Systemic treatment for elderly patients with NSCLC – what is the evidence?

Dr Yvonne Summers

Disclosure

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- Advisory honoraria – Eli Lilly, Boehringer Ingelheim, Roche

What is "Elderly"?

- Epidemiologic literature uses ≥65 years
- Clinical trials use ≥70 years[1,2]
- Variation between chronological vs biological age
- Changes in changes in metabolic excretory pathways with age
  - 30% reduction in function of P450 microsomal system in healthy elderly vs younger counterparts
  - GFR reduces by 1ml/min every year over age 40

1. Pallis et al. *Ann Oncol* 2010;21(4):692-706.
2. Azzoli et al. J Clin Oncol 2009; 27(36):6251-66.

Comprehensive Geriatric Assessment (CGA)

- Evaluation of:
  - Co-morbidities
  - Functional status
  - Cognitive function
  - Nutritional status
  - Psychological status
  - Social support
  - Medications
- Helps to predict chemotherapy toxicity, post-operative morbidity & mortality and overall survival in cancer patients
- Useful to help guide cancer treatments
- Better than performance status alone
- However, time consuming – abbreviated versions needed

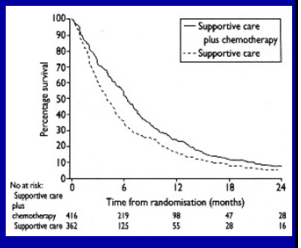
NSCLC in Elderly Patients

- NSCLC is the leading cause of death due to cancer in patients aged ≥65 years[1]
- The median age at diagnosis with NSCLC is 70 years[2]
- Predicted that incidence of NSCLC in older patients will increase by over 50% by 2030[3]
- Despite the increasing incidence of lung cancer in the elderly population, elderly patients continue to be under-represented in cancer-treatment trials
- Despite its demonstrated survival benefits, most elderly patients are not receiving chemotherapy, even with controls for co-morbidity and PS[4]

1. Hayat et al SEER program Oncologist; 2007.
2. Pallis et al. *Ann Oncol* 2010; 21(4):692-706.
3. Smith et al J Clin Oncol 2009; 27; 2758-65
4. Davidoff et al. *J Clin Oncol* 2010;28(13):2191-7.

Chemotherapy for NSCLC in Elderly Patients

- NSCLC Collaborative Group 1995 meta analysis of platinum based therapy showed no evidence of significantly worse outcome by age
- Concerns about efficacy and tolerability in older patients
- Trials conducted exclusively in elderly populations have established feasibility and potential benefits of cytotoxic chemotherapy

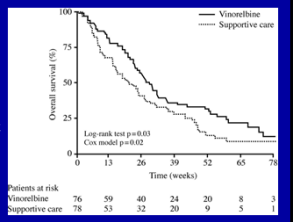


NSCLC Collaborative Group BMJ 1995;311

Chemotherapy for NSCLC in Elderly Patients (cont)

Elderly Lung Cancer Vinorelbine Italian Study Group (ELVIS)

- Stage IIIB/IV previously untreated NSCLC
- Age ≥70 years, median 74yrs, range 70-86yrs, n=161
- PS 0 (18%), PS1 (58%), PS 2 (24%)
- Vinorelbine 30mg/m^2 (D1,8) vs BSC
- No 2nd line therapy
- Median survival 28wks vs 21wks (p=0.03), 1 year survival 32% vs 14%
- Vin treated patients scored better on QoL functioning scales and reported fewer lung cancer related symptoms
- Tolerable toxicity – neutropenia & constipation

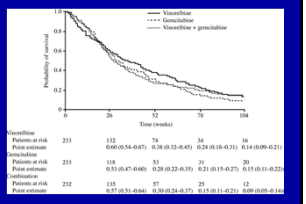


ELVIS Investigators JNCI 1999; 91

Chemotherapy for NSCLC in Elderly Patients (cont)

Muliti centre Italian Lung Cancer in Elderly Study (MILES)

- Stage IIIB/IV previously untreated NSCLC
- Age ≥70 years, median 74yrs, 39% ≥75 years, n=698
- PS 0 (29%), PS1 (52%), PS 2 (19%)
- Vinorelbine 30mg/m^2 (D1,8) vs Gemcitabine 1200mg/m^2 vs Vin 25mg/m^2 +Gem 1000mg/m^2 D1&8, 6 cycles
- Median survival 36wks vs 28wks vs 30wks(ns), 1 year survival 38% vs 28% vs 30%
- QoL similar across 3 arms
- Toxicity worse with doublet

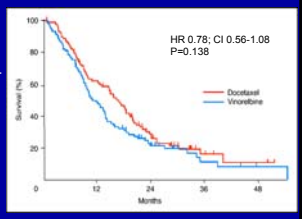


MILES JNCI 2003; 95, 362-72

Chemotherapy for NSCLC in Elderly Patients (cont)

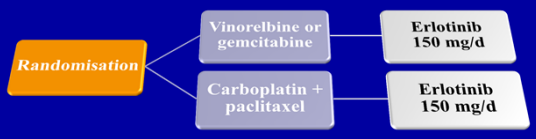
West Japan Thoracic Oncology Group Study of Docetaxel vs Vinorelbine (WJTOG 9904)

- Stage IIIB/IV previously untreated NSCLC
- Age ≥70 years, median 76yrs, range 70-86 years, n=186
- PS 0-1 (97%), PS 2 (3%)
- Docetaxel 60mg/m^2 (D1) vs Vinorelbine 25mg/m^2 (D1,8), 4 cycles
- PFS 5.5 vs 3.1 months (p<0.001)
- Median overall survival 14.3 vs 9.9 months, 1 year survival 58% vs 36%
- More neutropaenia with Docetaxel but not neut sepsis or infections
- Greater improvement is disease related symptoms (appetite & fatigue) with docetaxel



