

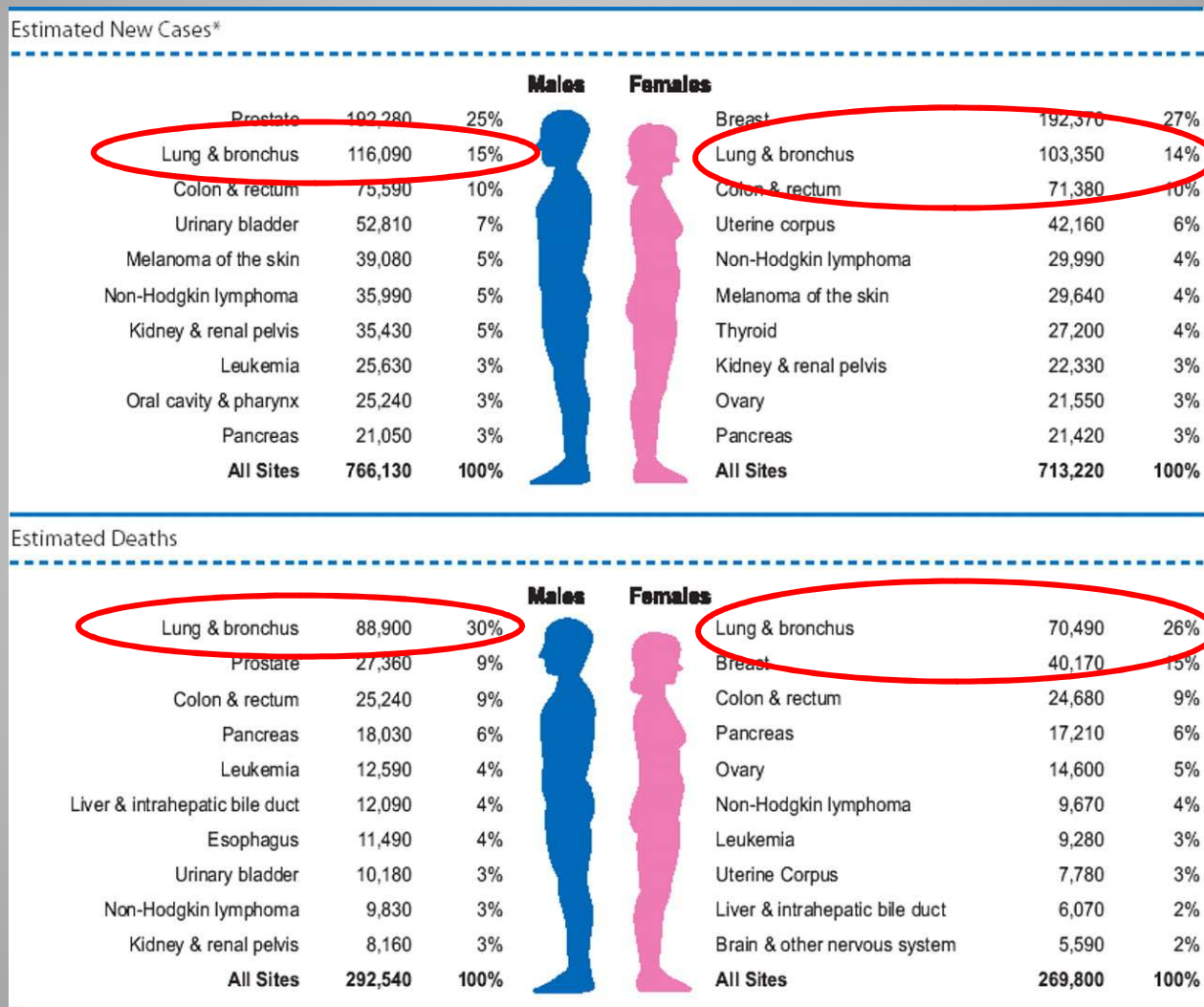


Istituto Palazzolo-Fondazione Don Gnocchi - Milano  
Fondazione IRCCS Istituto Nazionale Tumori - Milano  
Istituto Oncologico Veneto (IOV) - Padova

# LA TERAPIA MEDICA DEL CARCINOMA DEL POLMONE NELL'ANZIANO

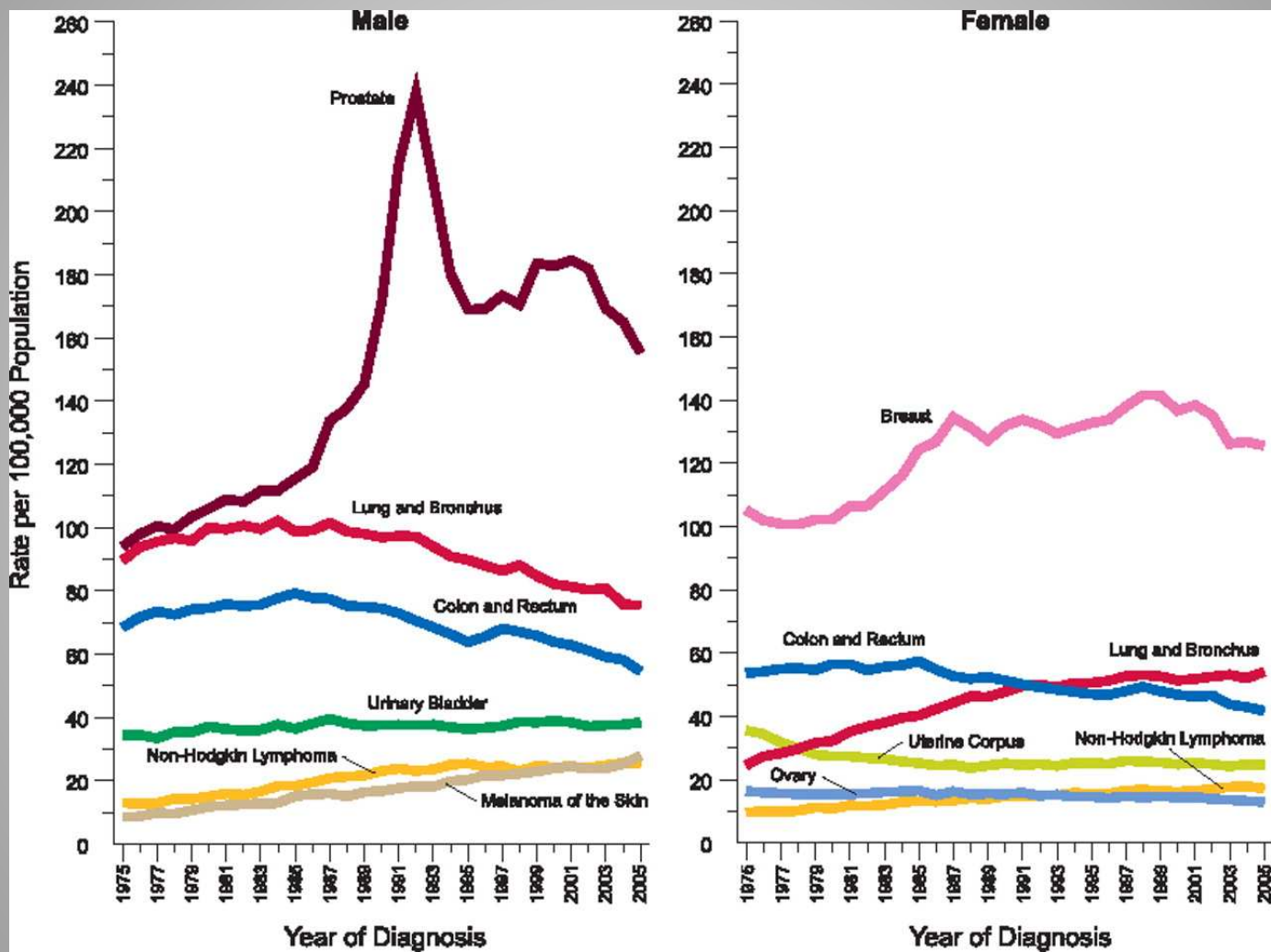
**Adolfo FAVARETTO**  
**S.S. ONCOLOGIA TORACICA**  
**ONCOLOGIA MEDICA 2**  
**IOV-IRCCS PADOVA**

