ICORG 05-03: Prospective Randomised Non-inferiority Phase III Trial Comparing 2 Radiation Schedules in Malignant Spinal Cord Compression (not proceeding with surgical decompression)

P. Thirion; L. Sullivan; A. Clayton-Lea; C. Small; O. McArdle; P. Kelly; I. Parker; J. O’Sullivan; D. Hacking; C. Collins; M. Pomeroy; M. Moriarty

All Ireland Cooperative Oncology Research Group
Background & Methodology

• Malignant Spinal Cord Compression (MSCC)
  • occurs in patients with advanced cancer, usually with bone involvement
  • is related to (nerve) spine compression by secondary deposit(s)
  • exposes to pain, paralysis, or incontinence
  • Is usually treated by decompressive surgery and radiotherapy

• Trial Objective:
  ▪ To compare prospectively 2 fractionation radiotherapy schedules (20 Gy / 5# vs. 10 Gy / 1#) in patients with malignant spinal cord compression not proceeding with surgical decompression.

• Trial design:
  ▪ ICH-GCP compliant prospective randomised non-inferiority phase III trial
  ▪ Power: 80%, significance level : 5%, +0.4 non-inferiority margin in mobility change at 5 weeks
  ▪ Sample size: 76 evaluable patients (alive at 5 weeks), requiring an
Methodology (2)

• Eligibility Criteria:
  - Pathologically proven metastatic cancer (excluding haematological/germ cell malignancies)
  - MRI documented treatment naïve symptomatic MSCC.

• Two arms:
  - Control arm: EBRT: 20 Gy / 5 #
  - Experimental arm: EBRT: 10 Gy / 1 #
  - Radiotherapy technique according to institutional practice, no central QA

• End-points:
  - Primary:
    - Change in mobility status at 5 weeks (Modified Tomita 3 points scale)
  - Secondary end-points:
    - Change in bladder control status at 5 weeks (In-house 3 points scale)
    - Acute & long-term toxicity (RTOG scale)
    - Overall survival
Results (1)

Patient Population Characteristics

- Accrual period: 2006-2014, 5 participating centres, showing the challenge of research in the area of palliative radiotherapy
- Main patient characteristics similar in both treatment arms

<table>
<thead>
<tr>
<th>Main Patient Characteristics</th>
<th>Eligible patients (116)</th>
<th>Evaluable patients (76)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control arm (38)</td>
<td>Experimental arm (38)</td>
</tr>
<tr>
<td>Age (Median, min-max)</td>
<td>68.7 (29.7 – 87.4)</td>
<td>68.7 (33.3 – 87.4)</td>
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<tr>
<td>KPS (Median, min-max)</td>
<td>60 (30-100)</td>
<td>70 (40 – 100)</td>
</tr>
<tr>
<td>Gender ratio (♀/♂)</td>
<td>36.2 % / 63.8 %</td>
<td>47.4 % / 52.6 %</td>
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<tr>
<td>Primary (Prostate / Breast/ Lung)</td>
<td>24.3% / 20 % / 19.1%</td>
<td>28.9% / 28.9% / 5.3%</td>
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<tr>
<td>Cervical / Thoracic / Lumbar / Sacrum / X levels</td>
<td>4.3% / 67% / 23.5% / 2.6% / 2.6%</td>
<td>2.6% / 65.7% / 21.1% / 5.3% / 5.3%</td>
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<tr>
<td>Baseline Mobility Status (Unaided / Walking with aid / Bed-bound)</td>
<td>41.7% / 25.3% / 33%</td>
<td>47.4% / 28.9% / 23.7%</td>
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<td>Baseline Bladder Function Status (Continent / Incontinent / Catheterised)</td>
<td>73% / 6.1% / 20%</td>
<td>68.4% / 10.5% / 21.1%</td>
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Results (2)

• Primary end-point:
  - No difference in change in mobility at 5 weeks between the 2 arms.
  - Only 10% of patients experienced an improvement, 58-68% of patients experiencing a stabilization.

• Secondary functional end-points:
  - No difference between treatment arms in bladder control change at 5 weeks, Neurological Deterioration-Free Survival (duration of functional stabilisation and improvement) and Overall Survival (median overall survival = 4 months).

• Toxicity (favourable):
  - Acute: 1 non-neurological G3 event (in experimental arm), no G4-5 toxicity.
  - Long-term: 2 non-neurological G3 events (1 in each arm), no G4-5 toxicity.
Conclusions

• ICORG 05-03 results:
  - Patient with MSCC treated by external beam radiation therapy alone have a poor vital and functional prognosis.
  - Radiotherapy alone provides only short term functional stabilisation.
  - 10 Gy -single fractionation radiation schedule provides similar outcome than 20 Gy / 5 fractions.

• In clinical daily practice:
  - Patient should be proposed Direct Decompressive Surgery followed by Radiotherapy when appropriate (current standard of care).
  - If patient not considered for surgery, a 10 Gy-single fraction schedule is a reasonable standard.

• Further clinical research is warranted and should be supported to improve the outcome of patients diagnosed with MSCC.