INTRODUCTION

Purpose:
- The clinical course of neuroendocrine (NET) patients remains poorly defined.
- We evaluated clinical outcomes and prognostic factors in 853 NET patients enrolled in a large, prospective outcomes study.

Characteristics of NET:
- Incidence ~ 5.25/100,000
- Diagnosis is increasing
- Prevalence estimated at >100,000
- Often pursue indolent course
- Hormone-secreting
- Common subtypes:
  - Carcinoid – small bowel is most common site
  - Pancreatic Endocrine tumor

METHODS

Patient population:
- Case recruitment at the Dana-Farber Cancer Institute (DFCI) from 2003-2009
- 853 cases diagnosed 1958-2009
  - 190 pancreatic NET
  - 321 small bowel carcinoid
  - 342 other carcinoid
- Clinical information recorded from time of initial diagnosis
  - Updated at 6-month intervals following study enrollment

Statistics:
- Kaplan-Meier plot with the log-rank test
- Cox proportional hazards regression analysis adjusting for:
  - age, sex (M,F), race
  - metastasis at initial diagnosis (M0 fully resected, M1 metastatic)
  - tumor subtype (small bowel, pancreatic NET, other carcinoid)
  - histologic grade (unknown, poor, moderate, welldifferentiated)
  - octreotide treatment (Y/N/ref)
- Subgroups of Small Bowel Carcinoids and Pancreatic NET also analyzed separately

RESULTS

Table 1: Baseline Characteristics of the patient population

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (N=853)</th>
<th>Small Bowel Carcinoid (N=321)</th>
<th>Pancreatic NET (N=190)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Dx</td>
<td>60.7 (71.2%)</td>
<td>56.0 (63.1%)</td>
<td>63.3 (74.3%)</td>
</tr>
<tr>
<td>Gender M/F</td>
<td>375 (44.1%)</td>
<td>181 (56.5%)</td>
<td>194 (74.6%)</td>
</tr>
<tr>
<td>Grade of Differentiation</td>
<td>118 (36.9%)</td>
<td>62 (19.3%)</td>
<td>56 (24.2%)</td>
</tr>
<tr>
<td>Histology</td>
<td>240 (74.8%)</td>
<td>138 (42.9%)</td>
<td>102 (42.6%)</td>
</tr>
<tr>
<td>Octreotide treatment (Y/N)</td>
<td>703 (84.9%)</td>
<td>382 (119.4%)</td>
<td>321 (165.7%)</td>
</tr>
</tbody>
</table>

Table 2: Baseline Survival Characteristics of the patient population

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (N=853)</th>
<th>Small Bowel Carcinoid (N=321)</th>
<th>Pancreatic NET (N=190)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Deaths</td>
<td>210 (24.6%)</td>
<td>66 (20.6%)</td>
<td>144 (75.3%)</td>
</tr>
<tr>
<td>Median F/U</td>
<td>4.65yrs (2.96, 7.25)</td>
<td>3.93yrs (2.53, 6.38)</td>
<td>5.38yrs (3.85, 8.51)</td>
</tr>
<tr>
<td>Stage M0-M1</td>
<td>312 (97.2%)</td>
<td>181 (56.5%)</td>
<td>194 (74.6%)</td>
</tr>
<tr>
<td>Median F/U</td>
<td>4.65yrs (2.96, 7.25)</td>
<td>3.93yrs (2.53, 6.38)</td>
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</tbody>
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DISCUSSION

Clinical characteristics of all patients:
- Follow-up time: initial diagnosis to last known follow-up
  - Median F/U: 4.45 years
  - 80% at 8.63 yrs
  - 90% at 11.7 yrs
  - 210 (24.6%) deaths occurred
  - 46% male, 54% female
  - 44% M0, 55.9% M1
  - Median OS for the entire cohort was 12.8 yrs.

Overall survival and disease free survival of resected (M0) patients:
- Median OS was not reached
- 5-yr OS was 94%
- 5-yr DFS was 65%
- Median time to recurrence was 7.9 yrs
  - 9 yrs for small bowel carcinoid
  - 4.6 yrs for pancreatic NET
  - 10 yrs for other carcinoid

Overall survival of metastatic (M1) patients:
- Median OS was 7.6 yrs
  - 12.5 yrs for small bowel carcinoid
  - 4.7 yrs for pancreatic NET
  - 4.6 yrs for other carcinoid

Prognostic Factors for resected patients:
- Higher risk of recurrence:
  - Older age, male gender, pancreatic primary site, and poor histologic grades were significantly associated

Prognostic Factors for metastatic patients:
- Overall survival and survival since metastasis:
  - The same factors were associated with shorter survival but
    - Panoramic origin is no longer significant
    - Small bowel origin is protective

Octreotide treatment:
- Suggested improved survival for patients since time of metastasis
  - M1 adjusted HR = 0.83, p=0.29
  - M0+M1 adjusted HR = 0.78, p=0.12

CONCLUSIONS

Pancreatic primary site increases the risk for recurrence after resection
Small Bowel primary site increases the chance for survival after metastasis compared to Pancreatic NET

Octreotide may be associated with improved survival after metastasis

Tumor recurrences, when they occur, may develop more than 5 years after initial diagnosis.