# Ten Leading Cancer Types for the Estimated New Cancer Cases and Deaths USA 2009



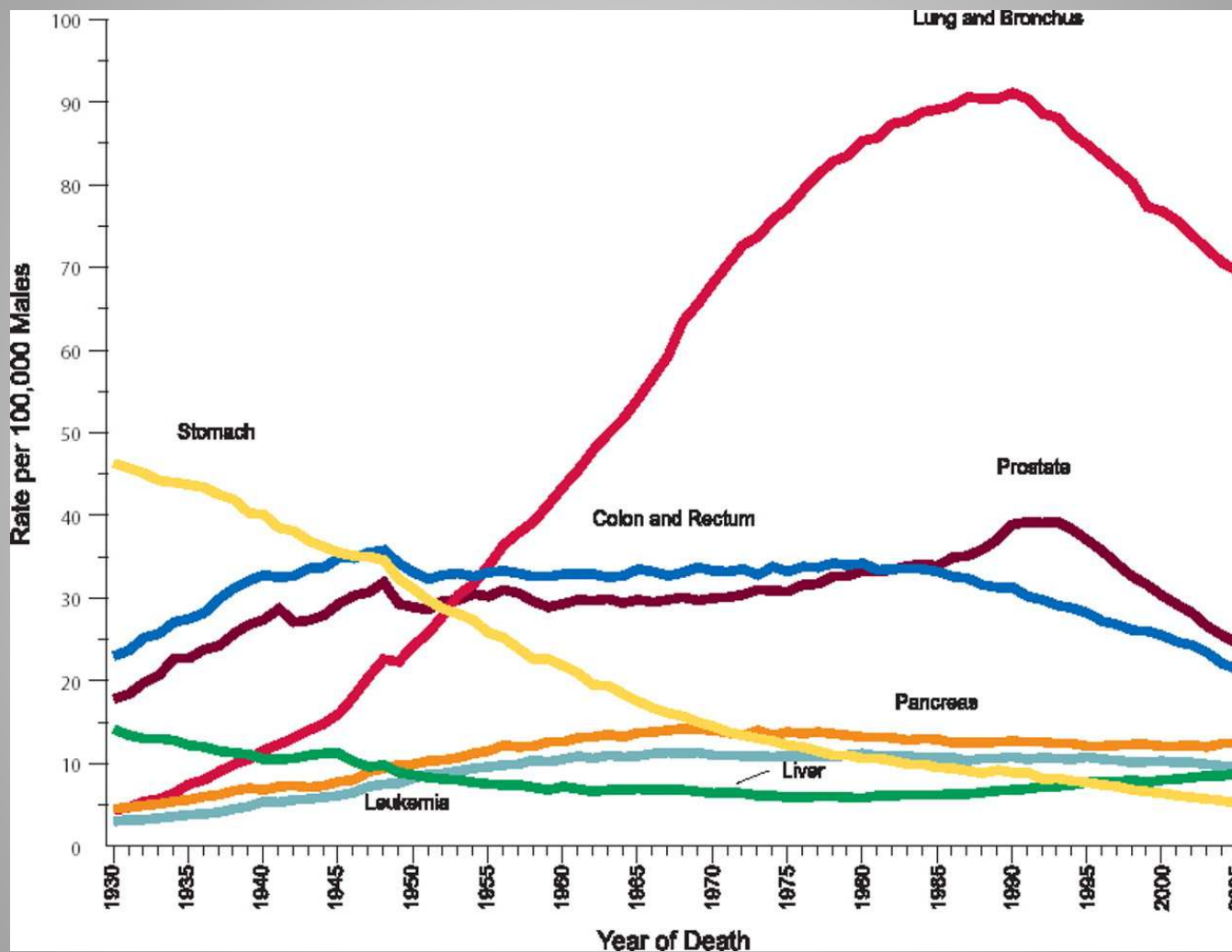
Jemal A CA Cancer J Clin 2009

# Annual Age-adjusted Cancer Incidence Rates Among Males and Females for Selected Cancer Types, US, 1975 to 2005



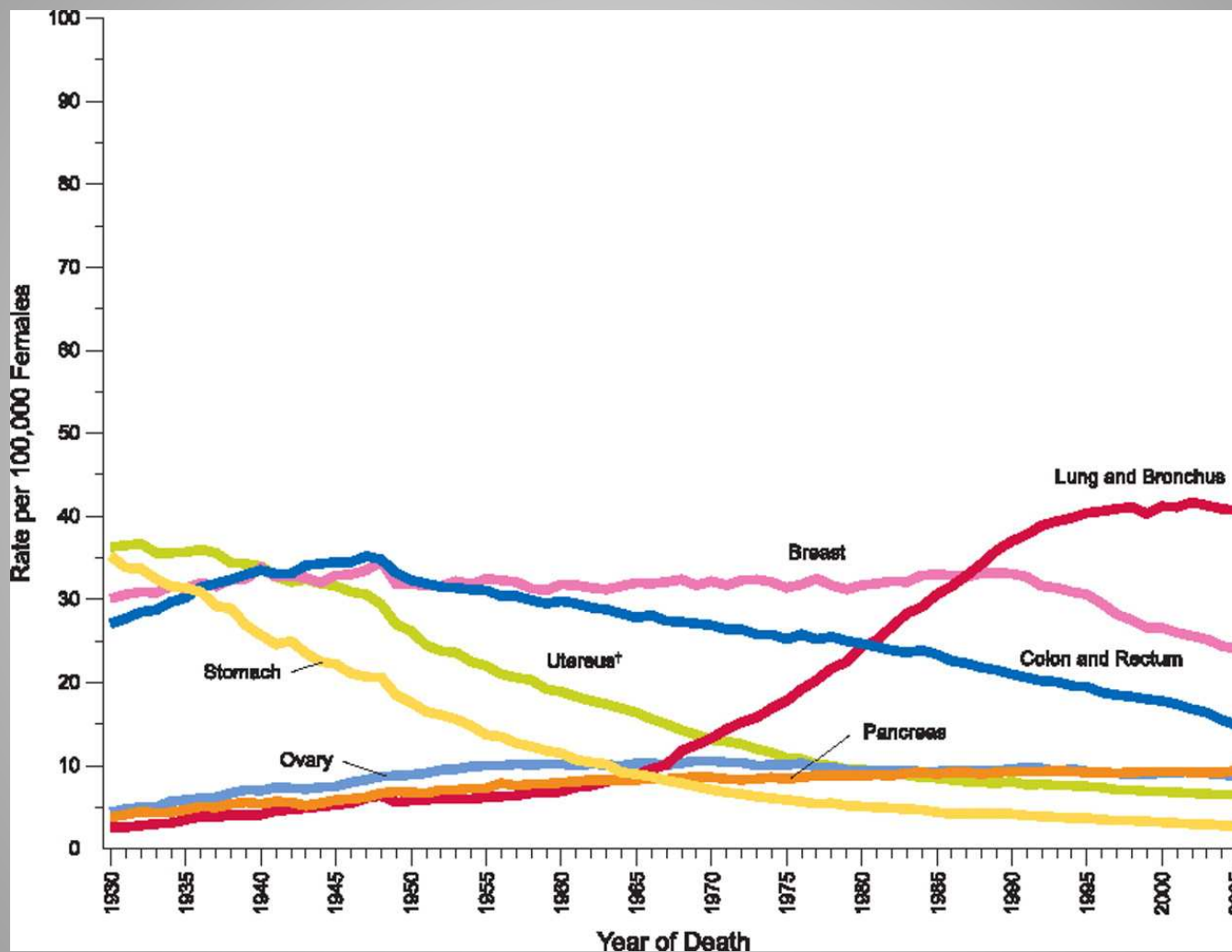
Jemal A CA Cancer J Clin 2009

## Annual Age-adjusted Cancer Death Rates Among Males for Selected Cancer Types, US, 1930 to 2005



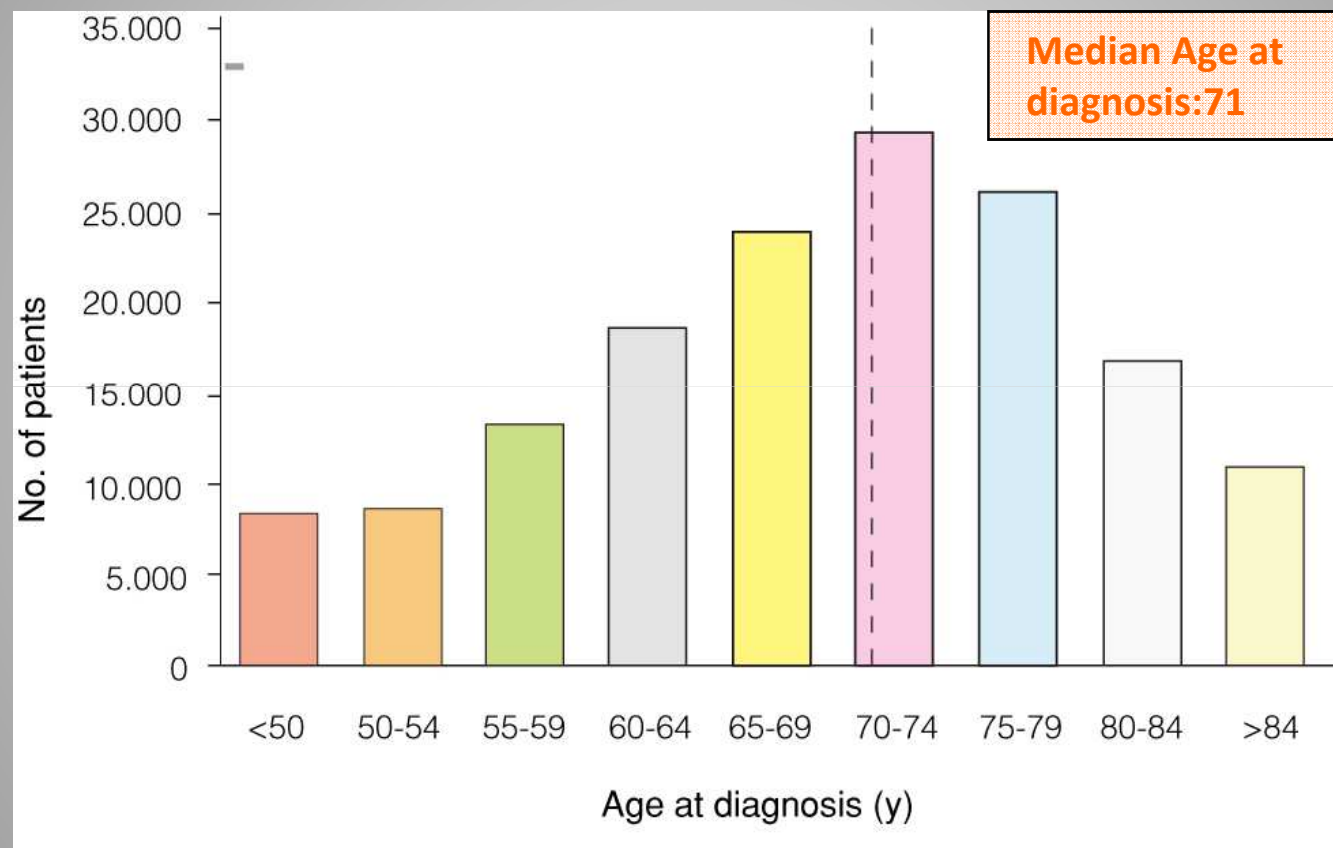
Jemal A CA Cancer J Clin 2009

