International collaboration on a very rare cancer: Adrenocortical Carcinoma

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CONSENSUS MEETING AND CONFERENCE
Improving the Methodology of Clinical Research on Rare Cancers Hotel Bedford Brussels, February 10th 2012
ADRENOCORTICAL CANCER EPIDEMIOLOGY

• Incidence: 0.5-2 cases per million population per year

• Women are more often affected than men (ratio: 1.5)

• Age distribution: bimodal with a first peak in childhood and a second higher peak in the fourth and fifth decade

• An exceptionally high annual incidence has been reported for children in Southern Brazil
Management of patients with adrenal cancer: recommendations of an international consensus conference

D E Schteingart, G M Doherty¹, P G Gauger¹, T J Giordano², G D Hammer, M Korobkin³ and F P Worden

Ann Arbor 2003

Recommendations mainly based on expert opinion
Evidence level of available data very low
European ACC core Group Study
## Chemotherapy: prospective trials including more than 10 patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Drugs</th>
<th>Pts</th>
<th>(CR+PR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHEMOTHERAPY ALONE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Slooten, 83</td>
<td>CDDP + DOXO + CTX</td>
<td>11</td>
<td>18%</td>
</tr>
<tr>
<td>Decker, 91</td>
<td>DOXO</td>
<td>16</td>
<td>19%</td>
</tr>
<tr>
<td>Schlumberger, 91</td>
<td>CDDP + DOXO + 5FU</td>
<td>13</td>
<td>23%</td>
</tr>
<tr>
<td>Burgess, 93</td>
<td>CDDP + VP16</td>
<td>13</td>
<td>46%</td>
</tr>
<tr>
<td>Williamson, 00</td>
<td>CDDP + VP16</td>
<td>45</td>
<td>11%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>98</td>
<td>18%</td>
</tr>
<tr>
<td><strong>CHEMOTHERAPY + MITOTANE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bonacci, 98</td>
<td>CDDP + VP16 + MIT (3-9 g/d)</td>
<td>18</td>
<td>33%</td>
</tr>
<tr>
<td>Khan, 00</td>
<td>STZ + MIT (1-4 g/d)</td>
<td>22</td>
<td>36%</td>
</tr>
<tr>
<td>Abraham, 02</td>
<td>VP16 + DOXO + VCR + MIT (6 g/d)</td>
<td>36</td>
<td>22%</td>
</tr>
<tr>
<td>Berruti, 05</td>
<td>CDDP + DOXO + VP16 + MIT (1-4 g/d)</td>
<td>72</td>
<td>49%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>148</td>
<td>42%</td>
</tr>
</tbody>
</table>
An academic intention to treat study

**Design:**
- randomized
- prospective
- controlled
- open-label
- multi-center
- international
- parallel-group
- phase III trial

Second line therapy as phase II trial

Recruiting, follow-up, analysis
60+28+6 months = 7 years
# FIRM-ACT Recruitment per country

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>AUS</th>
<th>CAN</th>
<th>GER</th>
<th>F</th>
<th>Italy</th>
<th>NL</th>
<th>N</th>
<th>PL</th>
<th>SWE</th>
<th>US</th>
<th><strong>Total</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population in million</strong></td>
<td>8</td>
<td>28</td>
<td>33</td>
<td>82</td>
<td>64</td>
<td>60</td>
<td>16</td>
<td>5</td>
<td>38</td>
<td>9</td>
<td>311</td>
<td></td>
</tr>
<tr>
<td><strong>centers (n)</strong></td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>11</td>
<td>9</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>39</td>
</tr>
<tr>
<td><strong>patients (n)</strong></td>
<td>1</td>
<td>3</td>
<td>9</td>
<td>103</td>
<td>71</td>
<td>35</td>
<td>28</td>
<td>5</td>
<td>6</td>
<td>26</td>
<td>17</td>
<td>304</td>
</tr>
</tbody>
</table>

Patients are randomized from June 12, 2004 until Sept 17, 2009
Etoposide, doxorubicin, cisplatin, and mitotane versus streptozotocin and mitotane for advanced adrenocortical carcinoma – The FIRM-ACT study –


Submitted for publication
GALACCTIC TRIAL

OSI-906-301
A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of OSI-906 in Patients with Locally Advanced or Metastatic Adrenocortical Carcinoma
- Protocol Review

- Primary
  - To determine overall survival of single agent OSI-906 (Arm A) versus placebo (Arm B) in patients with ACC who received at least 1 but no more than 2 prior drug regimens
OSI 906-301: Countries
OSI 906 trial accrual completed:
139 Patients Randomized

Canada, 6
Poland, 1
Australia, 2
France, 19
Germany, 22
Italy, 15
UK, 6
Netherlands, 8

US, 60
Time lines of randomized studies in ACC

Firm-act accrual
Start  24/04/2004
End    02/10/2009
304 patients enrolled

GALACCTIC trial accrual
Start  15/02/2010
End    22/06/2011
139 patients enrolled
Conclusion

A multinational cooperation makes feasible prospective randomized clinical trials in ACC

Each participating center increases its expertise and the number of patients referenced