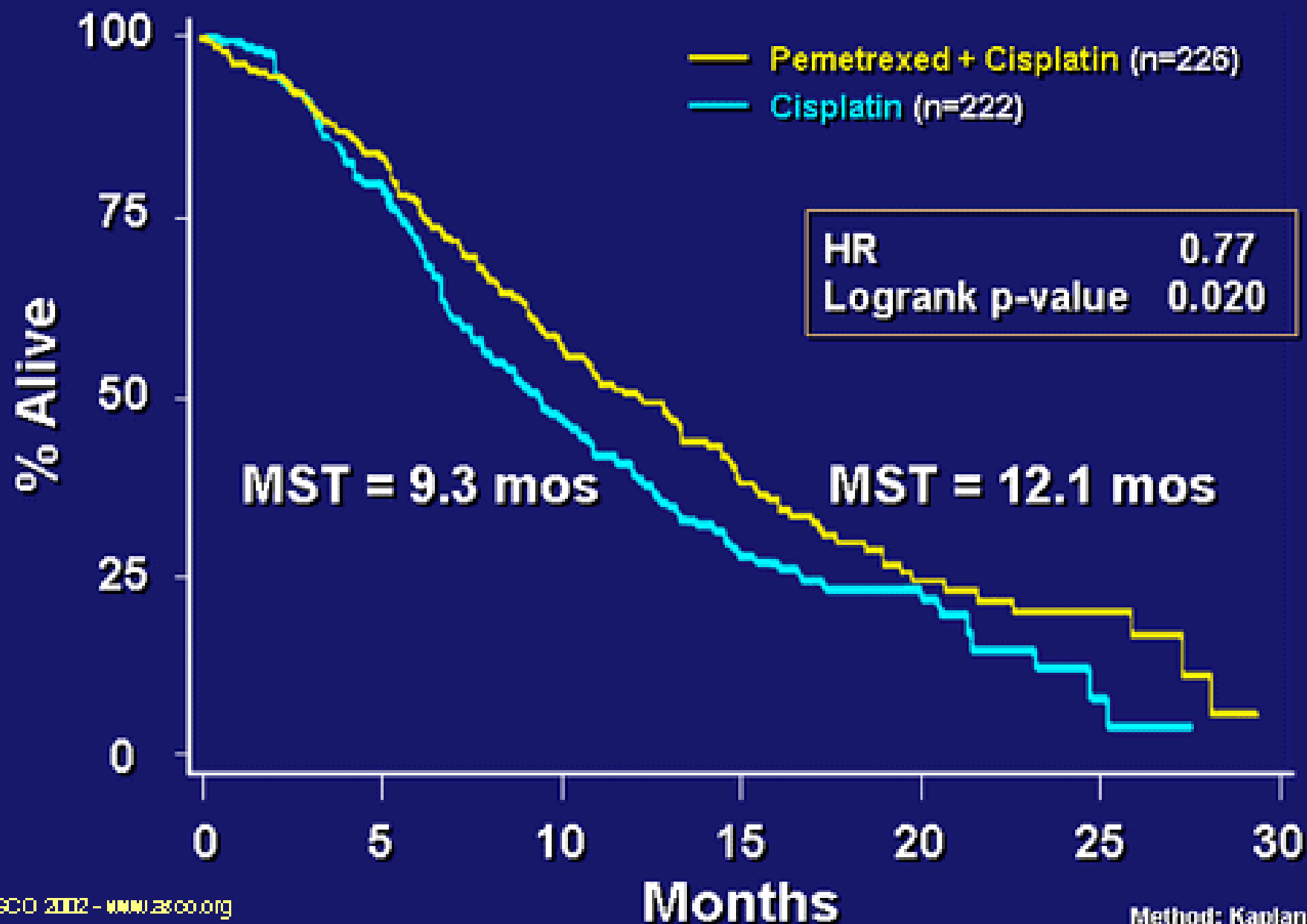
Trial design



Overall survival (3 arms)