## Annual Age-adjusted Cancer Death Rates Among Females for Selected Cancer Types, US, 1930 to 2005



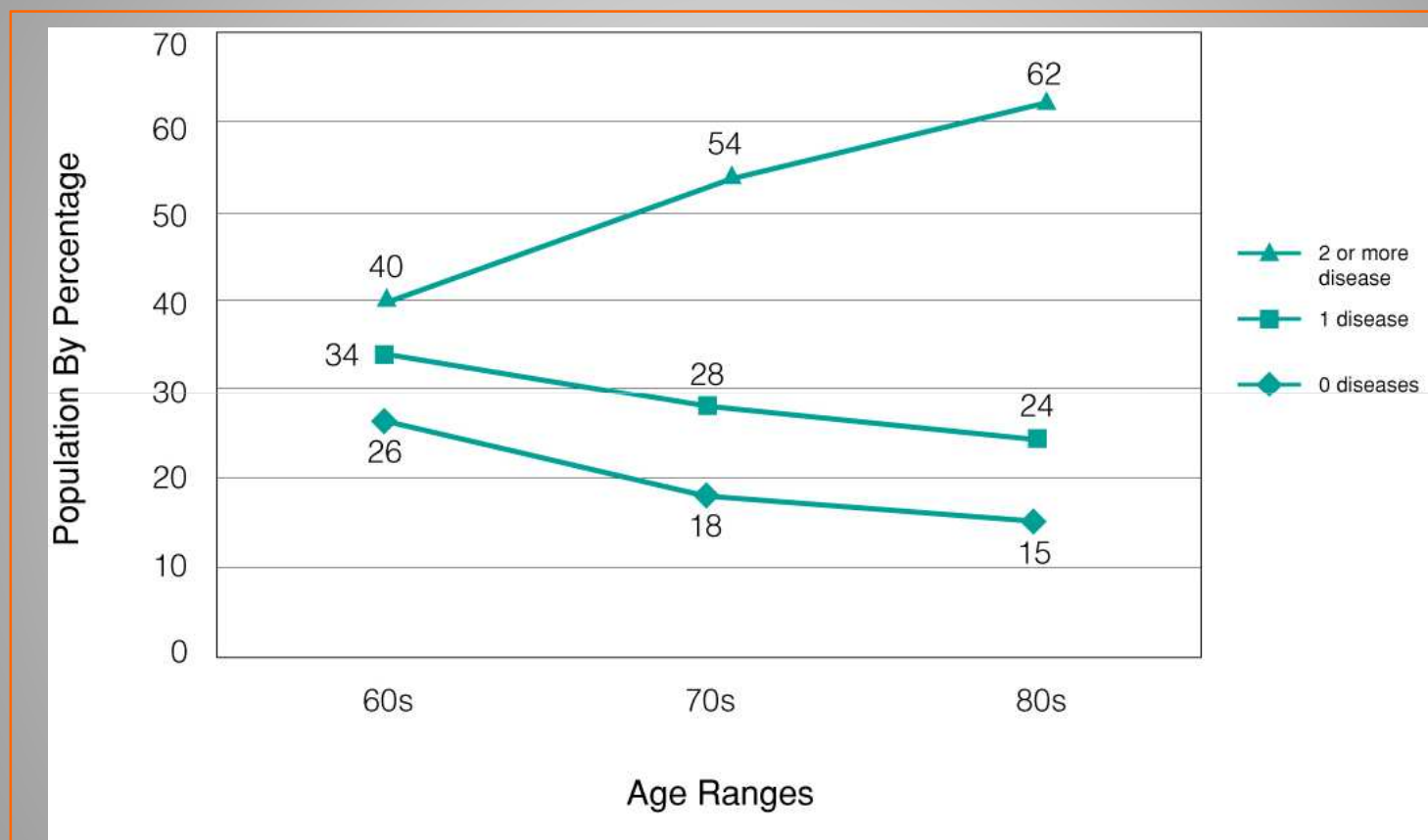
Jemal A CA Cancer J Clin 2009

## US NSCLC Incidence: Age at diagnosis

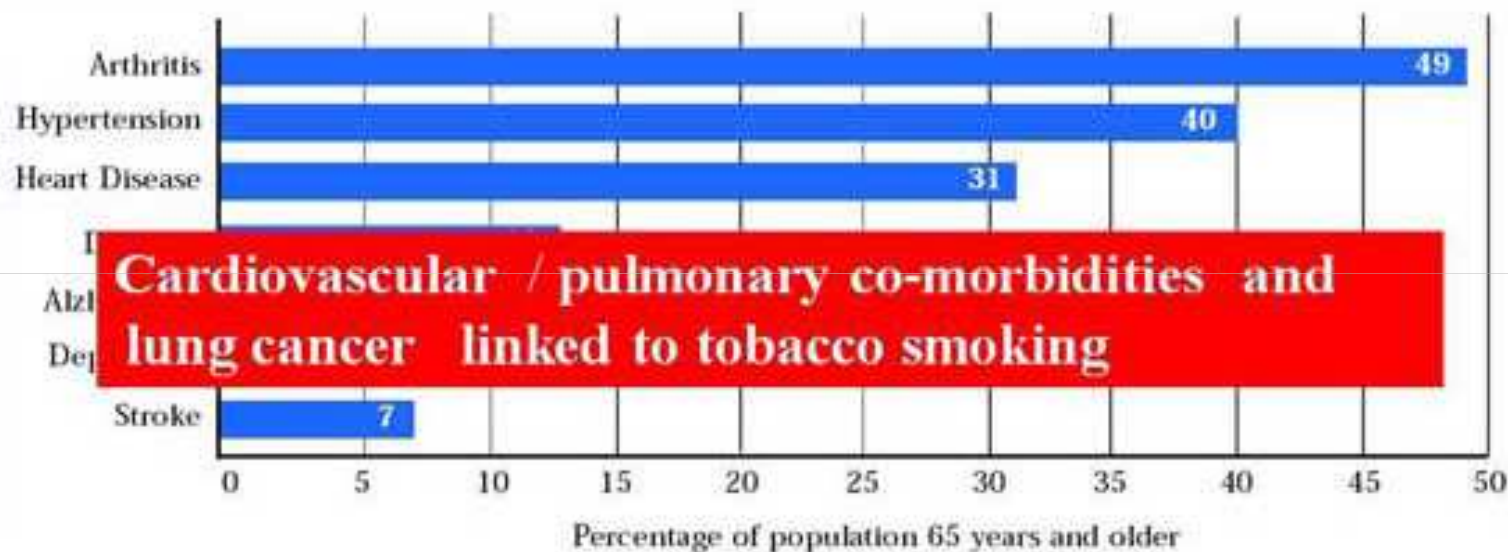


Data from SEER Cancer Statistics Review 1975-2001

## Comorbidity increases with age...

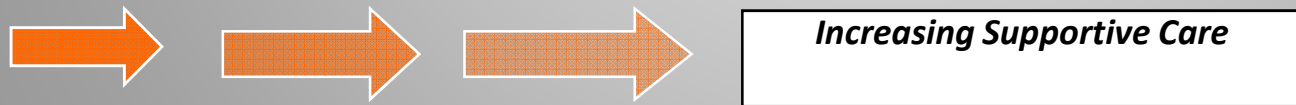
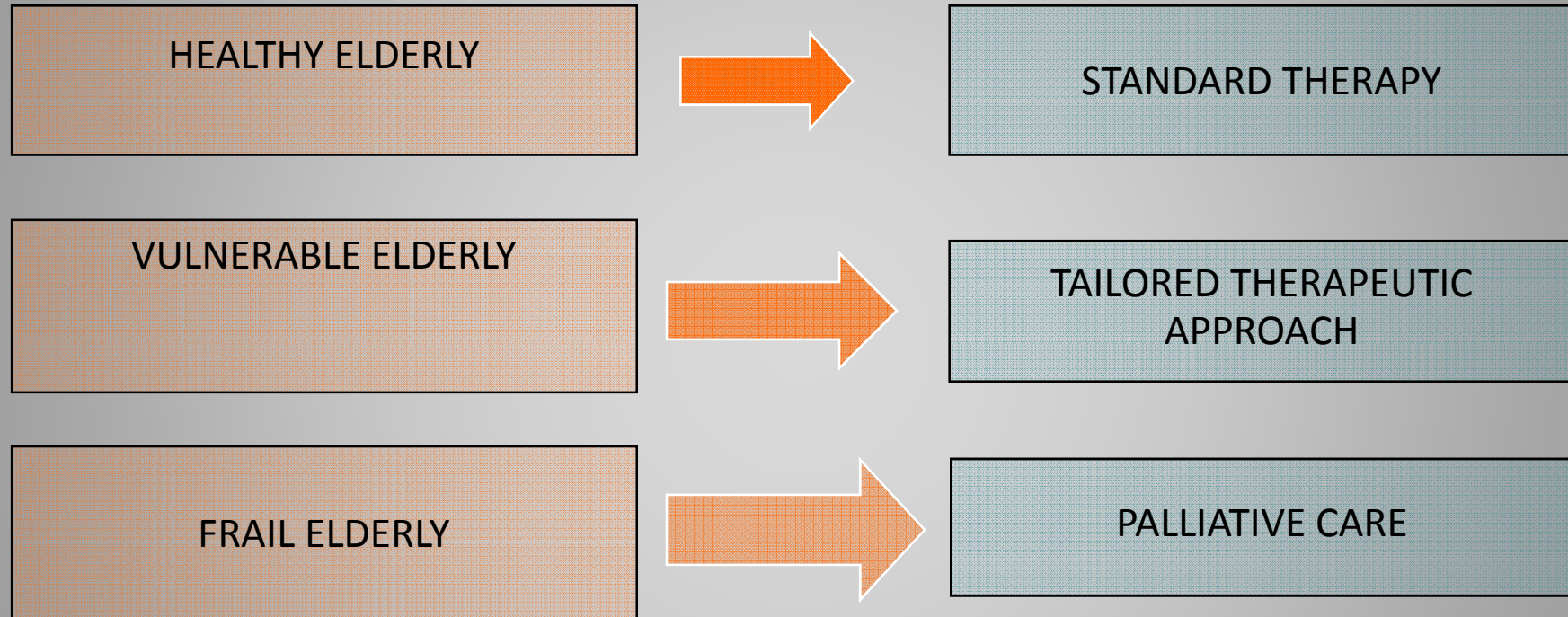


## DISEASE PREVALENCE IN THE ELDERLY



**Source:** Centers for Disease Control and Prevention/National Center for Health Statistics. Current Estimates from the National Health Interview Survey, 1995. Report 199, 1995.

