Current trials in Neuroendocrine Tumours: A systematic review

D.L. Chan1, E. Segelov2, J. Millican1, S. Singh3, N. Pavlakis4 for the CommNETS collaborators

Royal North Shore Hospital, Sydney, 1St Vincent’s Clinical School, University of New South Wales, Sydney, 2Sunnybrook Odette Cancer Centre, Toronto

Introduction/background

Trials in neuroendocrine tumours (NETs) have increased markedly in number over the last 10 years.

• No comprehensive registry of NET trials exists; researchers do not have ready access to a summary of open trials to identify research gaps.

• We aimed to systematically identify currently open, registered trials in NET

• To describe the current research landscape and
• To direct future trials

Methods

• Databases identified and searched for NET trials.

• 9 databases (clinicaltrials.gov, ISRCTN, clinicaltrialsregister.eu, ANZCTR, Canadiancancertrials.ca, 3CTN, UK clinical trials gateway, National Cancer Institute, NCIC), as well as conference abstracts (ENETs, ASCO, ASCO GI) searched.

• Ongoing trials and randomized data, particularly in areas

• Involving neuroendocrine tumours (Phase I trials for multiple solid tumour sites excluded)

• Classified into RCTs and single-arm trials by investigational agent's mode of action

Inclusion criteria:

• Prospective trials open/recently closed (<6 months) to accrual

• Involving neuroendocrine tumours (Phase I trials for multiple solid tumour sites excluded)

• Classified into RCTs and single-arm trials by investigational agent's mode of action

Sample search strategies:

Clinicaltrials.gov = “neuroendocrine”, “carcinoid” – restricted to open trials

Other websites – “neuroendocrine”

• Open NET trials were included and classified into randomised trials (RCTs), single-arm interventional trials and non-interventional trials. Unreported trials recently closed to accrual were also identified.

Results

Fig.1: Trial Flow Diagram

Table 1: Summary of search results

<table>
<thead>
<tr>
<th>Type of Agent</th>
<th>RCT</th>
<th>Single-arm</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatotstatin analogues</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>PRRT</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Antiangiogenic agents</td>
<td>3</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>mTOR inhibitors</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Novel drugs/combinations</td>
<td>5</td>
<td>28</td>
<td>33</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>54</td>
<td>71</td>
</tr>
</tbody>
</table>

• NB 8 trials (1 RCT, 7 single-arm) were excluded from time of abstract submission as they have reported results/closed to accrual.

• The RCTs identified are described in Figure 2.

Discussion

• This is the first systematic review of open trials in NET.

• Few current randomized trials investigate

• Treatment of Grade 3 NEC

• Surgical/locoregional therapies

• Several trials have recently investigated symptom control as a primary endpoint. Given the considerable impact of NETs on patients, ongoing research in this area is of high priority.

• The ongoing challenges of disease heterogeneity and patient accrual may argue for novel trial designs going forward.

Conclusions

• A wide range of systemic therapies are currently being investigated in treatment of NETs.

• Ongoing trials and randomized data, particularly in areas such as symptom control and locoregional therapies, are needed to improve the patient journey in NETs.