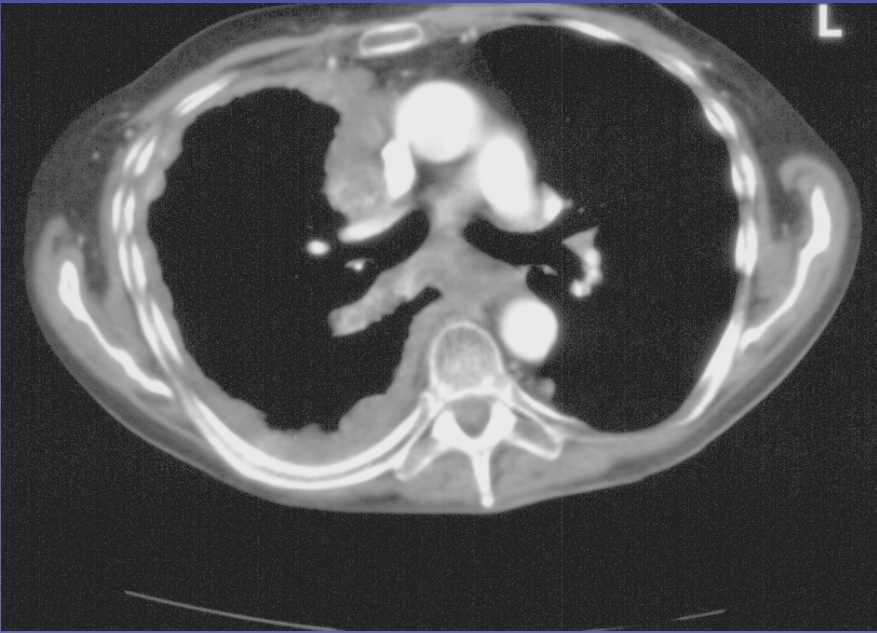
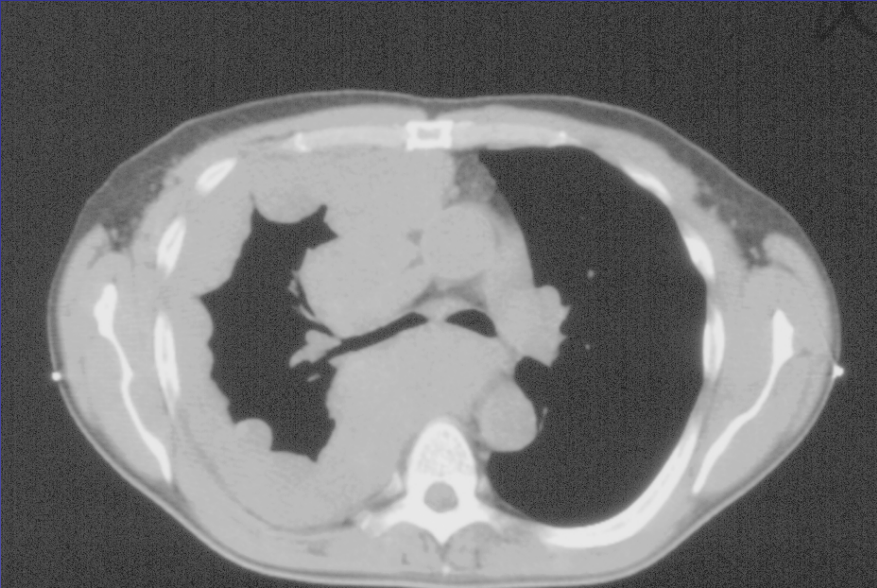


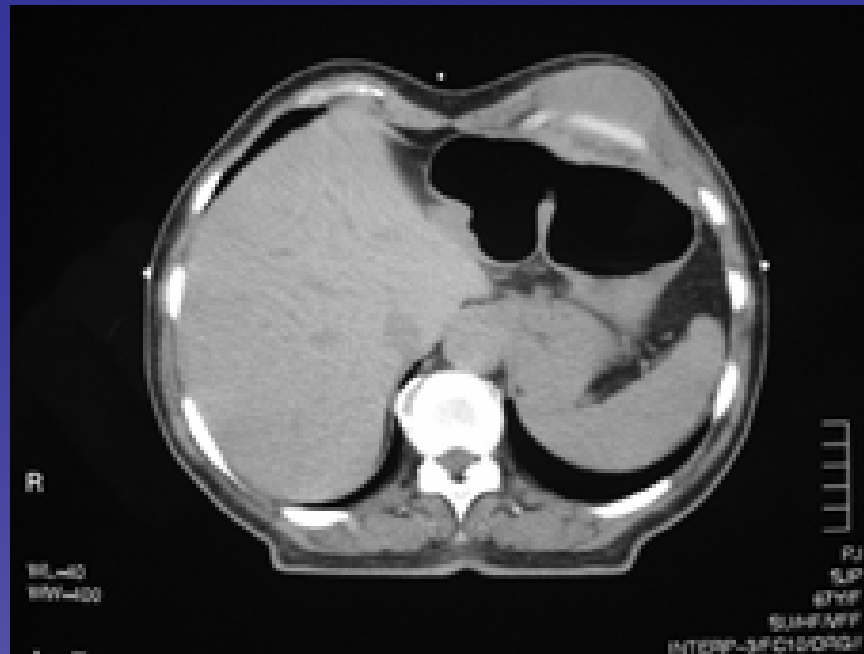
Survival: All Eligible Patients



Why would you have chemotherapy?

- *Prolong life – Yes with newer – probably not much with older*
- *Decrease symptoms*
- Maintain QOL
- Toxicity must be acceptable





What are the symptoms?

- Vague
- Breathlessness
- Pain
- Lethargy
- Reduced appetite
- Sweating

Symptomatic Response I

	No.	%
Overall	101/147	69
Dyspnoea	66/123	50
Cough	56/91	62
Pain	87/112	71
Malaise	39/82	44

Symptomatic Response II

- 2 patients had complete resolution of symptoms
- 19 (90%) of patients with an objective response also had a symptomatic response
- 70 (74%) of patients with no objective change had a symptomatic response
- 8 (40%) of patients with PD derived symptomatic benefit