# CGA



# Should Elderly Non–Small-Cell Lung Cancer Patients Be Offered Elderly-Specific Trials? Results of a Pooled Analysis From the North Central Cancer Treatment Group

*Aminah Jatoi, Shauna Hillman, Philip Stella, Erin Green, Alex Adjei, Suresh Nair, Edith Perez, Bipinkur Amin, Steven E. Schild, Rene Castillo, and James R. Jett*

**ELDERLY SPECIFIC**

**AGE UNSPECIFIED**

**Table 2.** Chemotherapy Regimens

N9921	N0022	98-24-52	N0026
Paclitaxel 50 mg/m <sup>2</sup> IV days 1,8,15; carboplatin AUC = 2 IV days 1,8,15; cycle length 28 d	Vinorelbine 60 mg/m <sup>2</sup> orally on days 1,8,15,22; cycle length 28 d	Docetaxel 100 mg/m <sup>2</sup> IV day 1; gemcitabine 800 mg/m <sup>2</sup> IV days 1,8,15; cycle length 28 d OR docetaxel 50 mg/m <sup>2</sup> IV days 1, 15; gemcitabine 2,500 mg/m <sup>2</sup> IV days 1, 15; cycle length 28 d OR docetaxel 75 mg/m <sup>2</sup> IV day 1; gemcitabine 700 mg/m <sup>2</sup> IV days 1,8,15; cycle length 28 d	Pemetrexed 500 mg/m <sup>2</sup> IV day 1; gemcitabine 1,250 mg/m <sup>2</sup> days 1,8; cycle length 21 d OR gemcitabine 1,250 mg/m <sup>2</sup> IV day 1; pemetrexed 500 mg/m <sup>2</sup> IV day 1; gemcitabine 1,250 mg/m <sup>2</sup> IV day 8; cycle length 21 d OR gemcitabine 1,250 mg/m <sup>2</sup> IV day 1; pemetrexed 500 mg/m <sup>2</sup> IV day 8; gemcitabine 1,250 mg/m <sup>2</sup> IV day 8; cycle length 21 d

Abbreviation: IV, intravenous.

## **CT for NSCLC: trials without age limits**

- **elderly pts eligible for such trials represent a selected subgroup probably with better prognosis & treatment compliance**
- **Data from that population can be misleading if generalized to the clinical practice.**
- **Studies with a minimum required age of 70 yrs make pts more representative of elderly pt population**

# Treatment of Elderly (>70 yrs) Lung Cancer Patient (CALGB 9730)

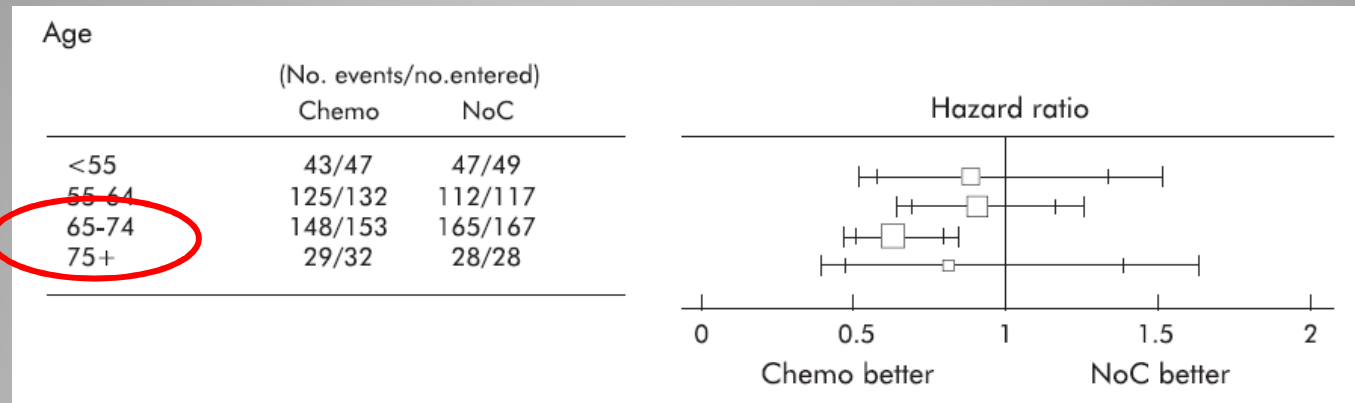
**Table 4.** Treatment Outcome Stratified by Age

	P	CP
No. of elderly patients (> 70 years)	78	77
Response rate		
%	21	36
95% CI	11 to 33	24 to 50
Survival*		
Median, months	5.8	8.0
95% CI	3.8 to 9.3	5.7 to 11
Survival, %		
1-year	31	35
95% CI	22 to 43	26 to 48
No. of younger patients (< 70 years)	199	207
Response rate		
%	15	28
95% CI	10 to 22	21 to 35
Survival, monthst		
Median	6.8	9.0
95% CI	5.6 to 8.6	8.2 to 10.8
Survival, %		
1-year	33	38
95% CI	27 to 41	32 to 45

Abbreviations: P, paclitaxel; CP, carboplatin-paclitaxel.

*Lilenbaum R JCO 2005*

## Overall Sv in Big Lung Trial

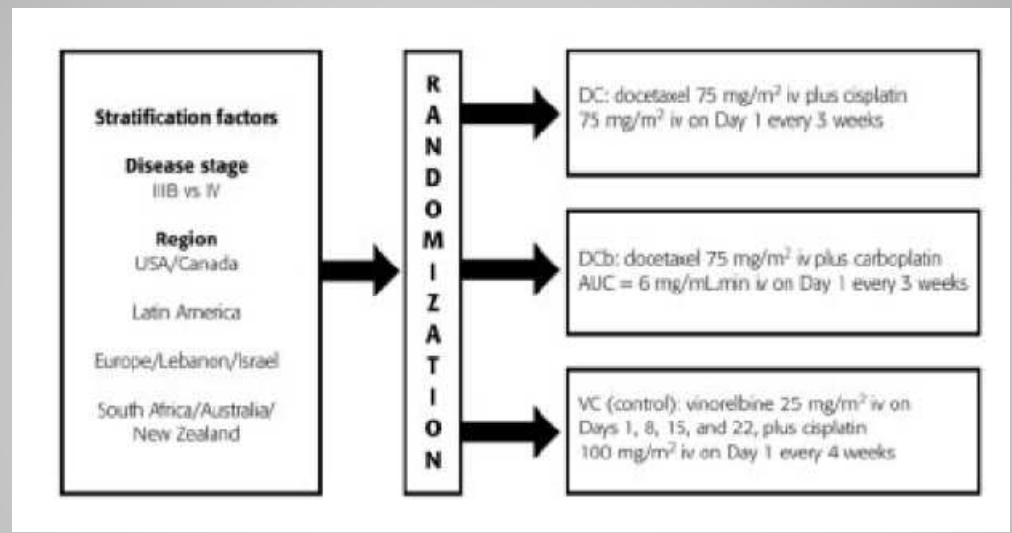


Hazard ratios and 95% and 99% confidence intervals for survival by subgroups

- Survival was related to stage ( $p = .0002$ ) and WHO PS ( $p = .0001$ )
- Pts with squamous histology survived longer than those with adenocarcinoma ( $p = .008$ ).
- No evidence that survival was related to age ( $p = .49$ ), sex ( $p = .33$ ), or chosen CT regimen ( $p = .99$ )

Spiro SG, Thorax 2004

# Survival analysis of elderly (>65yrs) and younger patients with A-NSCLC in the TAX 326 study



	Docetaxel 75 mg/m <sup>2</sup> + cisplatin 75 mg/m <sup>2</sup> q3w		Docetaxel 75 mg/m <sup>2</sup> + carboplatin AUC 6 q3w		Vinorelbine 25 mg/m <sup>2</sup> /w + cisplatin 100 mg/m <sup>2</sup> q4w <sup>a</sup>	
	Age < 65 yrs (n = 259)	Age ≥ 65 yrs (n = 149)	Age < 65 yrs (n = 288)	Age ≥ 65 yrs (n = 118)	Age < 65 yrs (n = 270)	Age ≥ 65 yrs (n = 134)
Median survival, months (95% CI)	11.0 (9.7–12.2)	12.6 (10.6–15.4)	9.7 (8.7–11)	9.0 (7.6–10.3)	10.1 (9.0–11.5)	9.9 (8.7–12.2)
One-year survival, % (95% CI)	44 (38–50)	52 (45–60)	37 (32–43)	39 (29–46)	41 (36–47)	41 (33–49)
Two-year survival, % (95% CI)	19 (14–25)	24 (16–32)	17 (12–22)	19 (11–27)	13 (9–18)	17 (10–24)

## The North Central Cancer Treatment Group Pooled Analysis on Elderly Pts Trials

- Elderly-specific trials, designed to provide a gentler treatment approach, showed no statistically significant difference in survival
- Participation in the elderly-specific trials did not affect negatively the efficacy of cancer therapy.
- Severe adverse event rates were more favorable in the elderly-specific trials both for nonhematologic and hematologic toxicity.
- Moreover these elderly specific trials recruited far older patients, the so-called "oldest of the old."

*JCO Dec 2005*

## The North Central Cancer Treatment Group Pooled Analysis on Elderly Pts Trials

**Table 4.** Adverse Events

	Age-Unspecified (n = 118)		Elderly-Specific (n = 104)		P
	No.	%	No.	%	
Patients with any grade 3+ event	112	95	63	61	< .001
Patients with any grade 3+ hematologic event	80	68	10	10	< .001
Patients with any grade 3+ nonhematologic event	95	81	59	57	< .001
Patients with grade 3+ neutropenia	66	56	9	9	< .001
Patients with grade 3+ dyspnea	21	18	20	19	.78
Patients with grade 3+ fatigue	30	25	9	9	.001
Patients with grade 3+ leukopenia	47	40	2	2	< .001
Patients with grade 3+ thrombocytopenia	16	14	1	1	< .001
Patients with grade 3+ febrile neutropenia	15	13	1	1	< .001

Incidence and severity of adverse events were worse among elderly patients participating in age-unspecified trials

Pts on the age-unspecified trials had better performance scores, yet after adjustment for factors as PS, still suffered higher toxicity

