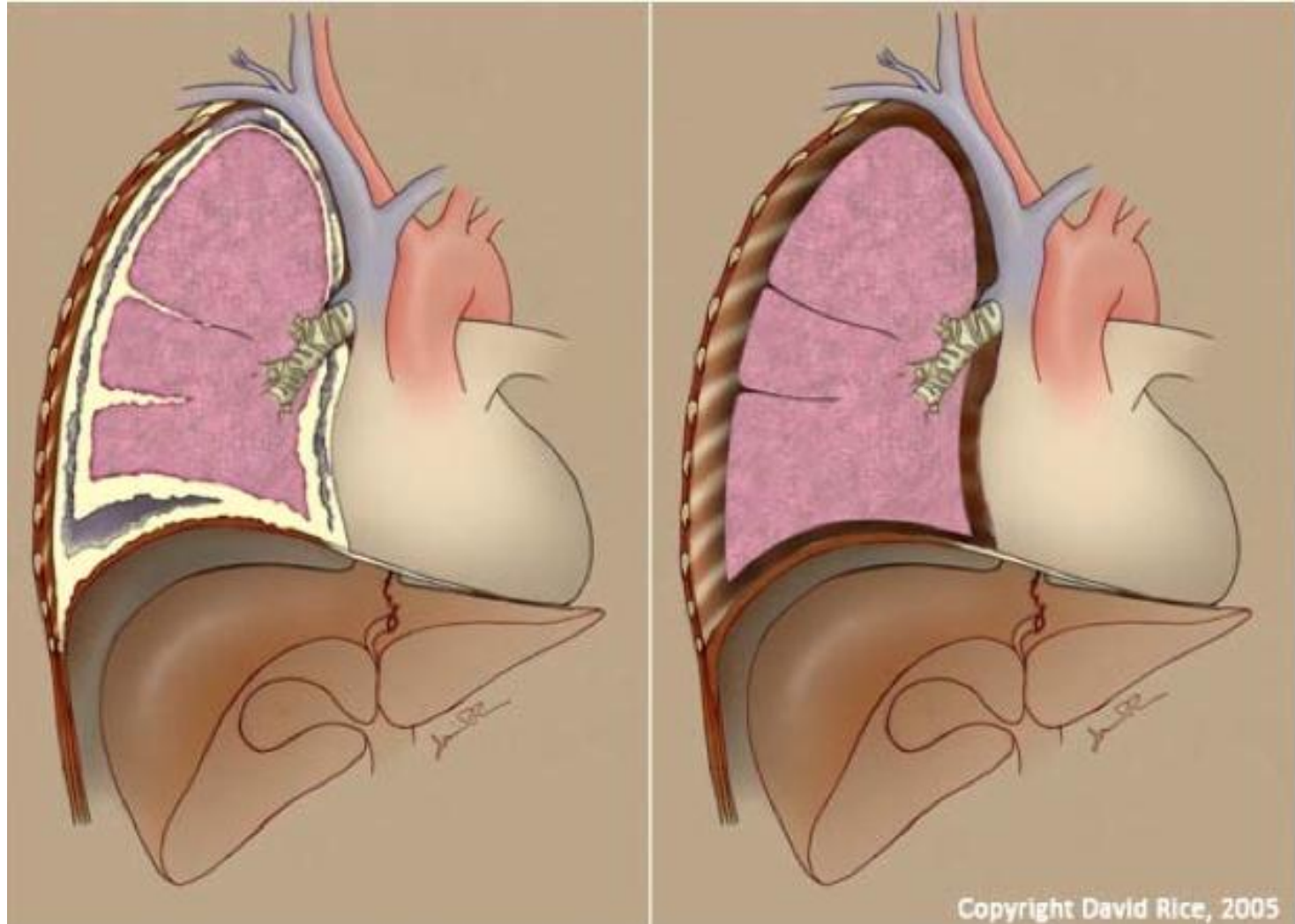


**2nd International Thoracic Oncology Congress, Dresden
16th – 18th September 2010**

**Malignant pleural
mesothelioma:
extention of surgery**

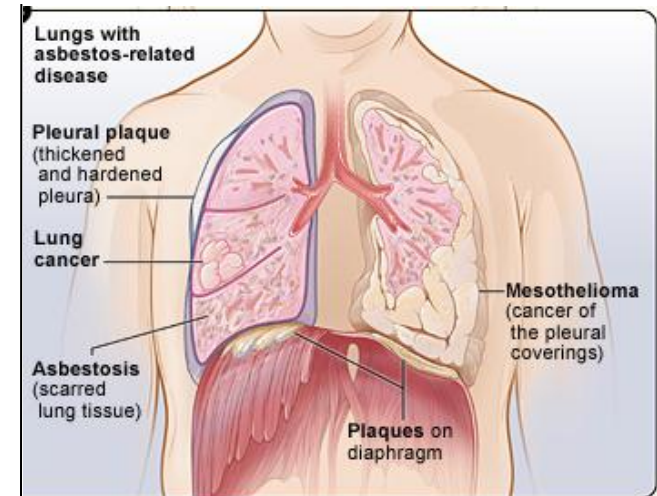
**Walter Weder MD
Professor of Surgery
University Hospital Zurich**

Malignant pleural mesothelioma



Operative Procedures

- ***Diagnostic***
 - pleural Bx, VATS
- ***Palliative for effusion control***
 - talk pleurodesis
VATS/open
 - parietal pleurectomy
VATS/open
- ***Curative Intent***
 - Pleurectomy /
Decortication (P/D)
 - Extrapleural
Pneumonectomy (EPP)



Multimodality therapy

- **Goal:**
 1. **curative therapy**
 2. **prolonged survival**
balanced with quality of live
- **Intervention:**
 - **radical resection/maximal cyto-reduction**
 - **systemic treatment**
 - **+/- radiotherapy**

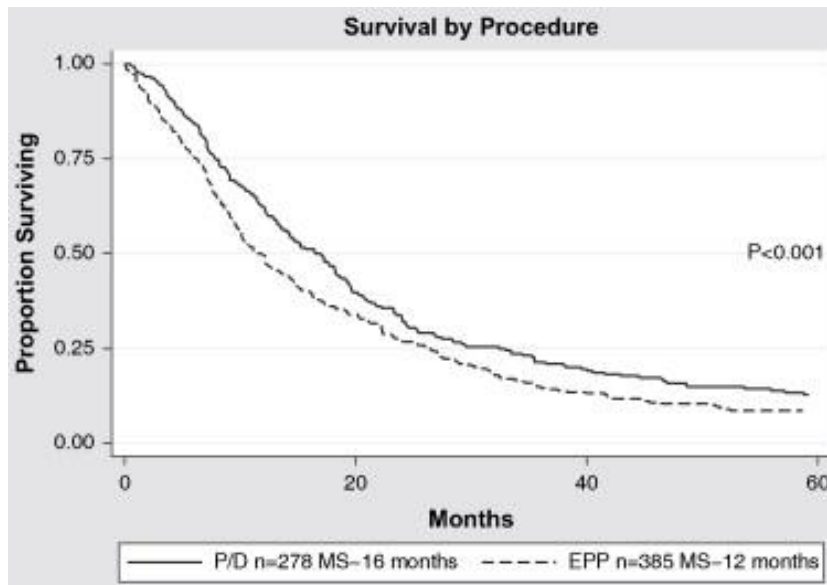
Dilemma

The role and type of surgery in MPM continues to be a matter of debate

- **no randomized study**
- **non-controlled case series**
 - **different staging systems**
 - **different patients selection/histology**
 - **different combinations of other treatments**
 - **different experience of a specialized surgical team**