Advanced Cancer-Related Breathlessness



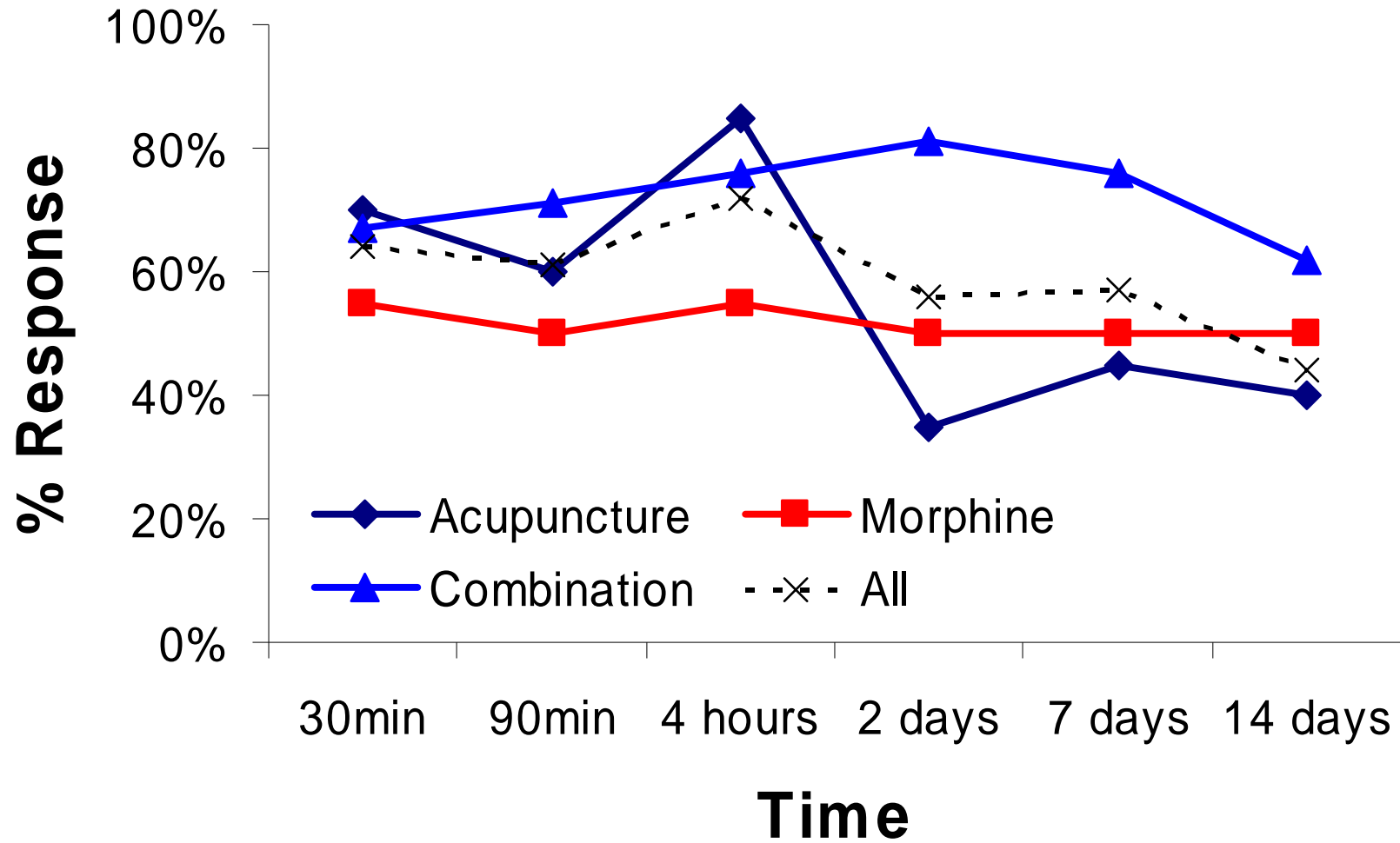
Acupuncture reduced shortness of breath in
subjective and objective measures

Filshie et al, 1996

RCT acupuncture v morphine v acupuncture + morphine

O'Brien M & Filshie J (underway)

