The Christie NHS Foundation Trust

Stage III NSCLC

What is the evidence-based for older patients?

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Manchester Radiation Related Research Group
SIOG Manchester

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Demographics

- ~1/3 NSCLC patients have stage III disease
- The median age at diagnosis of lung cancer is 71
  - 36% 75 years at diagnosis
- Over the last decade, the incidence of death from lung cancer has decreased in patients ≤50 years but increased in those ≥70 years

Parkin. Lancet Oncol 2001
De Ruysscher. Ann Oncol 2009

- Most lung cancer patients are former or current smokers
- High incidence of co-morbidities
  - COPD
  - Cardio-vascular
  - Multiple organ failure
  - Poor general condition
  - Nutritional deficiencies
  - Social/mental issues
  - Sedentarity

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What are the issues?

• Selection of patients
• Selection of treatment
  - Radical vs. palliative
  - CTRT vs. RT
• Impact of age/co-morbidities
  - Acute and long term side effects
  - Compliance to treatment
  - Prognosis
• Balance between toxicity/QOL/symptom control/survival
• Under-representation of the elderly in clinical trials
  - Patients above 70 tend to be excluded from clinical trials

Jatoi J Clin Oncol 2005
Jenneas Inter Med J 2006

Are we making progress in standard of care therapy and survival?

Van der Drift. JTO 2012
1989–2009 (n=147,760)

CASE

- 76 year old retired school teacher
- Presented with haemoptysis (1 episode)
- 30 pack year smoking history
- Chest X-ray: RUL mass
- PMH: Hypertension
- Active, walks 3 km / day
- PS 1, Respiratory score 1

Investigations
- CT scan - 4 cm RUL tumour and station 4R lymph node
- Bronchoscopy biopsy – endobronchial tumour, adenocarcinoma
- FEV1 70% predicted, KCO 60% predicted
- Creatinine clearance 80 ml/min

Treatment options for stage III NSCLC

- Concurrent CTRT
  - PS 0-1
  - Suitable for cisplatinum-based chemotherapy
  - Suitable for radical RT upfront
  - Able to cope with radiation oesophagitis
- Sequential CTRT
  - PS 0-2
  - Suitable for cisplatinum-based chemotherapy
  - Not suitable for radical RT upfront
- Radical RT
- Palliative RT
- Role of surgery is not well defined
**Inclusion criteria in CTRT studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>PS</th>
<th>Upper age limit</th>
<th>Weight (HR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RTSG 94-10 (Curran 2011)</td>
<td>PS 1-2</td>
<td>70</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>HFXG (Future 2009)</td>
<td>ECOG 0-2</td>
<td>70</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>COG-9404 (Javate 2008)</td>
<td>ECOG 0-1</td>
<td>70</td>
<td>&lt;5%</td>
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<tr>
<td>Czech Lung Cancer Group (Kvietkova 2004)</td>
<td>ECOG 0-2</td>
<td>70</td>
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<tr>
<td>CALGB 39301 (Vallee 2007)</td>
<td>CALGB 0-1</td>
<td>-</td>
<td>-</td>
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<tr>
<td>SWOG 0022 (Kelly 2008)</td>
<td>ECOG 0-1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HOC-UN 01-24 (Hirose 2008)</td>
<td>ECOG 0-1</td>
<td>75</td>
<td>&lt;5%</td>
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<tr>
<td>OLCSS-0007 (Segovia 2010)</td>
<td>ECOG 0-1</td>
<td>75</td>
<td>-</td>
</tr>
<tr>
<td>WJTOG 0105 (Yamamoto 2010)</td>
<td>ECOG 0-1</td>
<td>75</td>
<td>-</td>
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</tbody>
</table>

**What were the most liberal inclusion criteria in RCTs evaluating CTRT?**

- Maximum age 74 years
- WHO performance status ≤ 2
- Weight loss <10% in the last 3 months
- Forced Expiratory Volume (FEV1) at 1 second ≥ 40% of the age-predicted value
- Adequate cardiac, renal and hematological functions.

**Concurrent CTRT in the elderly**

- Elderly patients benefit from concurrent CTRT (RTOG 9410, NCCTG)
  - Disease control and survival rates similar to those of younger patients
- Elderly patients experienced more myelosuppression
- Elderly patients also experienced greater non-hematologic toxicity
  - NCCTG BD vs. OD RT - more pneumonitis
  - RTOG 9410 seq vs. conc CTRT - more oesophagitis
- Elderly patients more likely to be hospitalised and to discontinue treatment

**Concurrent CTRT in the elderly - NCCTG phase III trial**

**Background:** JCOG0812 stopped early
- High treatment-related deaths: 4/46 (8.6%)
- 60% had RT field non-protocol compliant
- apparent OS difference (18.2 vs 14.1 mo) in favour of Carboplatin + RT

Review and introduction of RT QA programme

**JCOG 0801 - 200 patients >70**
- Carboplatin+RT (30mg/m2 daily x20)
- RT alone (60Gy / 6weeks)
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Survival benefit seen with CTRT
- median OS 22.4 vs 16.9 months

High G3/4 haematological toxicity with CTRT
- neutropenia 57.3%
- thrombocytopenia 29.2%
- G3 infection 12.5%

G3+ pneumonitis (1% CTRT vs 3% RT)
G3+ oesophagitis (1% CTRT vs 0% RT)

Radiotherapy only

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Stage</th>
<th>Median age and range</th>
<th>Survival</th>
<th>Grade 3 Toxicity</th>
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<tbody>
<tr>
<td>Gauden</td>
<td>362</td>
<td>I</td>
<td>(70-93)</td>
<td>34% at 5'</td>
<td>0</td>
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<tr>
<td>Foruta</td>
<td>32</td>
<td>I-II</td>
<td>79 (75-90)</td>
<td>40% at 2'</td>
<td>0</td>
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<tr>
<td>Benfill</td>
<td>36</td>
<td>I</td>
<td>77</td>
<td>55% at 2'</td>
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<tr>
<td>San Jose</td>
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<td>I-II</td>
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<td>50% at 3'</td>
<td>6%</td>
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<tr>
<td>Yu</td>
<td>80</td>
<td>I-II</td>
<td>76 (70-84)</td>
<td>55% at 2'</td>
<td>5%</td>
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<td>Persicozzi</td>
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<td>I-II</td>
<td>77 (75-83)</td>
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<td>Lonardi</td>
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<td>I</td>
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<tr>
<td>Tombselli</td>
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<td>I</td>
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<td>7%</td>
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<tr>
<td>Wanders</td>
<td>65</td>
<td>I-III</td>
<td>79 (75-90)</td>
<td>20% at 5'</td>
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Outstanding questions

<table>
<thead>
<tr>
<th>Questions</th>
<th>Solutions</th>
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</thead>
</table>
| How can we better select patients for aggressive treatments such as CTRT? | - Clinical trials for the elderly patients
- Little data for octogenarian
- Little data on the impact of age on biology of the disease
- Explore role of a CGA on treatment decision
- Collect population-based data? |
| Less toxic alternatives to CTRT? | - Explore targeted therapies+RT as an alternative to CTRT
- Adapt RT planning parameters (ie V20, MLD) according to age? |

Conclusions

- Elderly patients with lung cancer should neither be under-treated nor over-treated with RT or CTRT
- Arbitrary numerical definitions of age should not be used to make treatment decision
- Importance of an informed discussion with patients about the risk of side effects and chances of long term survival
- Take into account patients' wishes and expectations
- PS, stage and patient's preferences should be the main factors determining treatment