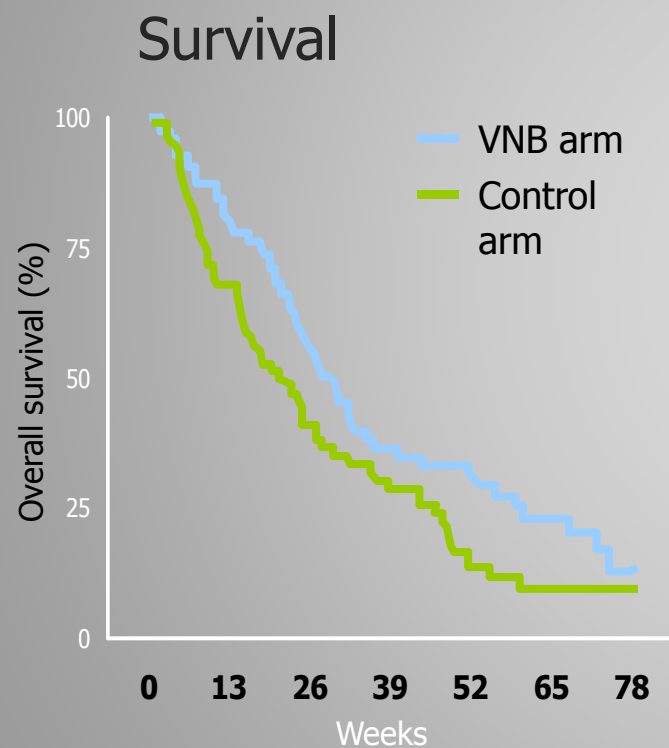
*JCO Dec 2005*

## Randomised phase III trials in elderly patients with advanced NSCLC

ELVIS, 1999	VNR Vs BSC	≥70	76	20	6.5
			78	NA	4.8
SICOG, 2000	VNR Vs VNR+GEM	≥70	60	15	4.2
			60	22	6.7
MILES, 2003	VNR or GEM Vs VNR+GEM	≥70	233	18	8.3
			233	16	6.5
			232	21	6.9
KUDOH, 2006	VNR Vs TXT	≥70	91	9.9	9.9
			89	22.7	14.3

# ELVIS study - Phase III

## Vinorelbine vs Best Supportive Care



Cox model  $p=0.02$

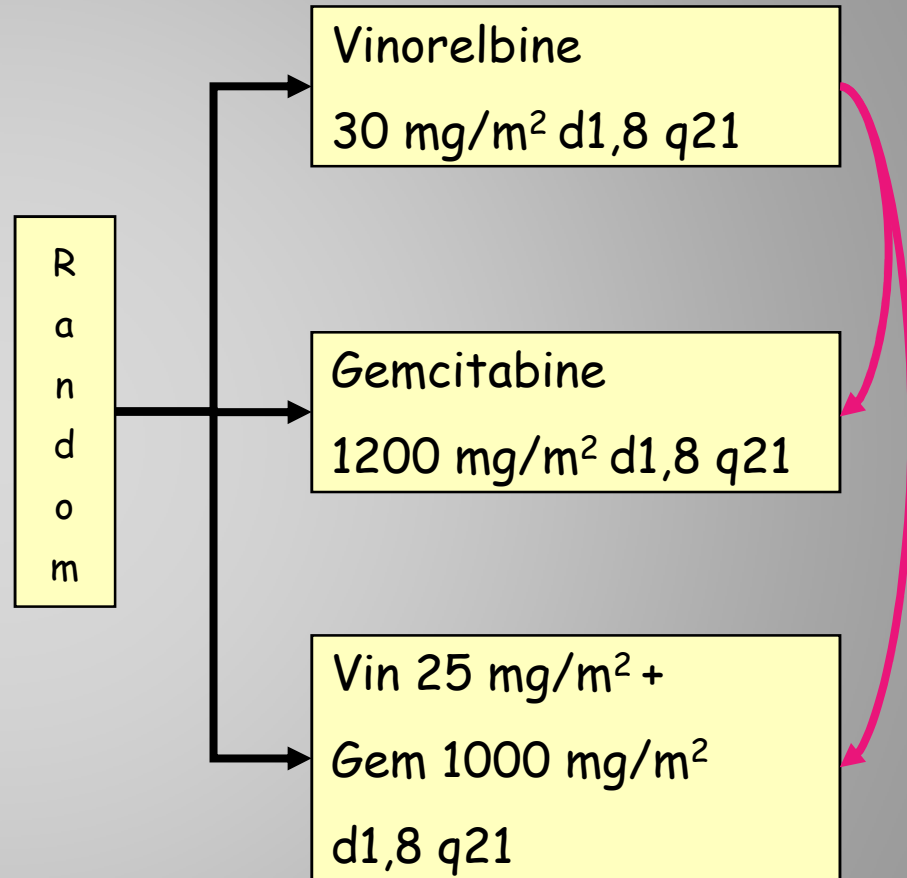
	VNB	BSC
Disease control (%)	50	—
Med Sv (months)	6.5	4.8
1 YS(%)	32	14

$p=0.03$

Gridelli, *JNCI* 1999

Is a 2-drug non-platinum based poly-CT more effective than single agent non-platinum treatment, in elderly patients with A-NSCLC?

- 707 randomized pts, >70 yrs, stage IV – IIIb : the largest prospective randomized trial of CT dedicated to elderly pts with A-NSCLC
- This study showed that poly-chemotherapy with gemcitabine plus vinorelbine is not more effective than gemcitabine alone and vinorelbine alone.



Gridelli C , JNCI 2003

VOLUME 23 · NUMBER 28 · OCTOBER 1 2005

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

# Pretreatment Quality of Life and Functional Status Assessment Significantly Predict Survival of Elderly Patients With Advanced Non–Small-Cell Lung Cancer Receiving Chemotherapy: A Prognostic Analysis of the Multicenter Italian Lung Cancer in the Elderly Study

*Paolo Maione, Francesco Perrone, Ciro Gallo, Luigi Manzione, Franco Vito Piantedosi, Santi Barbera, Silvio Cigolari, Francesco Rosetti, Elena Piazza, Sergio Federico Robbiati, Oscar Bertetto, Silvia Novello, Maria Rita Migliorino, Adolfo Favaretto, Mario Spatafora, Francesco Ferraiù, Luciano Frontini, Alessandra Bearz, Lazzaro Repetto, and Cesare Gridelli*

# A prognostic analysis of the MILES study

## Purpose

- To study the prognostic value for survival of baseline assessment of functional status, comorbidity and QoL
- 566 pts enrolled in the prognostic analysis study

## Geriatric Assessment

- **Functional status** (ADL\* & IADL\*\*)
- **Comorbidity** (Charlson scale & a 33-item check-list)
- **Quality of Life\*\*** (items 29 & 30 of EORTC QLQ-C30)

Analysis was performed by Cox model, stratified by treatment arm

\*Patients were categorized for ADL as with none versus 1 or more dependency

\*\*For IADL and QoL three categories representing the upper, intermediates and lower quarters of distribution were used

# A prognostic analysis of the MILES study

## Results

### ***Patients Characteristics***

- Median age: 74 years, range 70–84
- 229 patients (40%) were >75 years old
- Male gender 82%
- Stage IV: 69%
- Squamous cell carcinoma: 45% Adenocarcinoma: 34%
- A median of 3 organs were affected by cancer
- ECOG PS 2: 19% of patients
- $\geq 1$  comorbidity 89% of the patients
- $\geq 3$  comorbidity 40%
- Charlson score: 42% were in the lowest category (score 0)

## PROGNOSTIC FACTORS

# MILES-01

**Table 3.** Multivariate Analysis

Variable	HR	95% CL		P*
		Upper	Lower	
Sex				.07
Male (n = 465)	Ref			
Female (n = 101)	0.78	0.59	1.02	
Age, years				.69
< 75 (n = 337)	Ref			
75-79 (n = 210)	1.09	0.89	1.32	
≥ 80 (n = 19)	0.96	0.57	1.64	
Performance status				.006
0-1 (n = 460)	Ref			
2 (n = 106)	1.46	1.12	1.88	
Charlson score				.66
0 (n = 237)	Ref			
1 (n = 210)	1.06	0.85	1.32	
2 (n = 92)	1.12	0.85	1.48	
≥ 3 (n = 27)	0.84	0.52	1.36	
ADL				.44
No dependence (n = 482)	Ref			
One or more dependence (n = 84)	1.12	0.85	1.47	
IADL				.04
Better (n = 188)	Ref			
Intermediate (n = 217)	0.97	0.76	1.22	
Worse (n = 161)	1.31	1.00	1.71	

Quality of Life				.0003
Better (n = 119)	Ref			
Intermediate (n = 294)	1.62	1.24	2.10	
Worse (n = 153)	1.76	1.29	2.39	
Stage				.71
IIIb (n = 178)	Ref			
IV (n = 388)	1.04	0.85	1.28	
Histotype				.17
Other (n = 314)	Ref			
Squamous (n = 252)	1.14	0.94	1.39	
No. of sites of disease				.02
For each added site	1.13	1.02	1.24	
Center by No. of enrolled patients				.09
< 10 (n = 148)	Ref			
10-29 (n = 259)	1.19	0.94	1.52	
≥ 30 (n = 159)	1.34	1.03	1.74	

Abbreviations: HR, Hazard ratio of death; CL, confidence limits; Ref, reference category; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living.

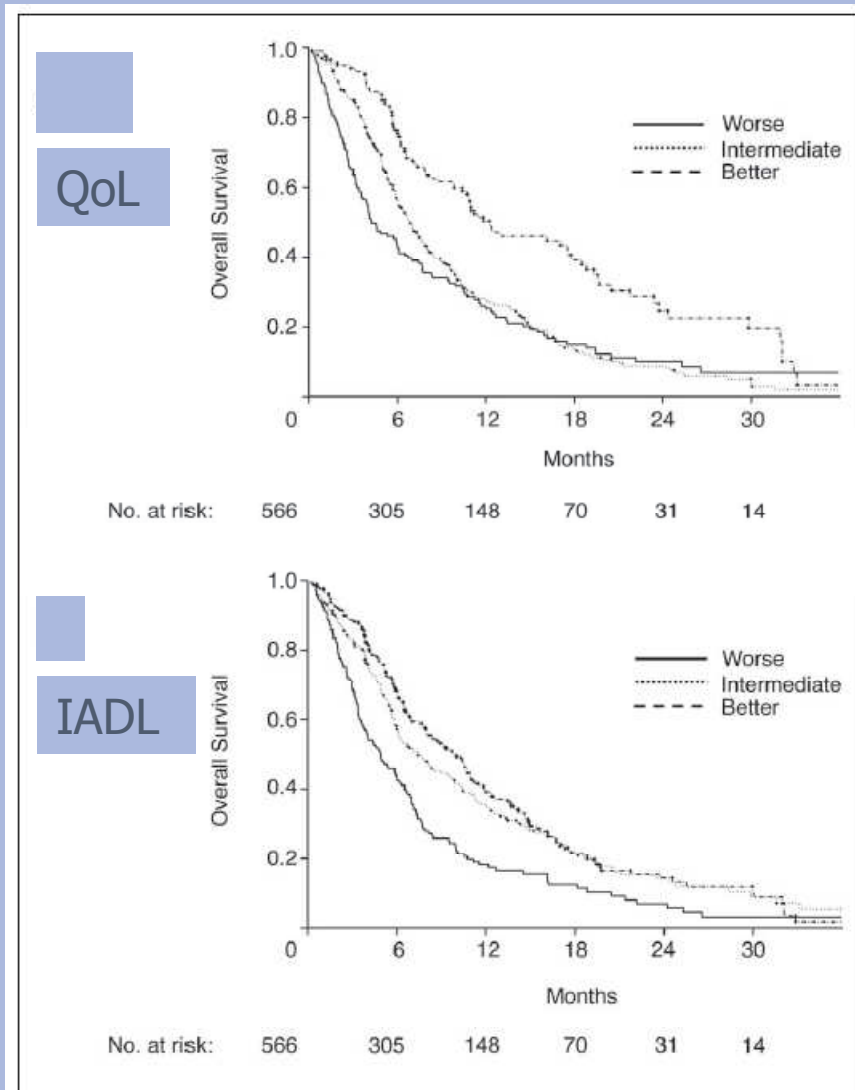
\*Likelihood ratio test.