Dyspnoea Response rate

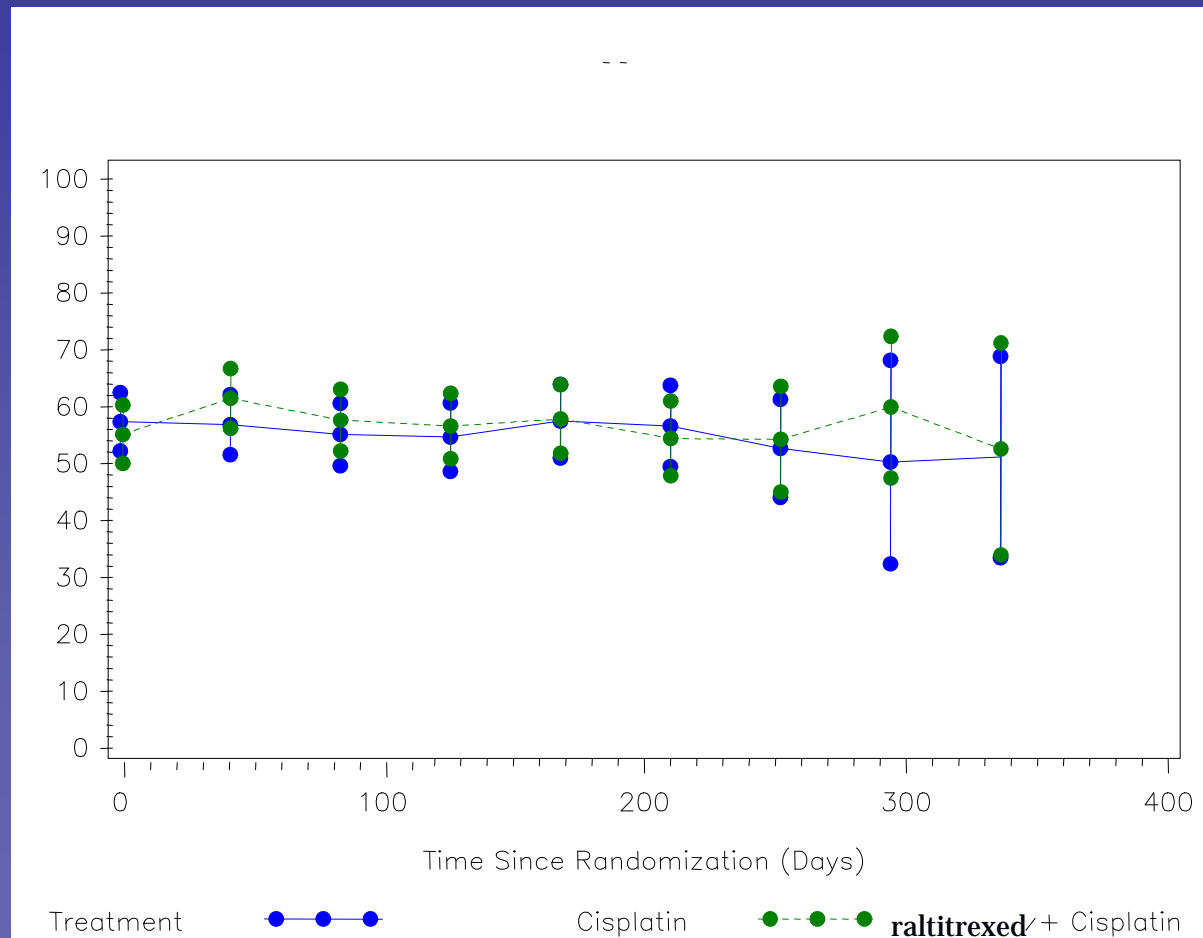


Over 50% of patients maintained a response to 1 week and 44% to 2 weeks.

Why would you have chemotherapy?

- *Prolong life – Yes with newer – probably not much with older*
- *Decrease symptoms – Yes but other things can also work*
- *Maintain QOL*
- *Toxicity must be acceptable*

Overall health/QoL: on-treatment (n=1013)



Toxicity pemetrexed plus cisplatin

Toxicity, n (%)	Pemetrexed + cisplatin (n=226)	Cisplatin alone (n=222)	p- value*
Laboratory (haematologic)			
Haemoglobin	11 (4.8)	0 (0.0)	0.001
Leukopenia	40 (17.7)	2 (0.9)	<0.001
Neutropenia	63 (27.9)	5 (2.3)	<0.001
Thrombocytopenia	13 (5.8)	0 (0.0)	<0.001
Non-laboratory			
Nausea	33 (14.6)	14 (6.3)	0.005
Fatigue	23 (10.2)	19 (8.6)	0.628
Vomiting	30 (13.3)	8 (3.6)	0.000
Diarrhoea	10 (4.4)	0 (0.0)	0.002
Dehydration	9 (4.0)	1 (0.5)	0.020
Stomatitis	9 (4.0)	0 (0.0)	0.004
Anorexia	5 (2.2)	1 (0.5)	0.216
Febrile neutropenia	4 (1.8)	0 (0.0)	0.123
Infection with grade 3–4 neutropenia	3 (1.3)	1 (0.5)	0.623
Rash	3 (1.3)	0 (0.0)	0.248

Why would you have chemotherapy?

- *Prolong life – Yes with newer – probably not much with older*
- *Decrease symptoms – Yes but other things can also work*
- *Maintain QOL/Toxicity must be acceptable*

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A Randomised Trial of Early Versus Delayed Chemotherapy in Symptomatically Stable Patients with Malignant Mesothelioma

