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

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What is “Elderly”? 

• Epidemiologic literature uses ≥65 years
• Clinical trials use ≥70 years1,2
• 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


Comprehensive Geriatric Assessment (CGA)

• Evaluation of:
  – Comorbidities
  – 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 years1
• The median age at diagnosis with NSCLC is 70 years2
• Predicted that incidence of NSCLC in older patients will increase by over 50% by 20303
• 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 PS4


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

Chemotherapy for NSCLC in Elderly Patients

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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 74 years, range 70-86 years, n=161
- PS 0 (18%), PS 1 (58%), PS 2 (24%)
- Vinorelbine 30mg/m² (D1,8) vs BSC
- No 2nd line therapy
- Median survival 28 weeks vs 21 weeks (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

Chemotherapy for NSCLC in Elderly Patients (cont)

Multi centre Italian Lung Cancer in Elderly Study (MILES)

- Stage IIIB/IV previously untreated NSCLC
- Age ≥70 years, median 74 years, 39% ≥75 years, n=698
- PS 0 (29%), PS 1 (52%), PS 2 (19%)
- Vinorelbine 30mg/m² (D1,8) vs Gemcitabine 1200mg/m² vs Vin 25mg/m² + Gem 1000mg/m² D1&8, 6 cycles
- Median survival 36 weeks vs 28 weeks vs 30 weeks (ns), 1 year survival 38% vs 28% vs 30%
- QoL similar across 3 arms
- Toxicity worse with doublet

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 76 years, range 70-86 years, n=186
- PS 0-1 (97%), PS 2 (3%)
- Docetaxel 60mg/m² (D1) vs Vinorelbine 25mg/m² (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 neutropenia with Docetaxel but not neut sepsis or infections
- Greater improvement in disease related symptoms (appetite & fatigue) with docetaxel

Platinum Doublet Chemotherapy

IFTC-0501 – Elderly Advanced NSCLC Patients

- 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/m² or gemcitabine 1,150 mg/m² d 1,8; Arm B: carboplatin AUC 6 every four weeks plus paclitaxel 90 mg/m² d 1,8,15.

Platinum 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

<table>
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<tr>
<th>Grade</th>
<th>Arm A</th>
<th>Arm B</th>
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Mortality due to toxicity was 1.8% (n=3) in Arm A and 4.4% (n=12) in Arm B.

Overall Survival –IFCT-0501

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<tr>
<th>Time (months)</th>
<th>Median OS: 10.3 months (95% CI 8.3-13.1)</th>
<th>1-year OS: 45.1% (95% CI 38.2-51.8)</th>
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<td>PFS 6.0 vs 2.8 months, p&lt;0.0001</td>
<td>RR 27.1% vs 10.2%, p&lt;0.0001</td>
<td>1Y OS: 44.5% vs 26.4%, p&lt;0.0001</td>
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Quoix, Lancet 2011; 378 1079-88
"The rate of mortality due to toxicity was 1.83% in Arm A and 6.62% in Arm B (p<0.035)."
Biological agents in elderly patients with NSCLC

- IRESSA, HR=0.19, 95% CI 0.13, 0.26, p<0.0001
- Carboplatin / paclitaxel, HR=0.78, 95% CI 0.57, 1.06, p=0.1103

Progression Free Survival - IPASS
- Gefitinib in pts with EGFR activating mutations
- Overall survival for crizotinib-treated versus crizotinib-naive, ALK-positive patients

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

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. Disease-free survival, no toxicity difference, similar survival benefit.
- Elderly patients from the LACE meta-analysis showed similar survival benefit, similar toxicities but lower dose intensity than younger patients.
- Ontario Cancer Registry; n=5,304, 2001-06. Survival improved for all groups except ≥80 years.

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