P/D or EPP

Combined retrospective results of 3 centers including 663 patients stage I-IV



Early Stage:

P/D 35% vs. EPP 25%
($p < 0.001$)

Local Recurrences:

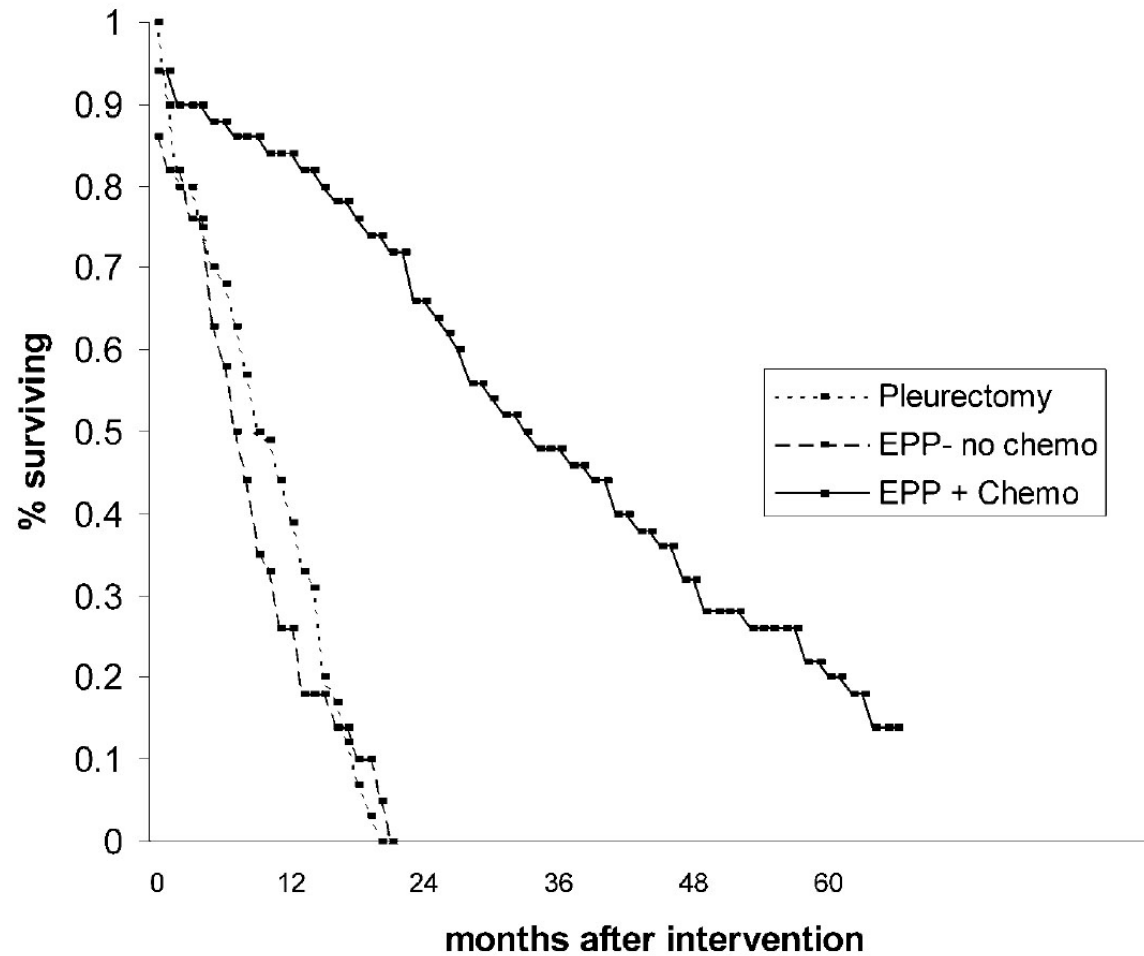
65% (P/D) vs 33%
(EPP)

Operative mortality:

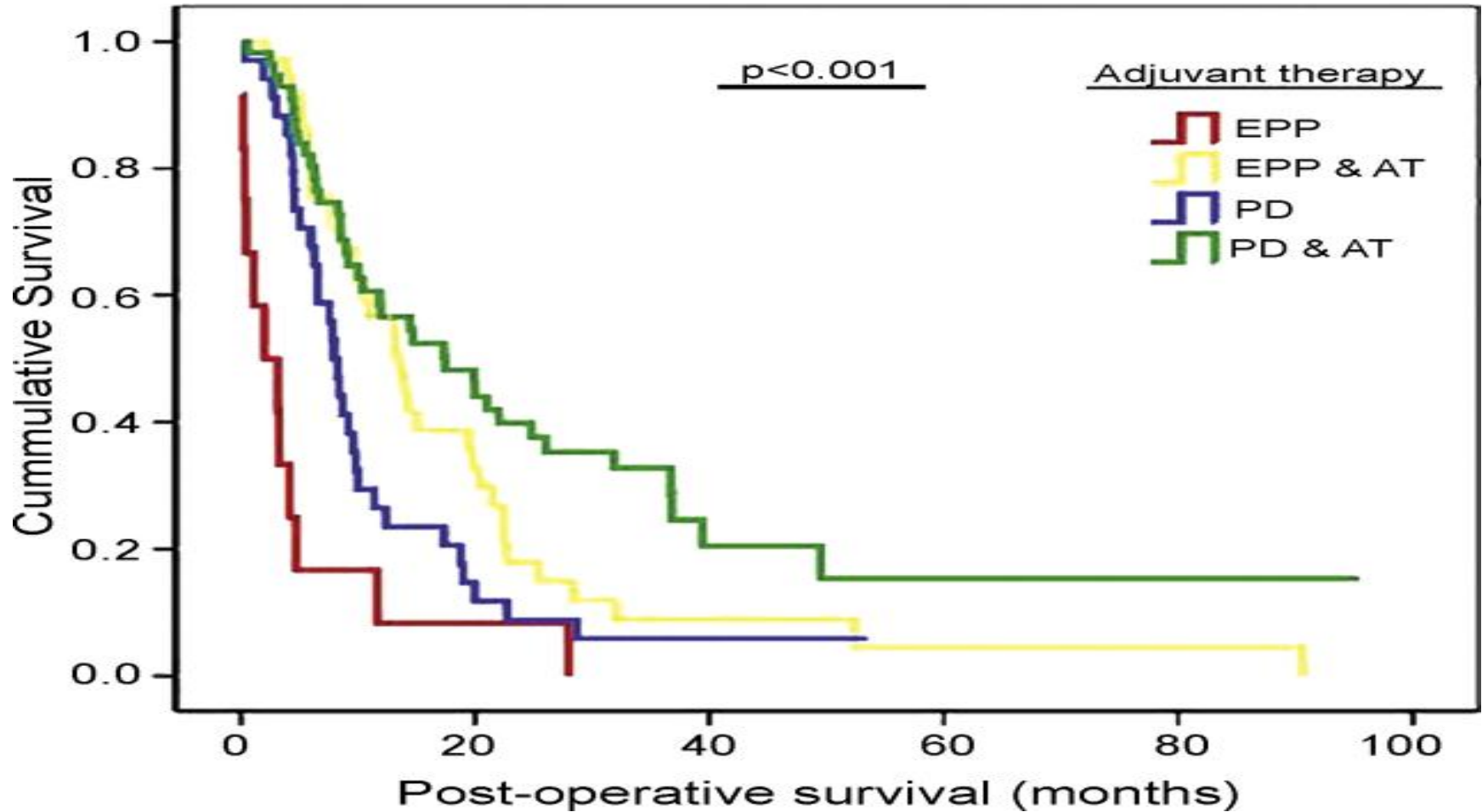
4% (P/D), 7% (EPP)