**Mary ER O'Brien, C Ryan, K Priest, C Corbishley, A Norton,
S Ashley, A Saini, T Eisen, N Rowell., IE Smith, R Sayer.**

**Initial
Clinic
Assess
ment**



**Review at
4 weeks
If
Symptom
Stable
Randomi
sed**



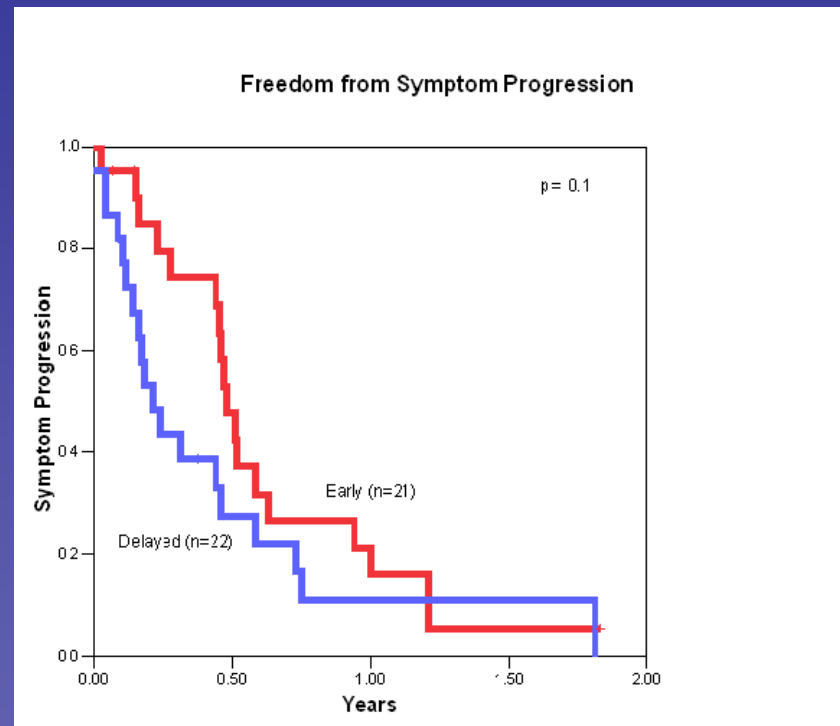
**Delayed
Group - BSC**
Regular FU with MVP
chemotherapy initiated
at loss of adequate
symptom control

**Early
Group
Immediate
Chemo**
MVP

MVP
Cisplatin
50mg/m²
Vinblastine
6mg/m²
Mitomycin
8mg/m²
3 weeks
Carboplatin
substitute
GFR
<40mls/ml
*

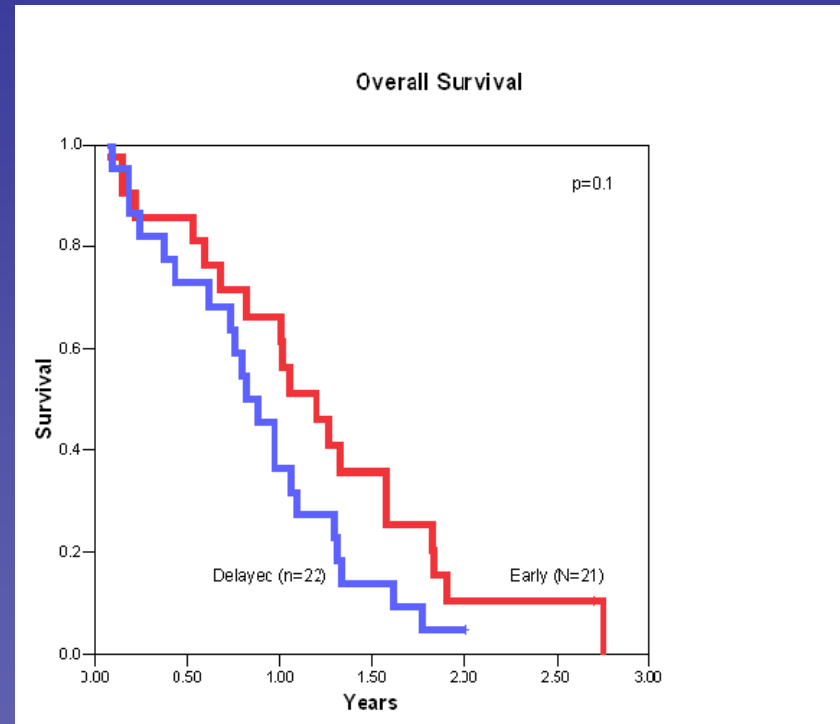
*MVP – Middleton et al, Andrepoulou et al 2004.

Symptom Progression



From date of randomisation time to symptom progression
25 weeks v 11 weeks.

Overall Survival



From the date of randomisation median survival
14 mths for the 'early' group v 10 mths for the 'delayed' group.
1 year 66% versus 36%

Changes in Quality of Life : Baseline -> Follow-up (3 mths)

	Early n=11		Delayed n=9 4 before, 5 after		Significance
<u>Functional Scales</u>	Mean & signif. from base		Mean & signif. from base		Early v Late
Physical Functioning	-4.7	P=0. 6	-12.7	<u>P=0.008*</u>	P = 0.5
Role functioning	-0.1	P=1. 0	-7.4	P=0.5	P = 0.6
Emotional functioning	-0.9	P=0. 9	-10.2	P=0.16	P = 0.3
Cognitive functioning	+3.4	P=0. 6	-9.3	P=0.13	P = 0.17
Social functioning	0.0	P=1. 0	-7.4	P=0.3	P = 0.7
Global Health	+1.6	P=0. 8	-12.8	P=0.15	P = 0.19

A negative change in the functional scales represents worsening function;