JCO Oct 2005

# MILES-01

## PROGNOSTIC FACTORS

Kaplan-Meier estimated overall survival curves according to Pretreatment QOL and IADL Categories



# A prognostic analysis of the MILES study

## Results

### *Survival*

- 462 patients dead out of 566 eligible for prognostic analysis (82%)
  - Median survival: 30 weeks (95% CI: 28-34)
  - 6-month and 1-year probabilities of surviving: 0.56 and 0.32
- 
- Baseline assessment of **QoL** (p= .0003) and **IADL** (p= .04) were significantly associated with prognosis
  - **ADL** (p= .44) and **Charlson** score (p= .66) had no prognostic value.
  - **PS 2** (p= .006) and the number of **metastatic sites** (p= .02) also predicted shorter survival



## The MILES-02 trial

Are typical cisplatin-containing doublets feasible in elderly patients with A-NSCLC?

**Arm A:** vinorelbine (25 mg/m<sup>2</sup> dd 1&8) + cisplatin (d1, dose-finding, then phase II)

**Arm B:** gemcitabine (1000 mg/m<sup>2</sup> dd 1&8) + cisplatin (d1, dose-finding, then phase II)

**Cisplatin was feasible:** at 60 mg/m<sup>2</sup> with gemcitabine  
at 40 mg/m<sup>2</sup> with vinorelbine

	<b>Cisplatin + Gemcitabine</b>	<b>Cisplatin + Vinorelbine</b>
<b>Pts enrolled:</b> 159		
<b>Phase 1</b> Recommended dose of cisplatin	60 mg	40 mg
<b>Phase 2</b> Pts treated without unacceptable toxicity (%)	50/60 (83.3)	50/61 (81.9)
Response Rate (%)	26/60 (43.3)	22/61 (36.1)
Median progression free survival	25.3 weeks	21.1 weeks
Median overall survival	43.6 weeks	33.1 weeks



# The MILES-02 trial



## Conclusion

- A cisplatin-based chemotherapy is feasible and active in the treatment of elderly patients with advanced NSCLC
- Namely, the combination of cisplatin given at 60 mg/m<sup>2</sup> and gemcitabine deserves comparison versus single-agent chemotherapy in this setting of patients

## Treatment of Non-small Cell Lung Cancer, Stage IV: ACCP Evidence-Based Clinical Practice Guidelines (2° Edition)

Mark A. Socinski, Richard Crowell, Thomas E. Hensing, Corey J. Langer, Rogerio Lilenbaum, Alan B. Sandler and David Morris *Chest* 2007; 132; 277-89 DOI 10.1378/chest 07-1381

### RECOMMENDATIONS

- 1.** In patients who have stage IV NSCLC and are elderly ( $\geq 70$  to 79 years old), single-agent chemotherapy is recommended for most. Grade of recommendation, 1A
- 2.** However, in patients who have stage IV NSCLC, are elderly ( $\geq 70$  to 79 years old), have good PS, and lack significant comorbidities, two drug combination chemotherapy is recommended as an option. Grade of recommendation, 1B
- 3.** In patients who have stage IV NSCLC and are  $\geq 80$  years old, the benefit of chemotherapy is unclear and should be decided on the basis of individual circumstances. Grade of recommendation, 2C

# Elderly Patients Benefit From Second-Line Cytotoxic CT

**Table 2.** Response Rate, Median Time to Progression, and Median Overall Survival

Outcome	Age ≥ 70 Years (n = 76)		Age < 70 Years (n = 462)	
	Pemetrexed (n = 40)	Docetaxel (n = 36)	Pemetrexed (n = 224)	Docetaxel (n = 238)
Objective response rate, %	5.0	5.6	9.8	9.2
Stable disease rate, %	60.0	41.7	43.3	47.1

Outcome	Age ≥70 Years (n = 86)		Age < 70 Years (n = 485)	
	Pemetrexed (n = 47)	Docetaxel (n = 39)	Pemetrexed (n = 236)	Docetaxel (n = 249)
Median time to progression, months	4.6	2.9	3.0	3.9
Median overall survival, months	9.5	7.7	7.8	8.0
% surviving at 12 months	20.4	23.1	30.8	30.8
% surviving at 24 months	6.1	10.6	10.6*	0*

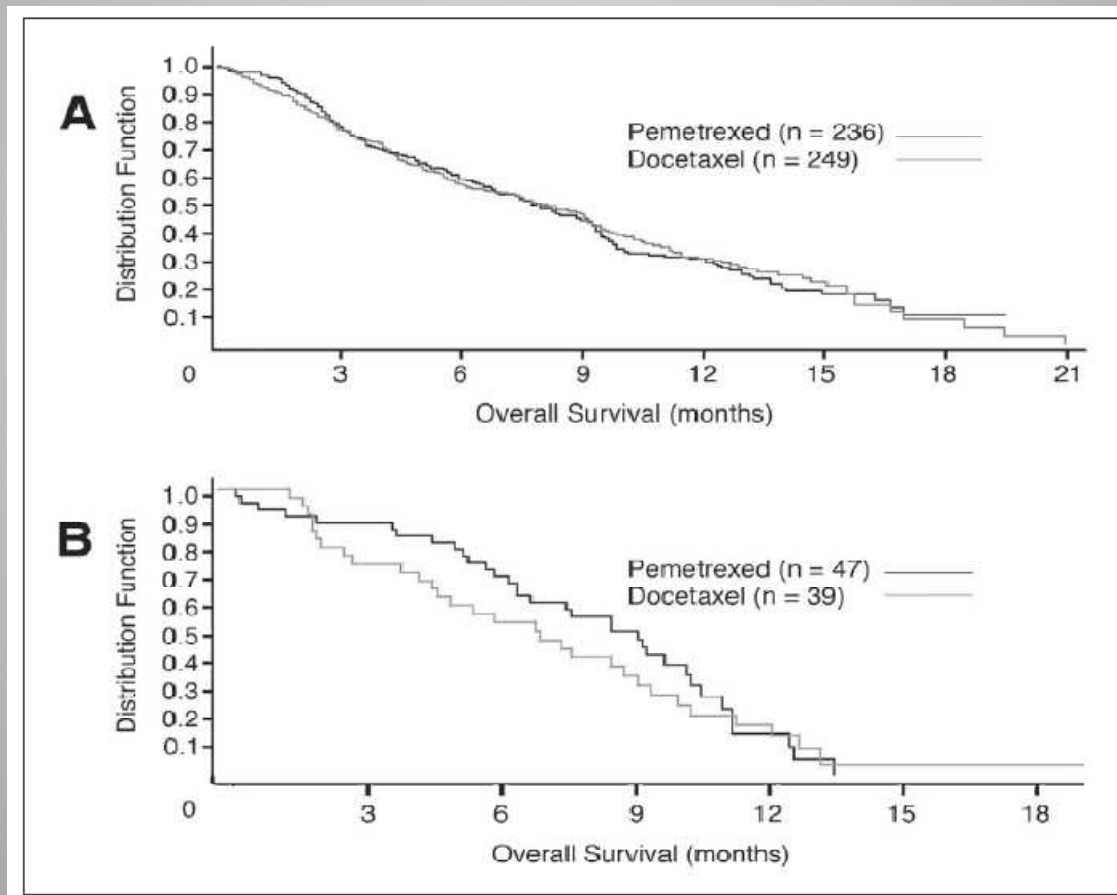
\*Estimated % difference is 10.6 ( $P = .0054$ ; 95% CI, 3.1 to 18.0).

Weiss, JCO 2006

## MEDIAN OVERALL SURVIVAL TIME

**(A) patients < 70 yrs: pemetrexed, 7.8 mos vs docetaxel, 8.0 mos  
(HR 1.02; 95%CI, 0.82 to 1.26)**

**(B) patients  $\geq$  70 yrs: pemetrexed, 9.5 mos vs docetaxel, 7.7 mos  
(HR 0.86; 95%CI, 0.53 to 1.42)**



Erlotinib (Tarceva™) Phase II study in elderly  
pts with untreated A-NSCLC  
*Jackman DM, Yeap BY et al.*

Erlotinib, an EGFR TKI, given @ 150mg/day p.o.