Prognosticator for longer overall survival: Multimodality approach

P/D or EPP



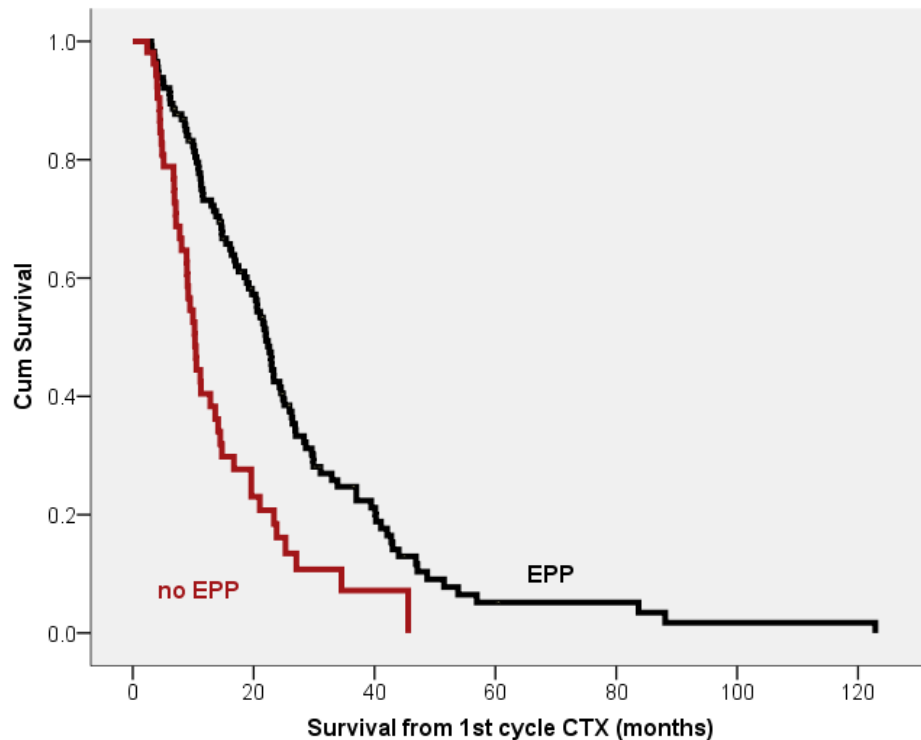
P/D or EPP



EPP in multimodality therapy

Investigator	CTX	EPP	RTX	MST (months)
Sugarbaker 1999	Adjuvant	183	+/-	19
Baldini 1997	Adjuvant	49	'+	22
Aziz 2002	Adjuvant	51		35
Weder 2007	Neoadjuvant:	45	+	23
Rea 2007	Neoadjuvant:	17	+	25.5
Krug 2009	Neoadjuvant	54	+	29
de Perrot 2009	Neoadjuvant	45	+	59 if N ₂ neg.
EORTC 2009	Neoadjuvant:	42/59	+	18.4 (ITT)

10 year experience EPP + MM in Zurich



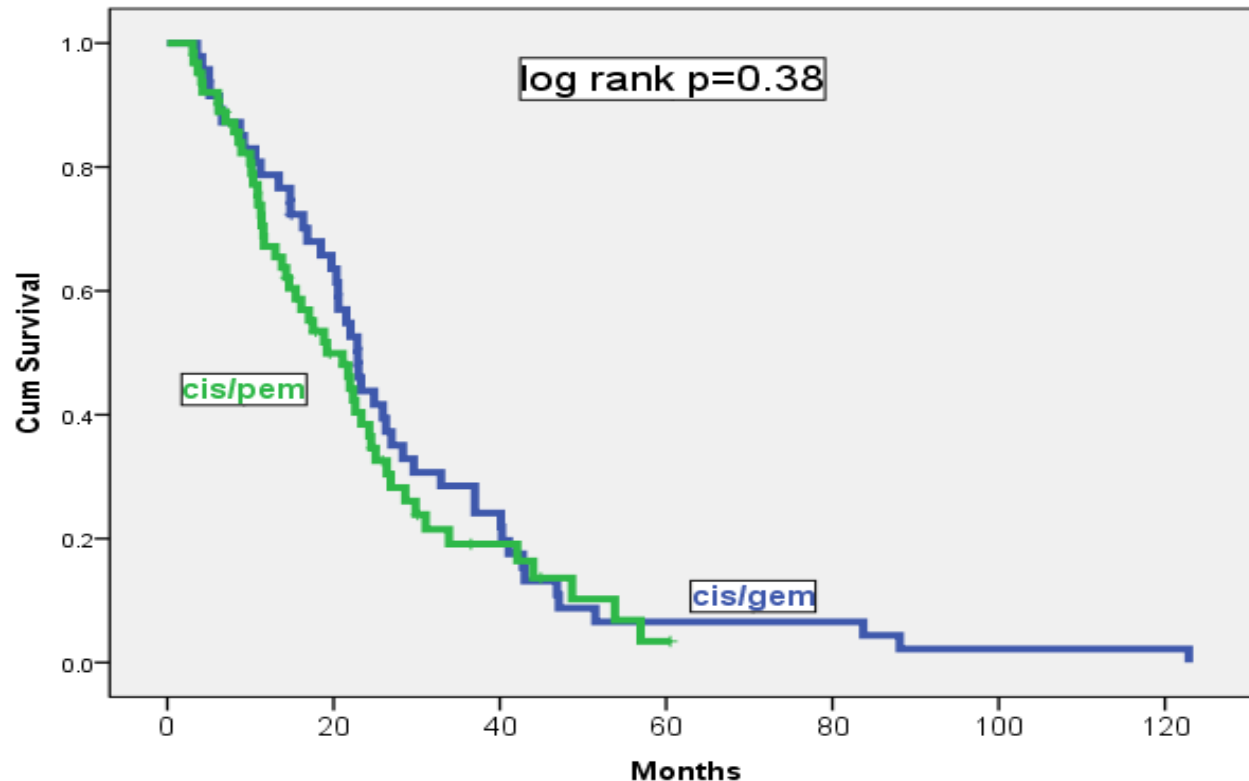
168 Patients ITT

114 EPP

71 with adjuvant Radiotherapy

- **Median OS 22 months EPP
10 months no
EPP**
- **Morbidity 34%
Mortality 4%**

OAS and Chemotherapy



Median OS:

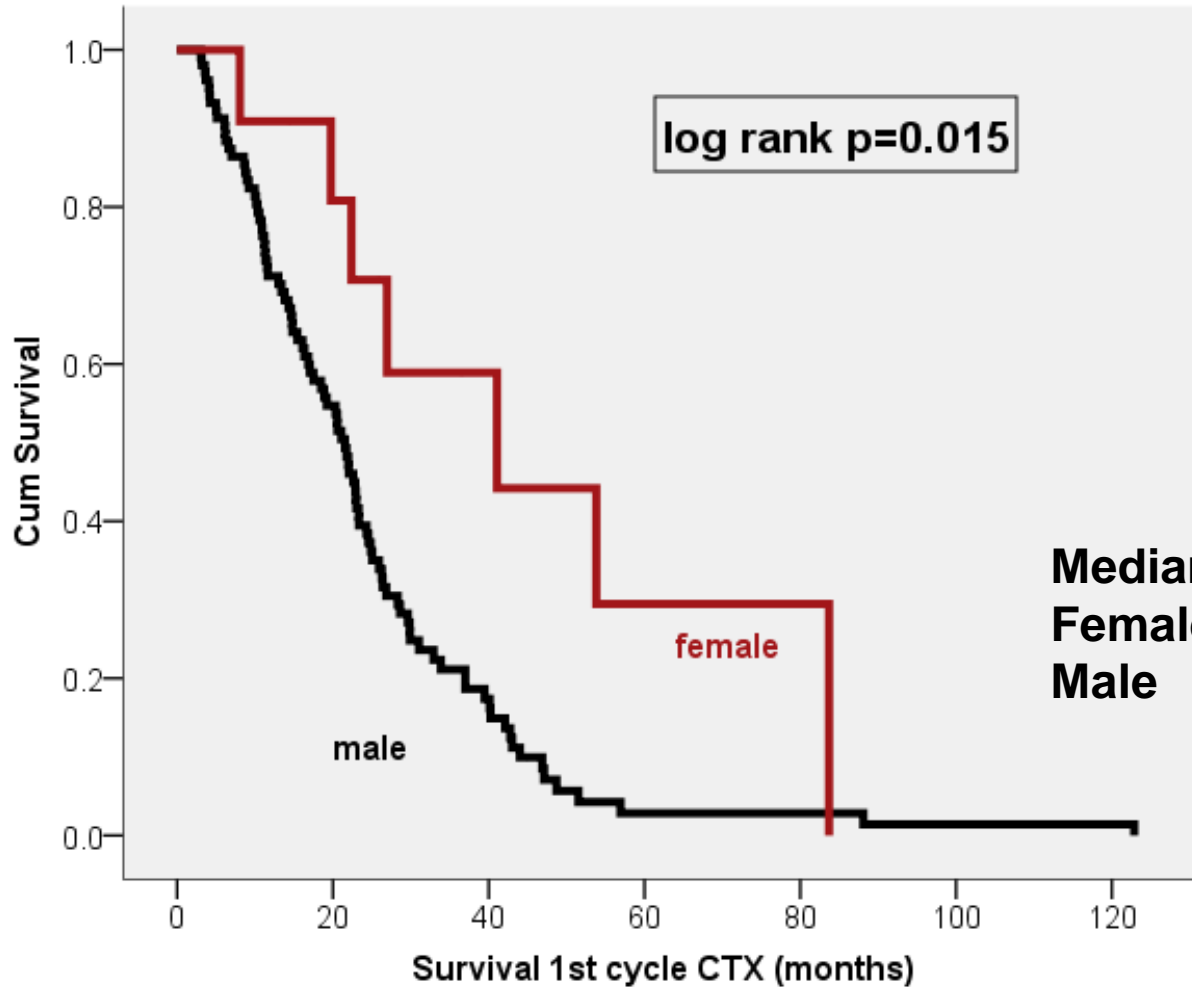
Cis/gem

23 months (95 % CI: 20; 26)

Cis/pem

19 months (95 % CI: 13; 25)

OAS and Sex

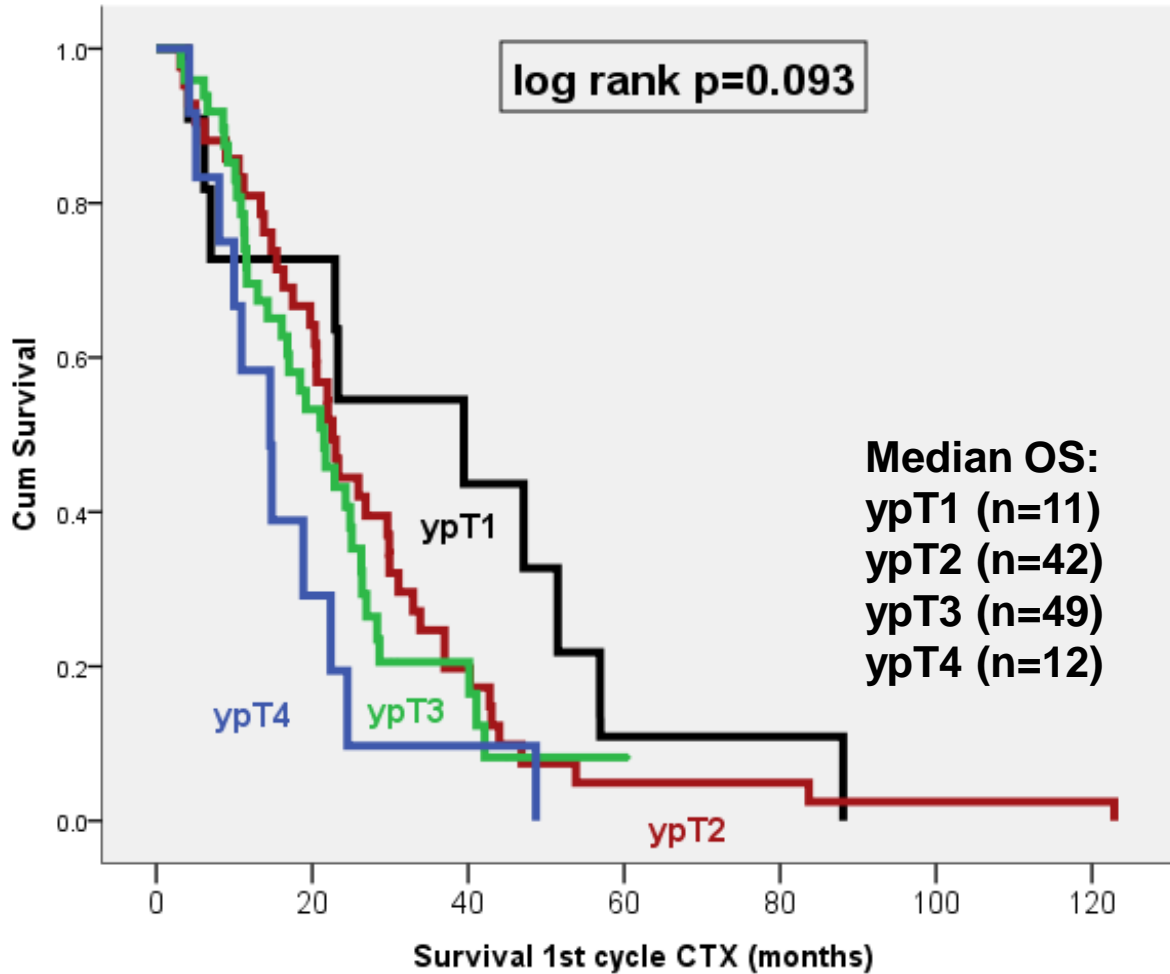


Median OS:

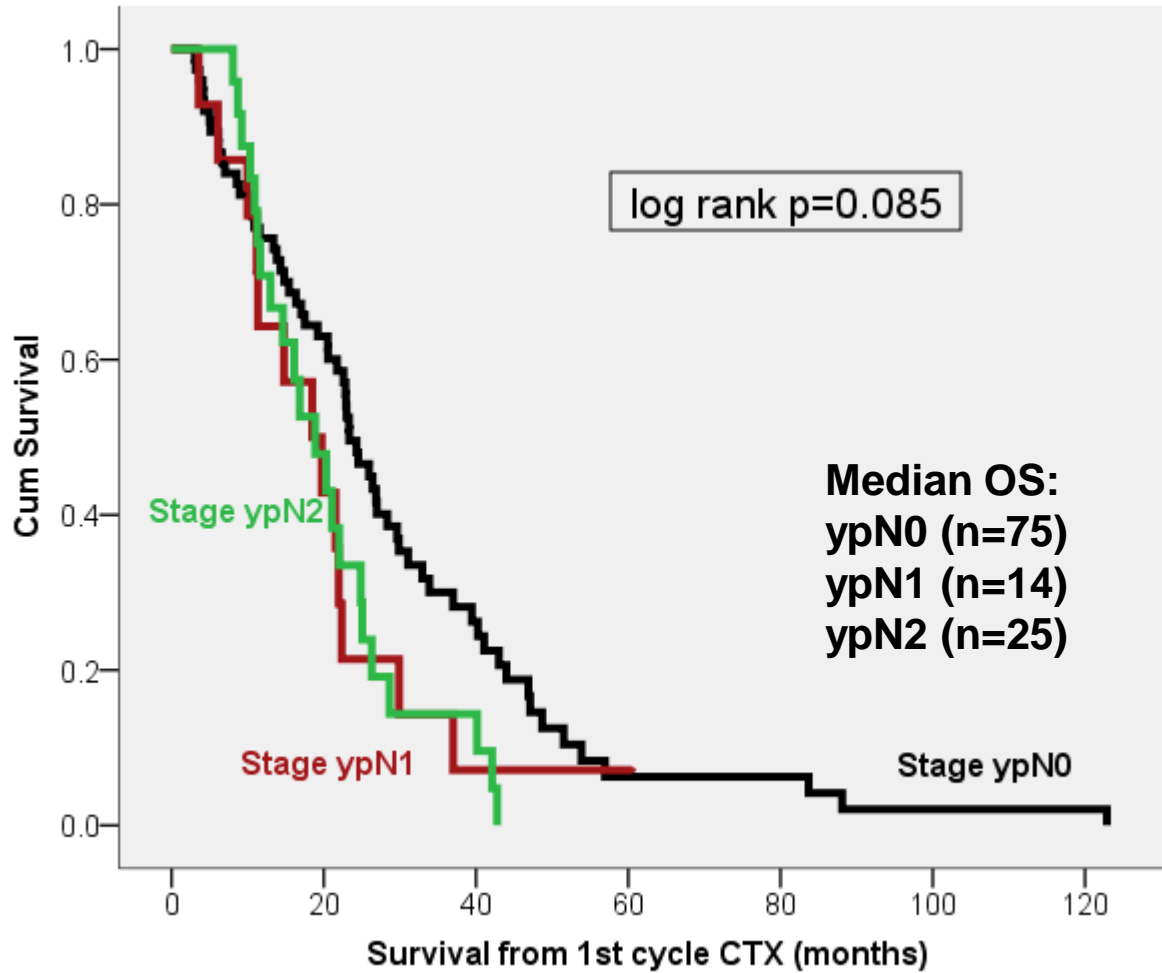
Female 41 months (95 % CI: 8; 74)

Male 22 months (95 % CI: 18; 25)

OAS and T-factor

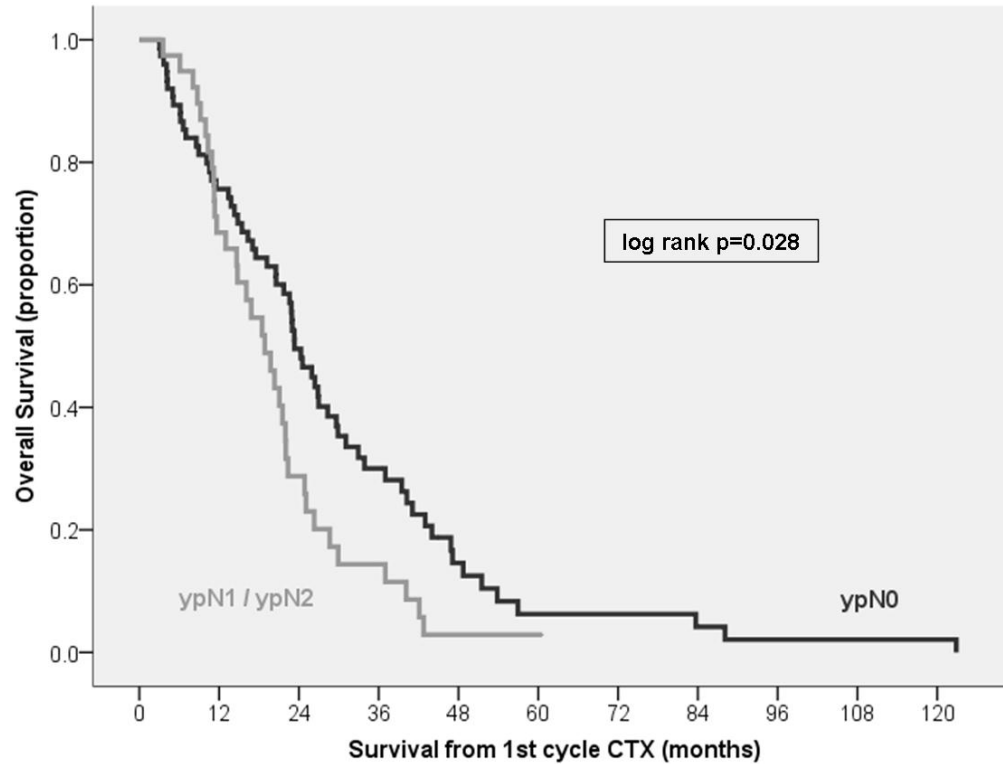


OAS and N-factor



23 months (95 % CI: 20; 27)
19 months (95 % CI: 9; 28)
19 months (95 % CI: 13; 25)