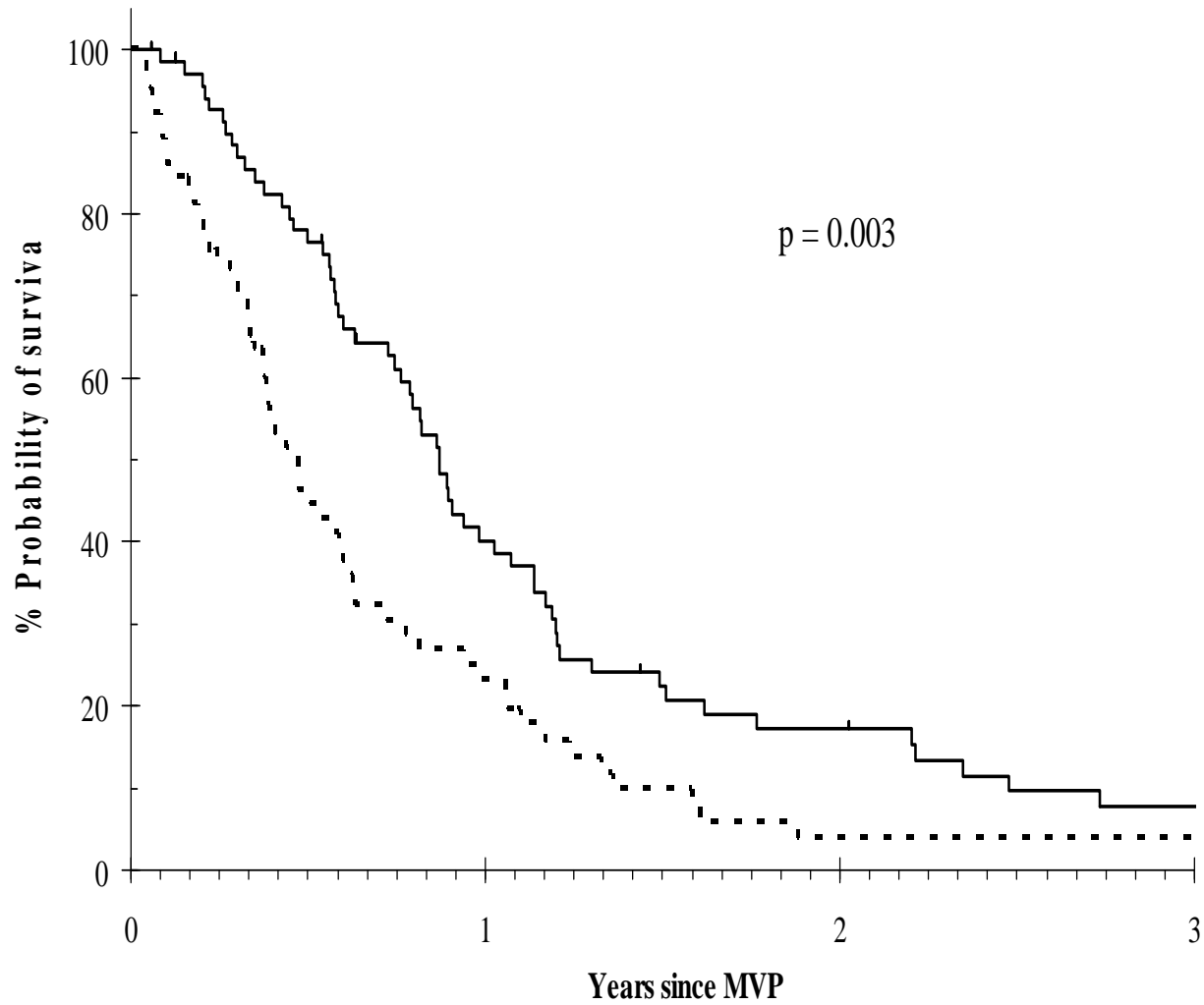
Changes in Quality of Life : Baseline -> Follow-up 2

<u>Symptom Scales</u>	<u>Early (mean)</u>		<u>Delayed (mean)</u> 4 before, 5 after		<u>Significance</u>
Fatigue	+14.4	P=0.07	+16.0	P=0.073	P = 0.9
Nausea / Vomiting	+3.0	P=0.6	+14.8	P=0.2	P = 0.4
Cough	+9.1	P=0.3	+11.1	P=0.5	P = 0.9
Haemoptysis	0.0		0.0		
Dyspnoea	+2.0	P=0.7	+14.8	<u>P=0.025**</u>	P = 0.1
Sore Mouth	0.0	P=1.0	+4.8	P=0.4	P = 0.5
Dysphagia	+3.0	P=0.3	+4.8	P=0.4	P = 0.8
Neuropathy	0.0	P=1.0	+4.7	P=0.4	P = 0.5
Alopecia	+15.2	P=0.05	+23.8	P=0.05	P = 0.5
Pain in Chest	+6.1	P=0.3	0.0	P=1.0	P = 0.7
Pain in other area	+3.3	P=0.7	+9.5	P=0.6	P = 0.7

a positive change in the symptom scales represents worsening symptoms

good = PS 0,1

PS 0/1 versus 2 – RMH data



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2nd line – yes or no

Pem ± Plat in 2nd-line MPM

- **Results –response**

	Pem alone	Pem+Cis	Pem+Crb
RR, % (95% CI)	12.1 (9.1–15.7)	23.8 (17.3–31.4)	16.8 (12.7–21.7)
CR, %	0	1.3	0.4
PR, %	12.1	22.5	16.5
SD, %	46.0	43.7	49.5
PD, %	37.1	27.2	30.9
Disease control rate (RR + SD), % (95% CI)	58.1 (53–63)	67.5 (59.5– 74.9)	66.3 (60.5– 71.8)
Median survival, months (95% CI)	N/A (8.8– NA)	14.0 (11.7– NA)	17.7 (17.7– NA)
One-year survival rate, % (95% CI)	54.7 (42.6– 66.8)	67.9 (48.6– 85.5)	65.5(54.6– 76.5)