Kudoh S et al. JCO 2006;24:3657-3663

Platinum Doublet Chemotherapy IFTC-0501 – Elderly Advanced NSCLC Patients



Study population and treatment

- 451 patients, stage IIIB/IV NSCLC, age 70-89, PS 0-2; no prior CT; life expectancy of at least 12 weeks; patient characteristics similar across both arms.
- Stratification by centre, PS 0-1 vs 2, age ≤80 vs >80, stage IIIB vs IV
- Arm A: 3-weekly single agent therapy with vinorelbine 30 mg/m^2 or gemcitabine 1,150 mg/m^2 d 1,8; Arm B: carboplatin AUC 6 every four weeks plus paclitaxel 90 mg/m^2 d 1,8,15.

Quoix, Lancet 2011; 378 1079-88

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Platinun Doublet Chemotherapy IFTC-0501 – Elderly Advanced NSCLC Patients

- 418 evaluable patients
- Median age 77 years, range 70-88 years
- PS 0-1 73%, PS2 27%
- Comprehensive Geriatric Assessment (MMSE, CCI, ADL score)
- Similar QoL scores

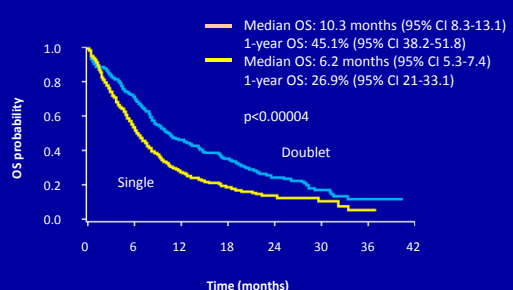
Haematological toxicity

Grade 3/4	Arm A		Arm B	p
	Gem (n=149)	Vin (n=61)	All (n=210)	(n=208)	
Neutropenia	7 (4.7)	23 (37.7)	30 (14.3)	113 (54.3)	<0.00001
Febrile neutropenia	0 (0.0)	6 (9.84)	6 (2.9)	20 (9.6)	0.004
Anaemia	3 (2.01)	6 (9.84)	9 (4.3)	16 (7.7)	0.14
Thrombocytopenia	2 (1.34)	0 (0.0)	2 (1.0)	13 (6.3)	0.004

Mortality due to toxicity was 1.8% (n=3) in Arm A and 4.4% (n=10)in Arm B

Quoix, Lancet 2011; 378 1079-88

Overall Survival –IFCT-0501



PFS 6.0 vs 2.8 months, p<0.0001
RR 27.1% vs 10.2%, p<0.0001
1YS 44.5% vs 25.4%, p<0.0001

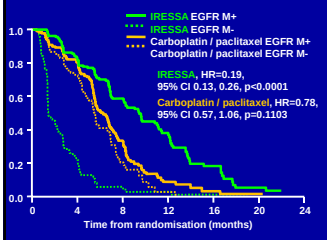
Quoix, Lancet 2011; 378 1079-88

Slide 11

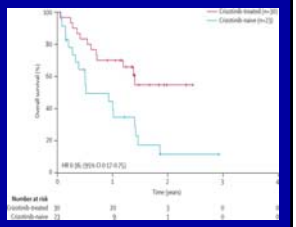
n13 " The rate of mortality due to toxicity was 1.83% in Arm A and 6.62% in Arm B (p<0.035)."

New text added
naomi.mccormick; 14-6-2010

Biological agents in elderly patients with NSCLC



Progression Free Survival -IPASS
Gefitinib in pts with EGFR activating mutations



Overall survival for crizotinib-treated versus crizotinib-naive, ALK-positive patients

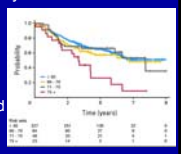
Mok et al. NEJM: 2009: 361. 10:947-57

Shaw et al. Lancet Oncol: 2011: 12. 11:1004

Adjuvant Chemotherapy in Elderly NSCLC Patients

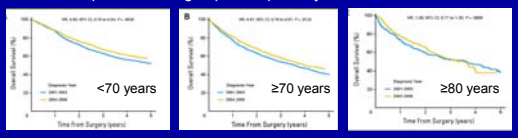
- No prospective data, elderly under-represented in trials – retrospective subgroup analysis, LACE meta-analysis & population data

Elderly (≥65 years) subpopulation analysis JBR-10. N=155. Dose intensity less, no toxicity difference, similar survival benefit[1]



Elderly patients from the LACE meta analysis showed similar survival benefit, similar severe toxicity but lower dose intensity than younger patients[2]

Ontario Cancer Registry; n=6,304; 2001-06.
Survival improved for all groups except ≥80 years[3]



1. Pepe et al. J Clin Oncol: 2007. 25:1553-61 2. Fruf et al. J Clin Oncol: 2008. 26: 3573-81 3. Cuffe et al. J Clin Oncol: 2012. 30:1813-21

Conclusions

- Selected older patients benefit from systemic treatment of NSCLC as much as younger patients
- Careful assessment (CGA) and discussion
- Individualise therapy according to molecular and histological characteristics where possible
- Patients with minimal co-morbidity and good PS should be considered for platinum doublet rather than single agent (more toxicity)
- Single agent is an option for those who can't tolerate doublet therapy
- Caution in over 80's