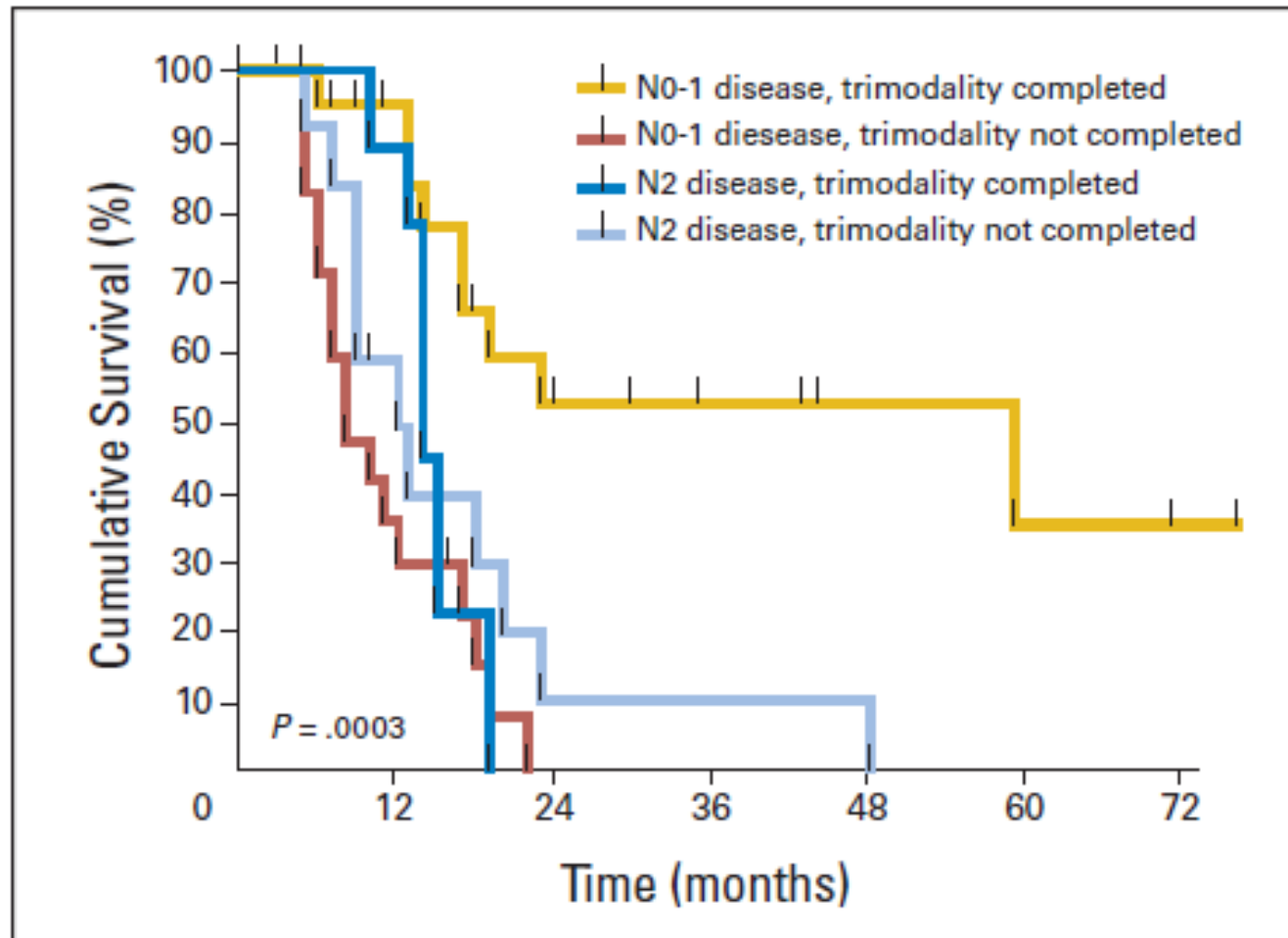
OAS N0 vs. N1/N2



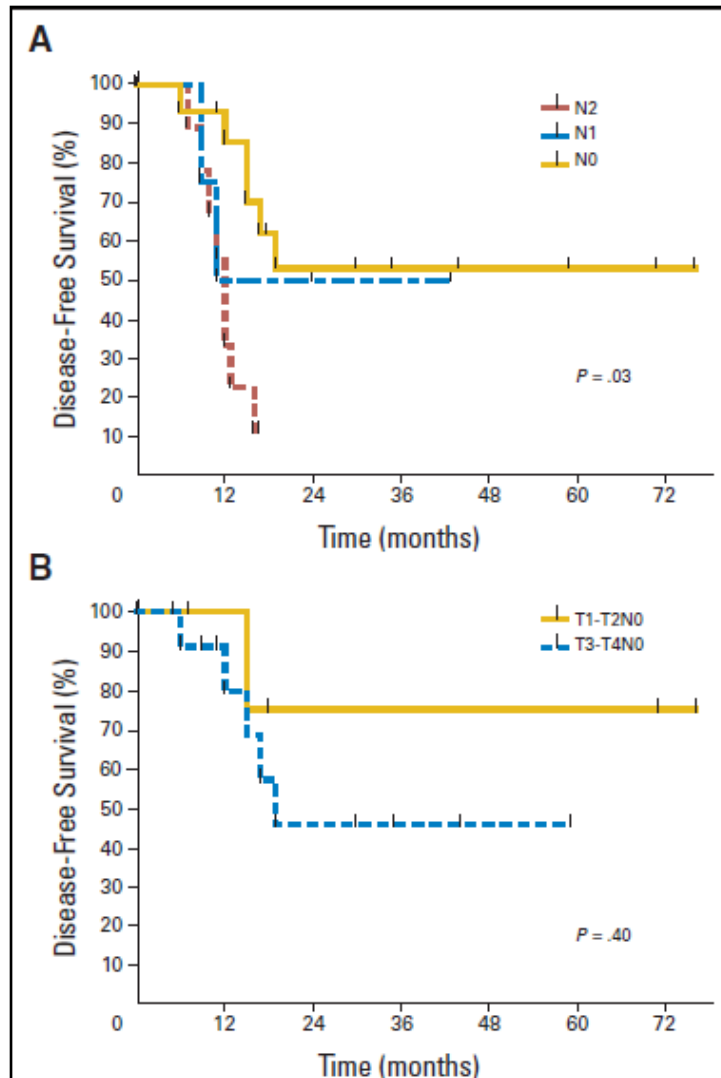
Patients at risk

ypN0	75	54	33	17	7	3	3	2	1	1	1
ypN1 / ypN2	39	26	10	5	1	1					

N-status and survival



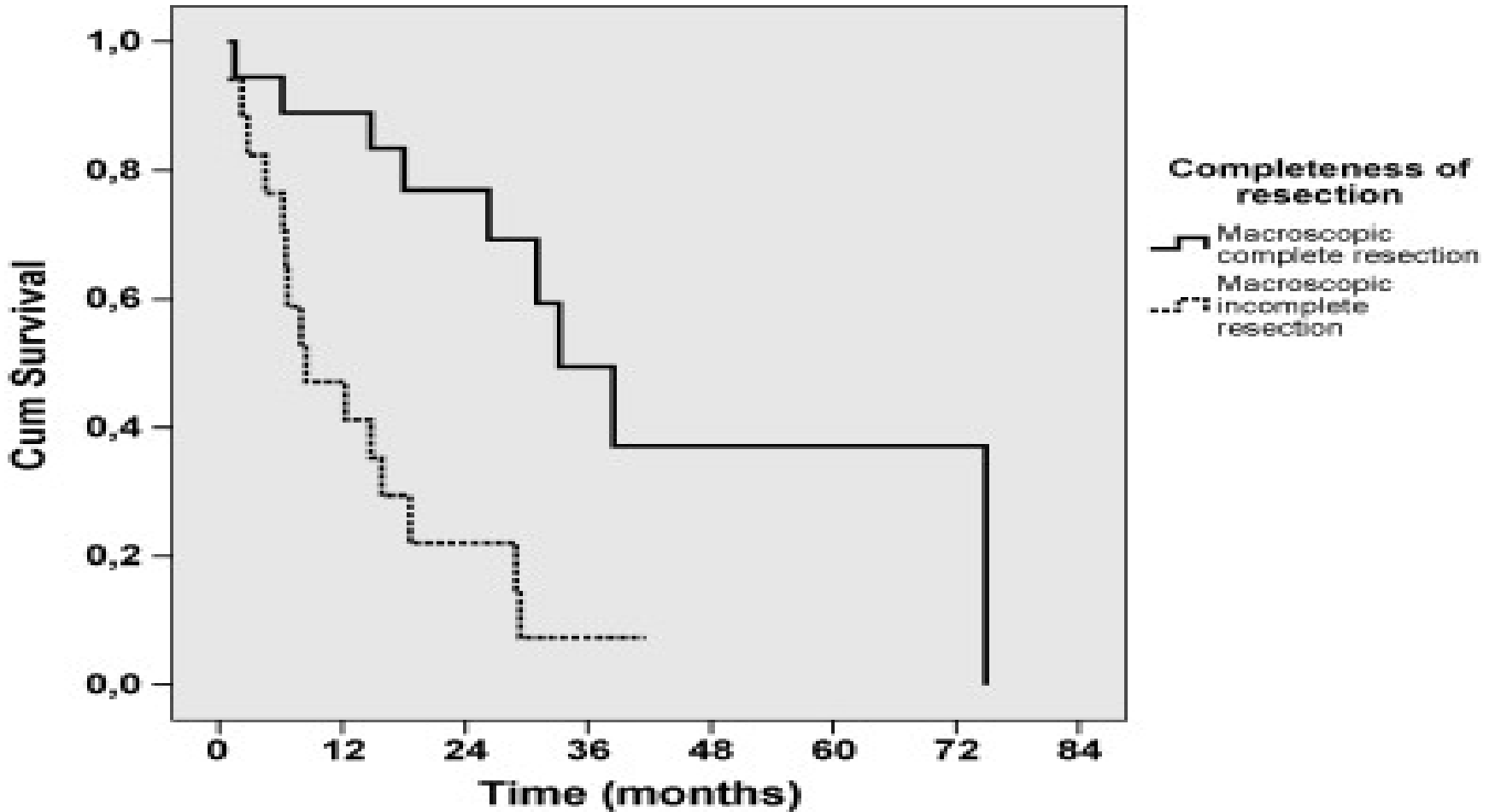
T-status and survival



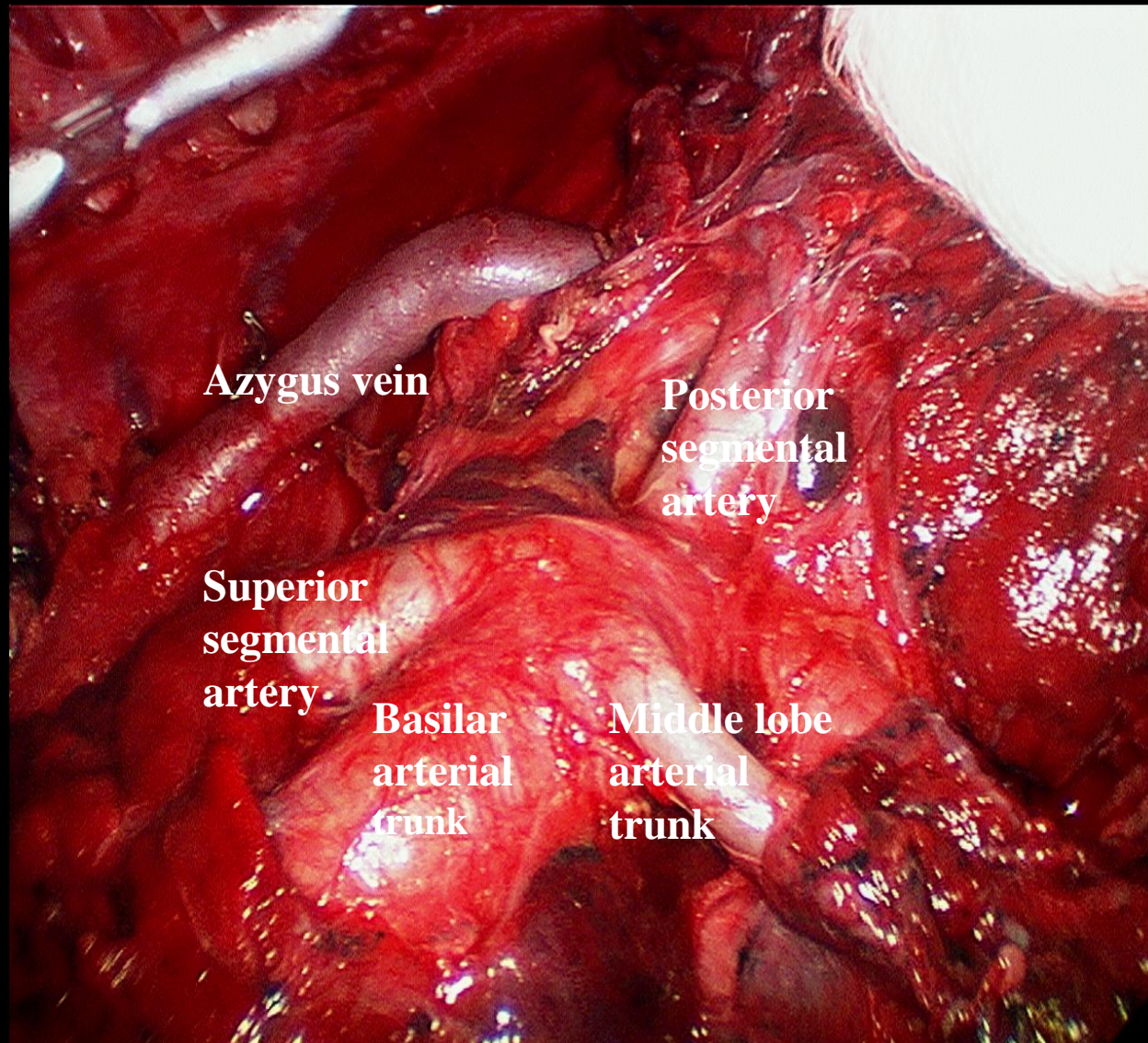
Series with P/D in multimodality therapy

Investigator	Patients	CTX Setting	P/D	Other Modalities	MST (months)
Ruffie 1989	332	Adjuvant	63	RTX	9.8
Branscheid 1991	301	Adjuvant	82	-	10.4
Allen 1994	96	Adjuvant	56	RTX	9
Pass 1998	48	Adjuvant	23	PDT, ICTX	22
Rusch 1999	231	Adjuvant	59	RTX	18.5
Bölükbas 2009	102	Adjuvant	35	RTX	30
Flores et al. 2008	663	Adjuvant	278	161	16