Stage IIIB wet, or IV, PS 0-2

Patient characteristics

Pts treated and evaluable	80 pts (40 F/40 M)
Median age	75 yrs (range 70-91);
ECOG PS 0/1/2 (%)	16/74/10
Histology adenocarcinoma	51%
squamous	9%
adenocarcinoma with BAC features	8%
BAC	5%,
other NSC	28%
smoking status (%) never	10
former	84
current	6

RESPONSE

PR	8	10%
SD	33	41%

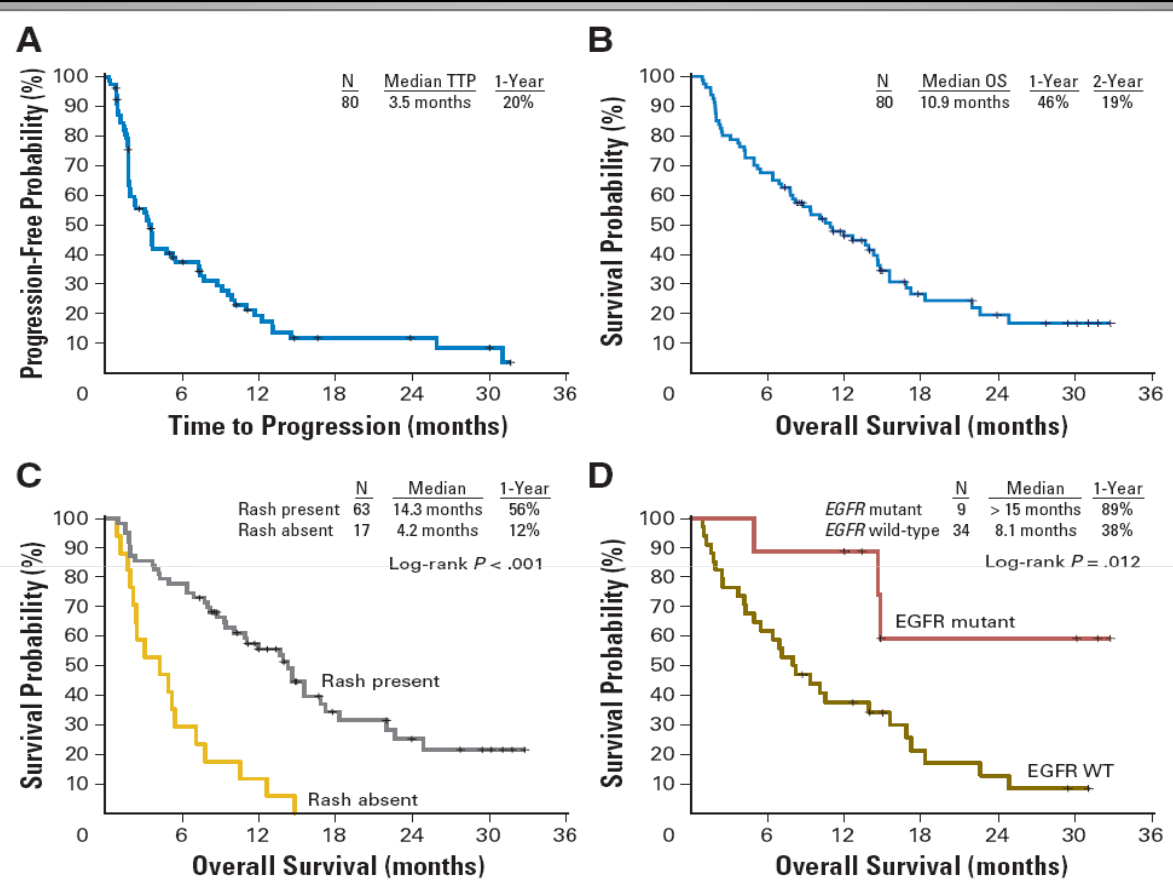
Med resp duration	8 months
Med SD duration	3.5 months

Toxicity

Skin rash	79%
Diarrhea	69%
ILD	4pts 1 death

*JCO, March 2007*

## Erlotinib Phase II study in elderly pts with untreated A-NSCLC



### CONCLUSION

- Erlotinib monotherapy is active and relatively well tolerated in chemotherapy-naive elderly patients with advanced NSCLC
- Erlotinib merits consideration for further investigation as a first-line therapeutic option in elderly patients.

# NCI-C BR.10 Adjuvant P-V *vs* Nil Study

## *Study Design*

- A phase III randomized trial of adjuvant cisplatin and vinorelbine versus observation after complete resection of stage IB or stage II NSCLC
- Accrual: From February 1994 to April 2001

## *Study Population*

- Elderly pts were defined as age >65 and young pts as age ≤65
- The chemotherapy regimen was 3 cycles every 28-day of:  
vinorelbine 25 mg/m<sup>2</sup> dd. 1, 8, 15, and 22 cisplatin 50 mg/m<sup>2</sup> dd 1, 8

età	<65	>65
# pts	327	<b>155</b>
Over Sv 5aa CT	66%	<b>70%</b>
Nil	58%	<b>46%</b>
Dis Spec Sv 5aa CT	73%	<b>73%</b>
Nil	60%	<b>56%</b>

# NCI-C BR.10 Adjuvant P-V *VS* Nil Study

Table 1. Summary of Prognostic Factors by Age Group for All Randomly Assigned Patients

Factor	Total No. of Patients	Young (≤ 65 years; n = 327)		Elderly (> 65 years; n = 155)		P
		No.	%	No.	%	
<b>Treatment</b>						
Chemotherapy	242	165	50.5	77	49.7	.87
Observation	240	162	49.5	78	50.3	
<b>Country</b>						
Canada	234	161	49.2	73	47.1	.66
United States	248	166	50.8	82	52.9	
<b>Sex</b>						
Male	314	207	63.3	107	69.0	.22
Female	168	120	36.7	48	31.0	
<b>Pathologic subtype</b>						
Adenocarcinoma	256	189	57.8	67	43.2	.001
Squamous	179	103	31.5	76	49.0	
Cther	47	35	10.7	12	7.7	
<b>Performance status</b>						
0	236	173	52.9	63	40.9	.01
1	245	154	47.1	91	59.1	
<b>Ras mutation status</b>						
Present	117	89	27.2	28	18.1	.08
Absent	333	216	66.1	117	75.5	
Unknown	32	22	6.7	10	6.5	
<b>Nodal status</b>						
N0	219	148	45.3	71	45.8	.91
N1	263	179	54.7	84	54.2	
<b>T staging</b>						
T1	70	46	14.1	24	15.5	.68
T2	412	281	85.9	131	84.5	
<b>Stage of disease</b>						
IB	219	146	45.3	71	45.6	.96
IIA	70	46	14.1	24	15.5	
IIB	193	133	40.7	60	38.7	
<b>Smoking history</b>						
Nonsmoker	26	20	6.1	6	3.9	.56
Smoker	451	304	93.0	147	94.8	
Unknown	5	3	0.9	2	1.3	
<b>Race/ethnicity</b>						
White	226	154	47.1	72	46.5	.89
Cther	256	173	52.9	83	53.6	
<b>Pack-years</b>						
< 20	97	69	21.1	28	18.1	.44
≥ 20	385	258	78.9	127	81.9	
<b>Baseline anemia</b>						
None	231	150	45.9	61	39.3	.19
≥ Grade 1	251	177	54.1	74	47.7	
<b>Surgery</b>						
Pneumonectomy	113	83	25.4	30	19.4	.34
Lesser resection	331	219	67.0	112	72.3	
Cther	38	25	7.7	13	8.4	

## NCI-C BR.10 Adjuvant P-V *vs* Nil Study

età	<65	>65
PS 0 pts	57%	<b>36%</b>
Toxicity		=
Dose Intensity VNR DDP		↓
Treatment Completed	56%	<b>40%</b>
Treatment Refused	23%	<b>40%</b>

Pepe, C. et al. *J Clin Oncol*; 25:1553-1561 2007

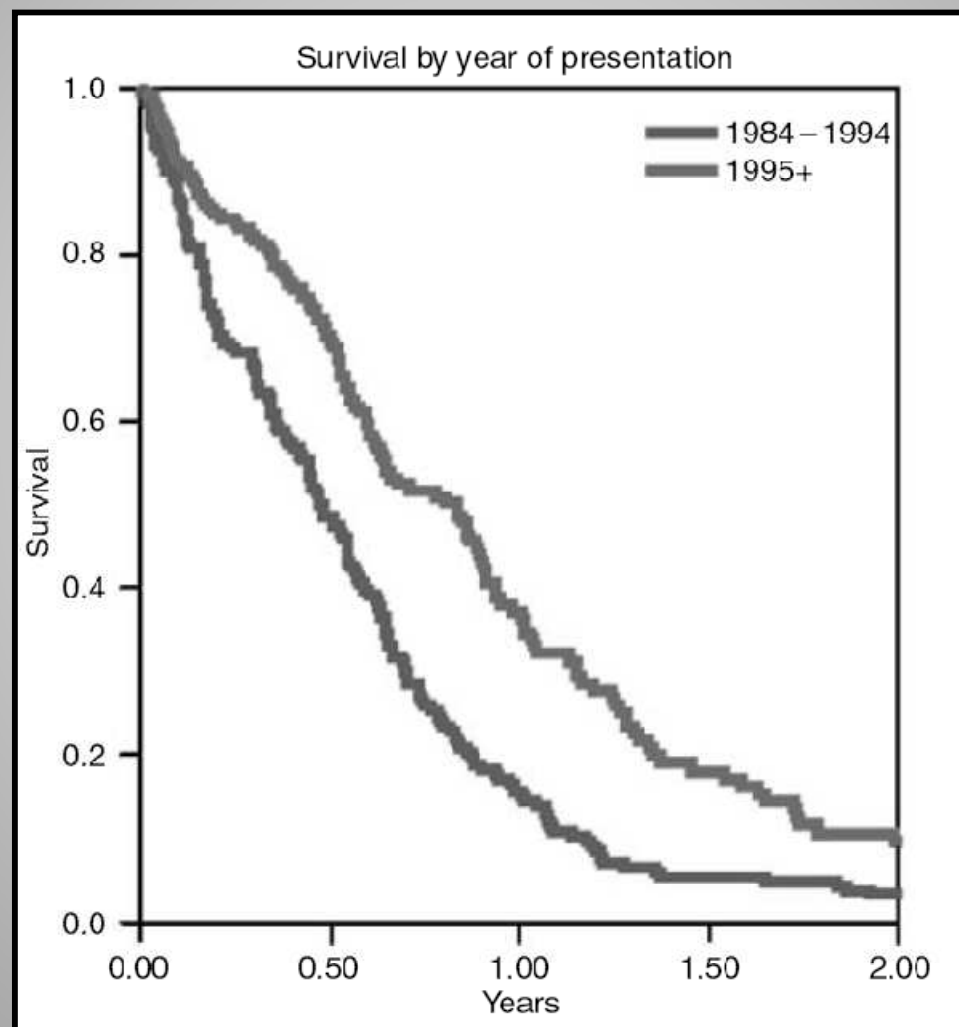
## Demographic data and treatment modalities stratified by year of presentation in 322 SCLC elderly patients treated between 1982-2003