Chemotherapy

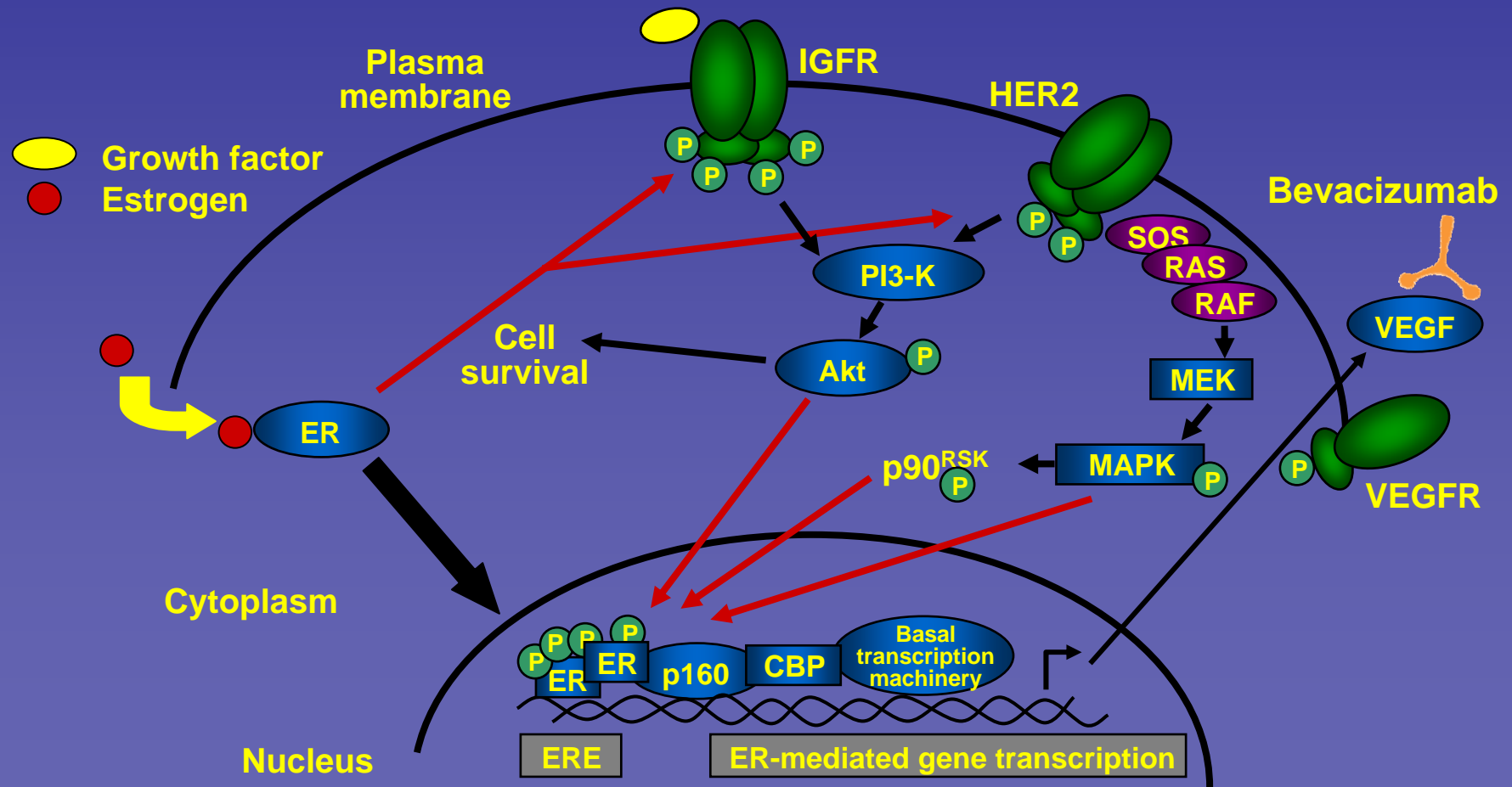
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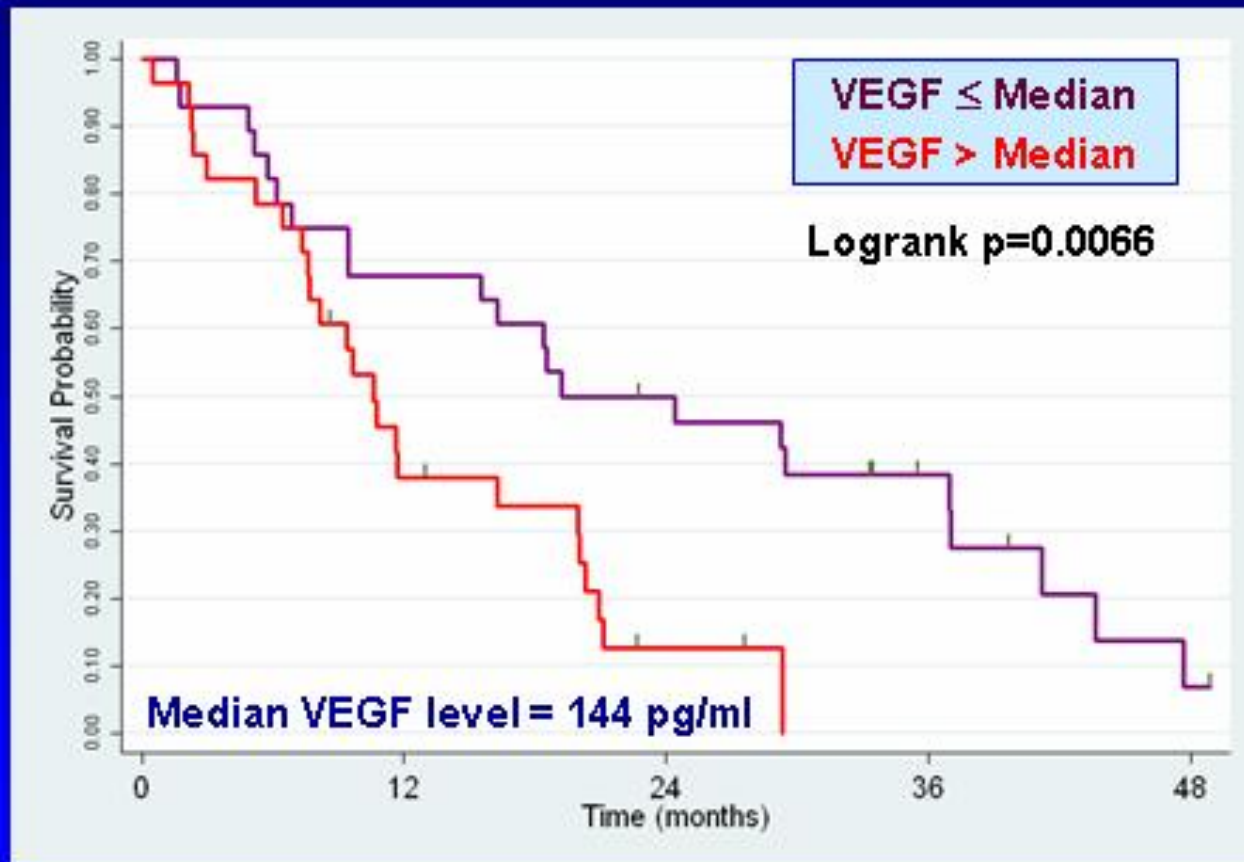
2nd line – yes or no

