Hyperthermia combined with radiation in cervical cancer

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² iThemba LABS, National Research Foundation, South Africa
³ Department of Basic Medical Sciences, Ghent University, Belgium
HYPERTHERMIA COMBINED WITH RADIATION IN CERVICAL CANCER

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South Africa
South Africa

- Limited resources

46% of the population make use of private healthcare (stats SA 2011).
Gauteng is in urgent need of an additional linear accelerator that can serve both private and state patients.

South Africa

- Limited resources
  - Not enough Linacs
  - PET and CT machines were not working for 6 months
- Poverty
  - Transport problems
  - Missed appointments
  - Lost to follow ups
- Patients present at advanced stage of disease
- Immunocompromised
  - Can’t use Cisplatin as a radiosensitiser

Can we help overcome the challenges of third world healthcare?


Aim

To determine the clinical effects of the addition of modulated electro-hyperthermia to the standard treatment protocols LACC patients.

OUTCOMES:

- Local disease control at 6 months (PET scan)
- 2 year Survival
- Toxicity: early and late
- Quality of Life

Materials and Methods

Sample group

- N=236 (current n=174 enrolled)
- Public Healthcare patients
- Ages 18-70 years
- FIGO staging: IIIB- IIIB squamous cell
- Comorbidities: Diabetes and hypertension
- Excluded: Contraindications to treatment
  Immunocompromised patients
  Renal dysfunction
Materials and Methods

Treatment Protocol

- External Beam Radiotherapy (EBRT): 50 Gy over 25 fractions
- Brachytherapy: High Dose Rate (Ir\textsuperscript{192}) 3 x 8 Gy doses
- Cisplatin: 1-2 doses 80mg/m\textsuperscript{2}

EHT Protocol: 2 x 55 min Rx/week

Materials and Methods

Adverse Events

* Common Terminology Criteria for Adverse Events (CTCAE) version 4.0

43 symptoms were graded and grouped into: Haematological, Ototoxicity, Neurotoxicity, Immunological, Rectal, Digestive, Dermatological, Urinary, Renal, Gynaecological

* Time Points:
  - Acute Toxicity: Weekly during treatment, 6 weeks post treatment, 3 months post treatment
  - Late Toxicity: Every 6 months post treatment
Materials and Methods

Quality of Life

- EORTC (CX 30) and cervix specific (CX24)
- EuroQoL (EQ-5D-5L)

- Time points:
  - Pre treatment
  - 6 weeks post treatment
  - 3, 6, 12, 18, 24, months post treatment

Results

First 100 patients:

Screening failure: 27%

Death
Development of contraindications or co-morbidities before or during treatment
Moved to palliative care after PET scan
Decided against treatment

HIV + : 52%   HIV - : 48%
## Results

### FIGO STAGE distribution

Excluding Screening failures

<table>
<thead>
<tr>
<th>FIGO STAGE</th>
<th>HT</th>
<th>no HT</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV+ 12</td>
<td>HIV- 14</td>
<td>Total 26</td>
<td>HIV+ 26</td>
<td>HIV- 21</td>
<td>Total 47</td>
</tr>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>4 33%</td>
<td>4 29%</td>
<td>8 31%</td>
<td>9 35%</td>
<td>3 14%</td>
<td>12 26%</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>0 0%</td>
<td>0 29%</td>
<td>0 0%</td>
<td>0 0%</td>
<td>1 5%</td>
<td>1 2%</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>8 67%</td>
<td>10 29%</td>
<td>18 69%</td>
<td>17 65%</td>
<td>17 81%</td>
<td>34 72%</td>
</tr>
</tbody>
</table>