Completeness of P/D



The Appearance of the Right Major Fissure After a Radical Pleurectomy

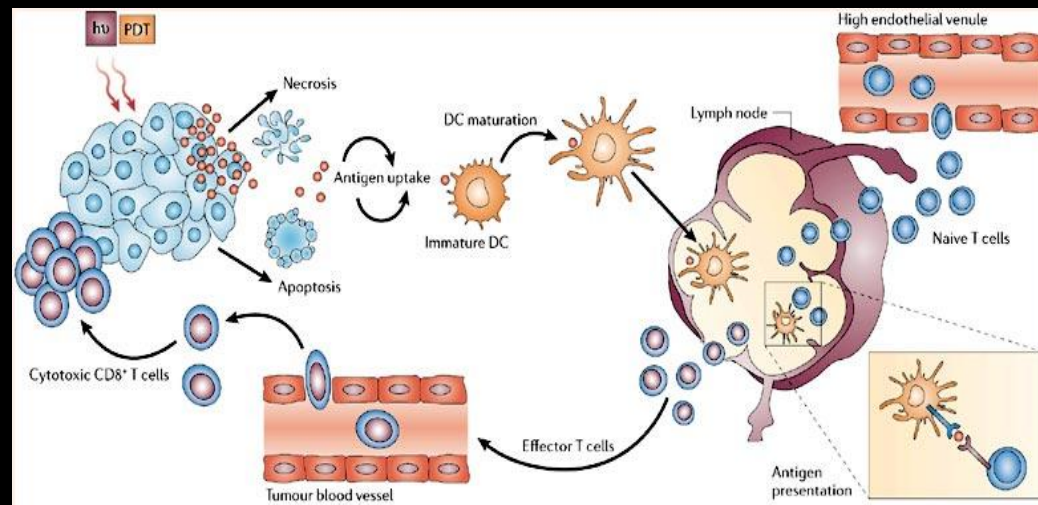
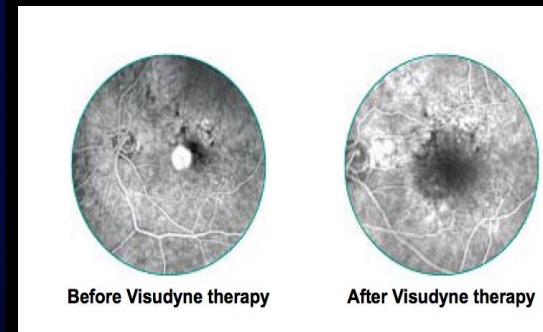
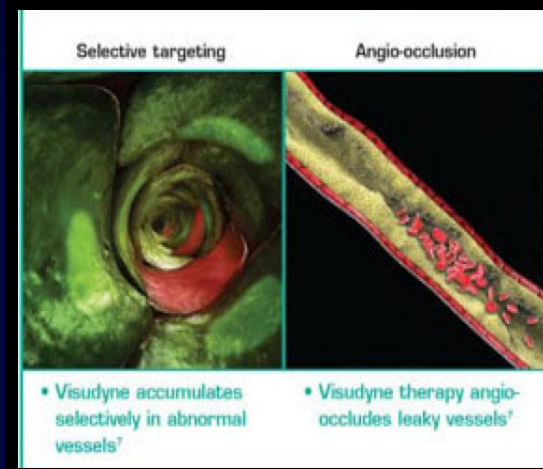


courtesy J. Friedberg

Mechanisms of PDT Effect

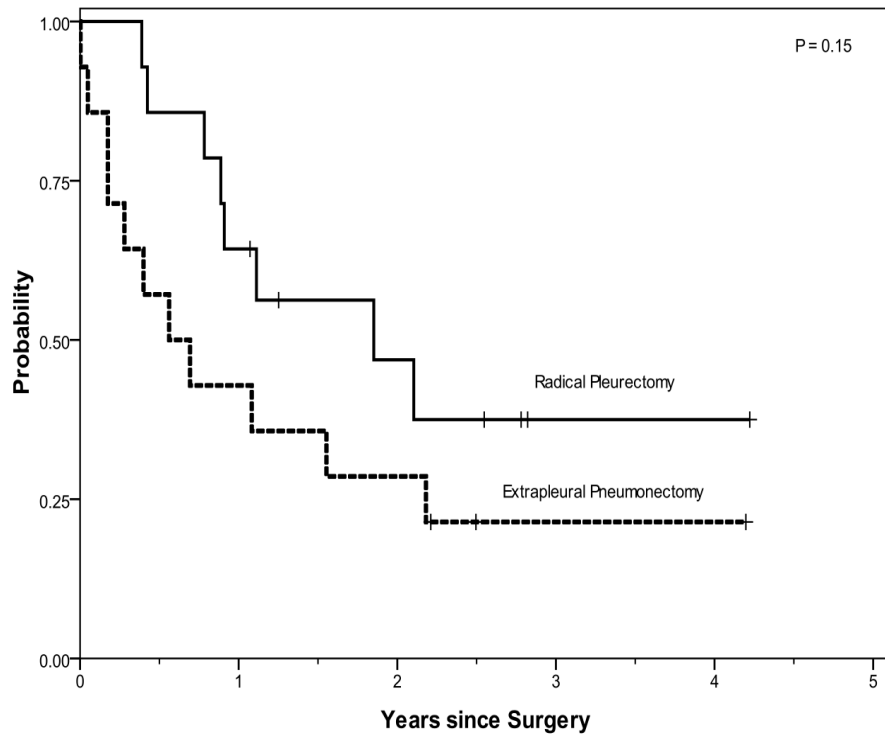
- Direct cell kill
 - Mitochondria
 - Cell membrane
 - Apoptosis
- Damage to neovasculature
- Immune response
 - Local
 - systemic

Cell Rupture

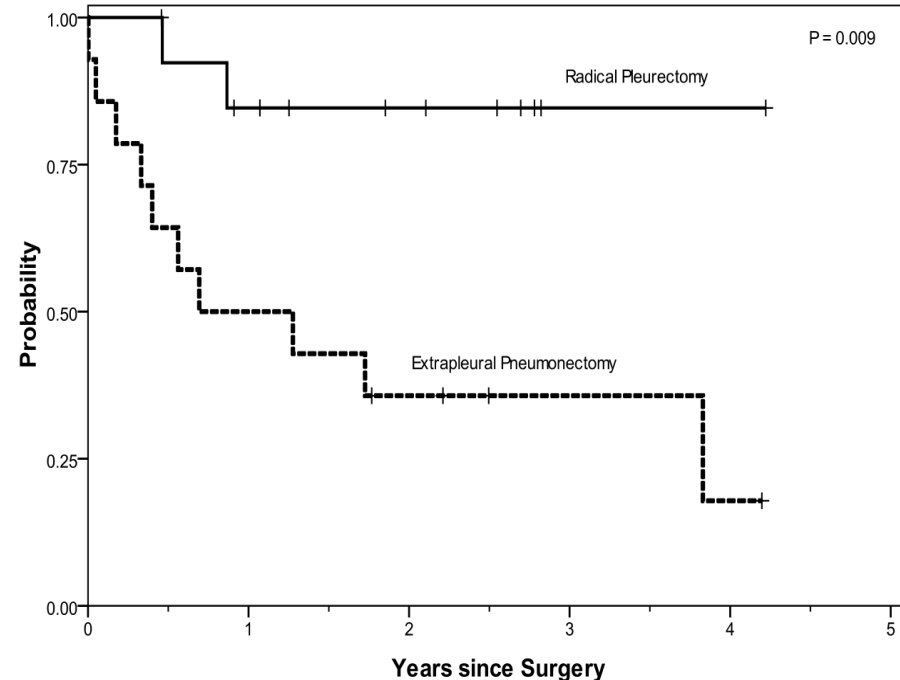


28 patients (14/14) having modified EPP or RP and PDT (86% stage III/IV)

Disease-Free Survival



Overall Survival



Summary

- **Series on multimodality treatment with radical surgery report better survival data than without surgery.**
- **EPP - as the most radical procedure - as well as P/D should be performed in experienced centres to ensure low local recurrence, low M&M rates as well as good quality of life.**

Summary

- **The selection of patients based on histology and extent of nodal involvement remains an issue of controversy and should be further investigated.**
- **Determination of molecular tumor characteristics should be an integrative part of further investigations in order to select patient groups who benefit from different therapies.**