– new treatments

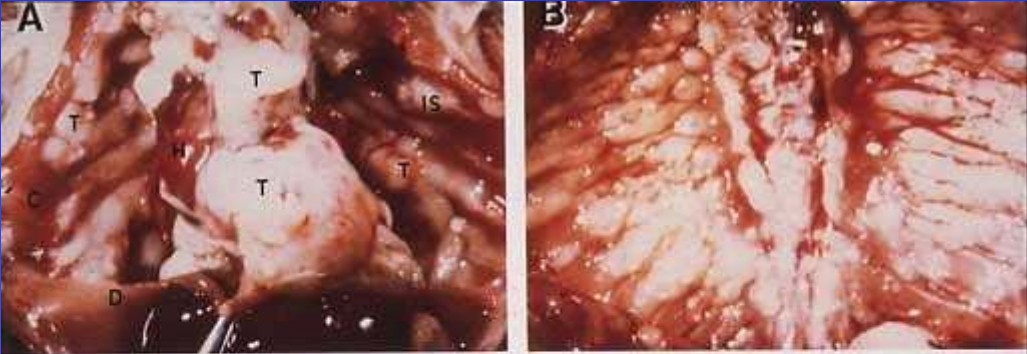
Bevacizumab Targets Vascular Endothelial Growth Factor (VEGF) - sorafenib



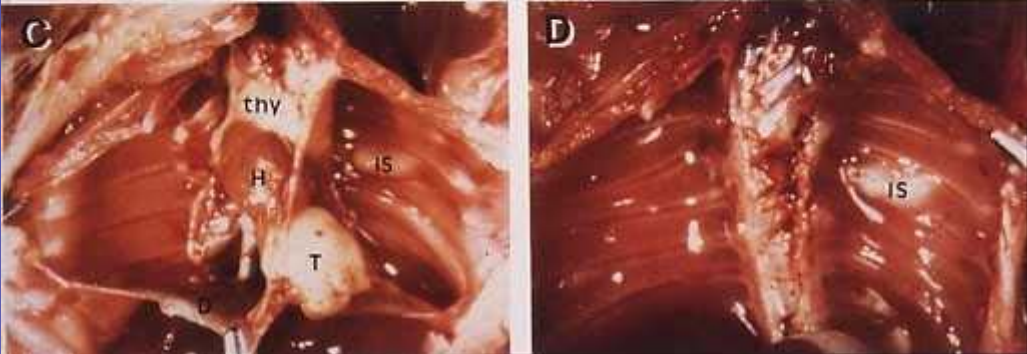
Overall survival by baseline VEGF level



before



after



Mouse mesothelioma treated by HSV-tk plus Gancyclovir

Chemotherapy

first line - yes

when – early yes

2nd line – for the future yes

3 YESs - x factor