### AGE distribution

Excluding Screening failures

<table>
<thead>
<tr>
<th>AGE</th>
<th>HT</th>
<th>no HT</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV+ 12</td>
<td>HIV- 14</td>
<td>Total 26</td>
<td>HIV+ 26</td>
<td>HIV- 21</td>
<td>Total 47</td>
</tr>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>&lt;30</td>
<td>0 0%</td>
<td>0 0%</td>
<td>0 0%</td>
<td>2 8%</td>
<td>0 0%</td>
<td>2 4%</td>
</tr>
<tr>
<td>30-50</td>
<td>7 58%</td>
<td>5 36%</td>
<td>12 46%</td>
<td>16 62%</td>
<td>4 19%</td>
<td>20 43%</td>
</tr>
<tr>
<td>&gt;50</td>
<td>5 42%</td>
<td>9 64%</td>
<td>14 54%</td>
<td>8 31%</td>
<td>17 81%</td>
<td>25 53%</td>
</tr>
</tbody>
</table>
## Results

### 6 month survival

Excluding non disease related deaths, n=71

<table>
<thead>
<tr>
<th>6 months</th>
<th>HT</th>
<th>no HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>HIV-</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>45</td>
</tr>
</tbody>
</table>

| HIV+     | 12 | 20 |
| HIV-     | 14 | 17 |
| Total    | 26 | 45 |

<table>
<thead>
<tr>
<th>Alive</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>12</td>
<td>100%</td>
<td>20</td>
<td>80%</td>
<td>37</td>
<td>82%</td>
</tr>
<tr>
<td>HIV-</td>
<td>13</td>
<td>93%</td>
<td>17</td>
<td>85%</td>
<td>37</td>
<td>82%</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>96%</td>
<td>37</td>
<td>82%</td>
<td>72</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Deceased</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>0</td>
<td>0%</td>
<td>5</td>
<td>20%</td>
<td>8</td>
<td>18%</td>
</tr>
<tr>
<td>HIV-</td>
<td>1</td>
<td>7%</td>
<td>3</td>
<td>15%</td>
<td>8</td>
<td>18%</td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
<td>4%</td>
<td>8</td>
<td>18%</td>
<td>9</td>
<td>18%</td>
</tr>
</tbody>
</table>

### Results: 6 month survival

**Alive at 6 months**

![Bar chart showing survival rates for HIV+ and HIV- groups with and without HT.](chart.png)
Results

6 month Local Disease Control
70 patients completed 6 month PET scan
1 patient was unable to lie still due to bone pain

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>1. Complete response</td>
<td>13</td>
<td>50%</td>
<td>17</td>
</tr>
<tr>
<td>2. Partial response</td>
<td>10</td>
<td>38%</td>
<td>10</td>
</tr>
<tr>
<td>3. No change</td>
<td>2</td>
<td>8%</td>
<td>2</td>
</tr>
<tr>
<td>4. Local progression</td>
<td>0</td>
<td>0%</td>
<td>7</td>
</tr>
<tr>
<td>5. Death d/t disease</td>
<td>1</td>
<td>4%</td>
<td>8</td>
</tr>
</tbody>
</table>

Frequency table, expected frequency, chi2 contribution
Fisher's exact = 0.058

Results: Quality of Life

Analysis of change from baseline score
(more than 30 points < or > )
And score at specific time points

AT INITIATION:

Worse in EHT group: Sexual worry, nausea,
Better in EHT group: role functioning
Results: Quality of Life

At 6 Weeks
Nausea and vomiting ↑ in HT group (p=0.0109)

At 3 Months
Pain ↑ in HT group (p=0.007)
Appetite ↑ in HT group (p=0.0221)

At 6 Months
Sexual worry↑ in HT group (p=0.0197)
Emotional functioning ↑ in HT group (p=0.0307)

Factors which may affect toxicity:

- HIV status:  No significant effect

- Hyperthermia (HT):  Significant effect in:
  On treatment and 6 weeks post treatment
  Diarrhoea:  ↑ Frequency of Grade I in HT
  Urinary pain:  ↑ Frequency of Grade II in non HT
  Cystitis:  ↑ Frequency of Grade II in HT
  at 3 months only
Discussion

- Positive trend in the six month survival
- Positive trend in local disease control
- Difference in Quality of Life and Acute toxicity is not significant
- Late side effects will be assessed with continued follow up.
- Overall survival will be followed up

Conclusion

- Initial results are promising with therapeutic benefit.
- Continued follow up and increased patient numbers needed to strengthen the results.
THANK YOU

Carrie Strauss
Ans Baeyens
Jeffrey Kotzen