	No. of patients (%)		
	1982-1994	1995-2003	Total
Patients	157 (49)	165 (51)	322
Sex			
Male	95 (64)	95 (58)	190 (59)
Female	62 (39)	70 (42)	132 (41)
Age (years)			
70-74	102 (65)	86 (52)	188 (58)
75-79	45 (29)	63 (38)	108 (34)
80+	10 (6)	16 (10)	26 (8)
Performance status			
0	10 (6)	5 (3)	15 (5)
1	88 (56)	52 (32)	140 (43)
2	39 (25)	77 (47)	116 (36)
3	15 (10)	29 (18)	44 (14)
4	4 (3)	1 (1)	5 (5)
Not known	1 (1)	1 (1)	2 (1)
Cisplatin-containing regimes	16 (10)	32 (19)	48 (15)
Carboplatin combinations	59 (38)	93 (56)	152 (47)
Nonplatinum single agents	60 (38)	23 (14)	83 (26)
Other non-platinum combinations	22 (14)	17 (10)	39 (12)

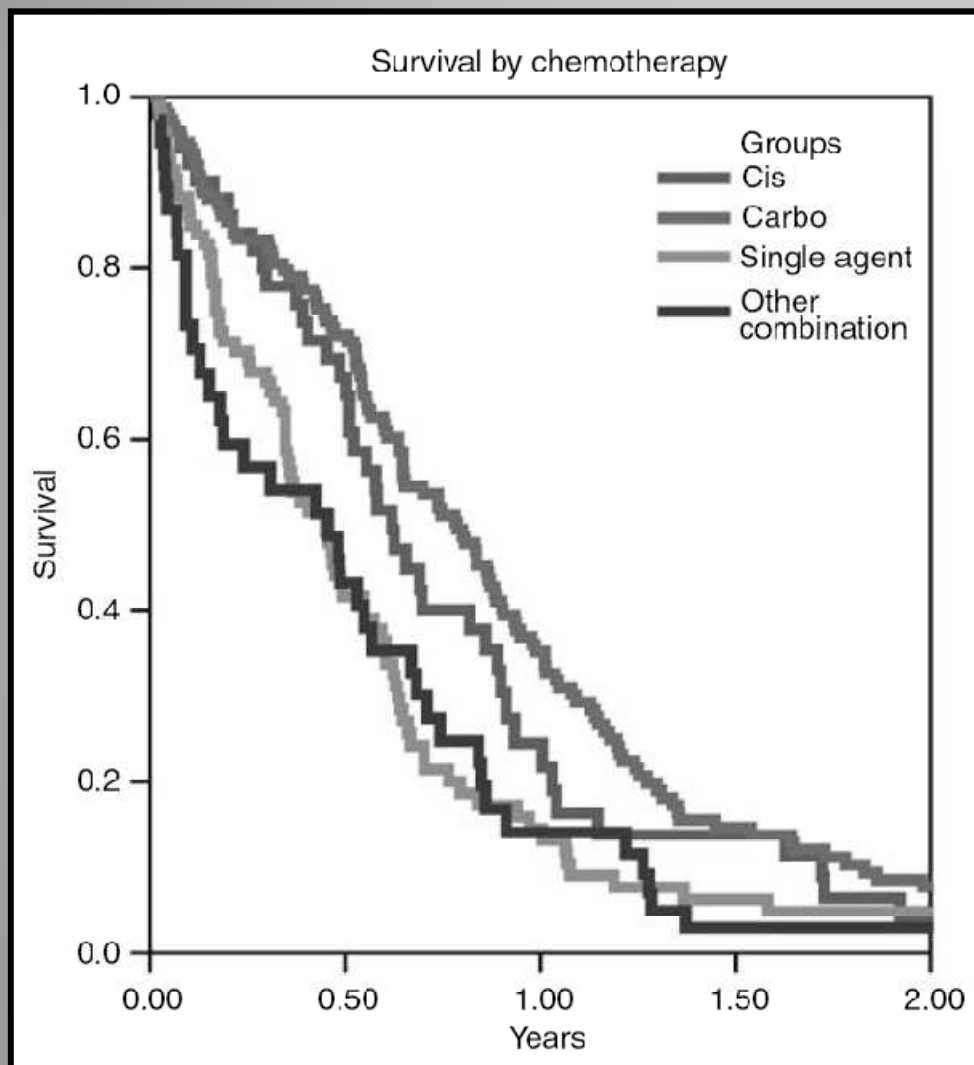
*Yau*

*BJC 2006*

## Survival differences among elderly SCLC patients between 1982–1994 and 1995–2003



## Survival differences among elderly SCLC patients between 1982–2003, by treatment



- Patients who received platinum combinations (carbo- or cisplatin) had significantly improved survival over those who received single agents or other combinations ( $P < 0.001$ )
- There was no significant difference between carboplatin and cisplatin ( $P = 0.7$ ).

*Yau BJC 2006*

# CONCLUSION

- This study suggests that there has been a significant improvement in survival for SCLC elderly patients (age >70 years) receiving treatment over the past 20 years despite the trend to treat more of the very elderly and patients with a worse PS
- This improvement is still present when patients are controlled for sex, stage and PS, suggesting that this is due to advances in patient management adjunctive therapies and in particular the use of platinum (and carboplatin)-based therapy rather than earlier presentation of the disease.

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ORIGINAL REPORT

# Platinum-Etoposide Chemotherapy in Elderly Patients With Small-Cell Lung Cancer: Results of a Randomized Multicenter Phase II Study Assessing Attenuated-Dose or Full-Dose With Lenograstim Prophylaxis—A Forza Operativa Nazionale Italiana Carcinoma Polmonare and Gruppo Studio Tumori Polmonari Veneto (FONICAP-GSTPV) Study

*Andrea Ardizzoni, Adolfo Favaretto, Luca Boni, Editta Baldini, Federico Castiglioni, Paola Antonelli, Franca Pari, Carmelo Tibaldi, Alfonso M. Altieri, Sante Barbera, Giancarlo Cacciani, Mario Raimondi, Lucia Tixi, Micaela Stefani, Silvio Monfardini, Antonio Antilli, Riccardo Rosso, and Adriano Paccagnella*

# STUDY DESIGN

- AIM of the STUDY  
to evaluate the therapeutic index of 2 platinum/etoposide regimens  
an attenuated dose (AD) arm  
a full-dose (FD) arm combined with prophylactic lenograstim
- A randomized phase II design was used
- A combined primary end point, named "therapeutic success", was used; it took into account activity, toxicity, and compliance
- A Therapeutic Success was defined as a patient receiving  
at least 3 cycles of CT at the planned dose and schedule  
having an objective response  
without (1) grade 3-4 nonhematological toxicity,  
(2) complications such as febrile neutropenia,  
infection, bleeding, or transfusion  
(3) any toxicity leading to hospitalization or death

# TREATMENT

- ATTENUATED DOSE CT

Cisplatin 25 mg/m<sup>2</sup> dd. 1-2  
Etoposide 60 mg/m<sup>2</sup> dd. 1-3

- FULL DOSE CT

Cisplatin 40 mg/m<sup>2</sup> dd. 1-2  
Etoposide 100 mg/m<sup>2</sup> dd. 1-3  
plus Lenograstim 5 µg/kg dd. 5-12

- 4 courses, q 3 weeks, were planned.
- Support Treatment: In both arms Amoxicillin+Clavulanic Acid was planned when leukopenia gr.4 occurred.

# RESULTS

**Table 1. Patient Characteristics**

Characteristic	AD Arm (n = 28)		FD Arm (n = 67)		Total (N = 95)	
	No.	%	No.	%	No.	%
<b>Sex</b>						
Male	27	96	53	79	80	84
Female	1	4	14	21	15	16
<b>Age, years</b>						
Median	74		73		73	
Range	70-80		70-79		70-80	
<b>ECOG PS</b>						
0	8	28	19	28	27	28
1	17	61	40	60	57	60
2	3	11	8	12	11	12
<b>Stage</b>						
Limited	16	57	36	54	52	55
Extensive	12	43	31	46	43	45
<b>CNS</b>	4	14	6	9	10	11
<b>Liver</b>	6	21	16	24	22	23

**Table 2. Primary Outcome**

	AD Arm (n = 28)		FD Arm (n = 67)		Total (N = 95)	
	No.	%	No.	%	No.	%
Therapeutic success	10	36	42	63	52	55
Therapeutic failure	18	64	25	37	43	45
Lack of objective response	13	46	6	9	19	20
Toxicity	3	11	9	13	12	13
Treatment-related death	—	—	1	1	1	1
Death unrelated to treatment	2	7	4	6	6	6
Patient refusal	—	—	2	3	2	2
Unknown	—	—	3	4	3	3

Abbreviations: AD, attenuated-dose; FD, full-dose.

# RESULTS

**Table 3. Objective Tumor Response and Survival**

	AD Arm (n = 28)		FD Arm (n = 67)		Total (N = 95)	
	No.	%	No.	%	No.	%
Complete remission	—	—	9	13.4	9	9.5
Partial remission	11	39.3	37	55.2	48	50.5
Stable disease	11	39.3	6	8.9	17	17.9
Progressive disease	4	14.3	4	6.0	8	8.4
Not assessable	2	7.1	8	11.9	10	10.5
Unknown	—	—	3	4.5	3	3.1
Overall response rate	11	39.3	46	68.7	57	60.0
95% CI, %	22.1 to 59.3		56.0 to 79.1		49.4 to 69.8	
Overall survival						
1 year, %	18		39		32	
2 year, %	0		12		9	
Median, weeks	31		41		38	

**Table 4. WHO Grade 3 and 4 Toxicities**

Toxicity	AD Arm (n = 28)		FD Arm (n = 67)		Total (N = 95)	
	No.	%	No.	%	No.	%
WBC	—	—	7	10	7	7
Hemoglobin	—	—	7	10	7	7
Platelets	—	—	8	12	8	8
Renal	—	—	1	1	1	1
Nausea/vomiting	1	4	4	6	5	5
Mucositis	—	—	2	3	2	2
Neurologic	—	—	2	3	2	2
Cardiac	1	4	—	—	1	1
Fatigue	1	4	3	4	4	4
Cutaneous	1	4	—	—	1	1

Abbreviations: AD, attenuated-dose; FD, full-dose.

# CONCLUSIONS

## In elderly patients with SCLC

- a full-dose Cisplatin/Etoposide regimen combined with prophylactic lenograstim is active and feasible
- attenuated doses of the same regimen are associated with a poor therapeutic outcome.