Carcinoid 2004
Update
Diagnosis and Treatment
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More cases being diagnosed

Rapid advances in diagnosis and treatment

Better use of established methods
IMAGING

- SPECT / CT (Fusion Scan)

- SSR dependent scintigraphy
  (OctreoScan, Lu$_{177}$ Octreotate Scan)
TRYPTOPHAN METABOLISM

Tryptophan
↓ Hydroxylase
5-Hydroxytryptophan (5-HTP)
↓ Decarboxylase
5-Hydroxytryptamine (Serotonin)
↓ Monoamine oxidase (MAO)
5-Hydroxyindole acetic acid (5-HIAA)
The APUD Concept

Amine Precursor Uptake and Decarboxylation Cells
ISOTOPE SCINTIGRAPHY (Scans) Not dependent on SSRs

- $^{18}F$ DG PET
- $^{18}F$ DOPA PET
- $^{11}C$ CLORGYLINE PET
- $^{11}C$ HARMINE PET
- $^{11}C$ 5-HTP PET
Treatments of Carcinoid Tumors and Syndrome

- Supportive
- Surgery
- Antiproliferative
Treatment Advances

- Gene alteration
- SOM-230
- Combination treatments:
  - Octreotide / Doxorubicine
  - Octreotide / Pegylated Alfa Interferon
- New isotopes:
  - \( \text{Lu}_{177} \) Octreotate, \( Y_{90} \) microspheres
- Aggressive surgery
- New chemotherapy drugs
Medical Supportive Treatments
Antidiarrheal Drugs

- Octreotide (Sandostatin)
- Cyproheptadine (Periactin)
- Diphenoxylate / atropine (Lomotil)
- Loperamide (Imodium)
- DTO
- Anticholinergics (Bentyl, Pro-Banthine, Pamine)
- Cholestyramine
- Pancreatic extract
Medical Supportive Treatments

Nutritional factors
- Diet
- Niacin
- MCT’s
- Hematinics (B$_{12}$, folate, iron)

Electrolytes
- Potassium, magnesium

Antiulcer medications
- H$_1$ and H$_2$ blockers (also for angioedema)

Antifibrosis
- ? Fish oil, colchicine
Medical Supportive Treatments

- **Nutritional factors**
  - Diet
  - Niacin
  - MCT’s
  - Hematinics (B$_{12}$, folate, iron)

- **Electrolytes**
  - Potassium, magnesium

- **Antiulcer medications**
  - H$_1$ and H$_2$ blockers (also for angio-edema)

- **Antifibrosis**
  - Fish oil ?, colchicine
Octreotide

- Carcinoid syndrome

- Biologic antitumor effect – stabilization, regression (anti-angiogenesis, upregulating SS receptors, synergistic with alpha interferon)

- Enhanced antitumor effect with very high dosage (Onco-LAR trials)

- Enhances chemotherapy (Adriamycin)
Antitumor Action of Octreotide

- Direct antimitotic effect
- Suppression of IGF-1
- Regulation of IGF binding protein
- Inhibiting effect on other growth factors (EGF, etc.)
- Inhibition of angiogenesis
- Regulation of immune response
- Induction of apoptosis
Surgery

- Bx for Dx
- Resection of primary (and secondaries) for:
  - cure, control of bleeding,
  - relief of obstruction,
  - exclusion of ischemic bowel
- Debulking:
  - Excision
  - Radiofrequency Ablation
  - Cryosurgery
  - HACE
- Heart valve replacement
- Relief of ascites – Denver shunt
- Stent placement
- Liver transplant
Surgery

- Biopsy for diagnosis

- Resection of primary and secondaries for: cure, control of bleeding, relief of obstruction, exclusion of ischemic bowel

- Debulking:
  - Excision
  - Radiofrequency ablation (RFA)
  - Cryosurgery
  - Hepatic artery chemoembolization (HACE)
Surgery (cont’d)

- Heart valve replacement
- Relief of ascites – Denver shunt
- Stent placement
- Liver transplant
## Antiproliferative Treatment (1)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Response %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biotherapy</strong></td>
<td></td>
</tr>
<tr>
<td>Octreotide (Sandostatin)</td>
<td>12-60</td>
</tr>
<tr>
<td>Octreotide /α IFN</td>
<td>40-85</td>
</tr>
<tr>
<td><strong>Radiotherapy</strong></td>
<td></td>
</tr>
<tr>
<td>Ext. beam</td>
<td>±</td>
</tr>
<tr>
<td>$^{131}$I MIBG</td>
<td>30-40</td>
</tr>
<tr>
<td>$^{111}$In</td>
<td>&gt;50</td>
</tr>
<tr>
<td>$^{90}$Y(Octreother, MicroSpheres)</td>
<td>&gt;50</td>
</tr>
</tbody>
</table>
# Antiproliferative Treatment (2)

<table>
<thead>
<tr>
<th>Agent (chemotherapy)</th>
<th>Response %</th>
</tr>
</thead>
<tbody>
<tr>
<td>5FU / Xeloda</td>
<td>&lt;25%</td>
</tr>
<tr>
<td>LCVN / 5FU / STDZ</td>
<td>± 40%</td>
</tr>
<tr>
<td>STDZ / Doxorubicin</td>
<td>&lt;40%</td>
</tr>
<tr>
<td>C.A.P. (Cytox / Adria / Cisplatin)</td>
<td>~40%</td>
</tr>
<tr>
<td>DTIC (Dacarbazine)</td>
<td>&lt;50%</td>
</tr>
<tr>
<td>Etopo / Cisplatin (for atypicals)</td>
<td>67%</td>
</tr>
<tr>
<td>CCNU / LCVN / 5FU</td>
<td>&gt;23%</td>
</tr>
</tbody>
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Antiproliferative Treatment (3)

<table>
<thead>
<tr>
<th>Agent (chemotherapy)</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>5FU/Irinotecan</td>
<td>? Poor</td>
</tr>
<tr>
<td>5FU/Gemcitabine</td>
<td>? Poor</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>? Poor</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>?</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>?</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>? Good</td>
</tr>
</tbody>
</table>
Antiproliferative Treatment (4)

- Bevacizumab (Avastin) +
- Temozolomide (Temodar) / Thalidomide/Capecitabine (Xeloda) ++
- Imatinib (Gleevec) +
- PS-341 (Proteosome inhibitor) ?
- Epothilone ?
- Gefitinib (Iressa) ?
- Oxaliplatin (Eloxatin) ?
- SUO 11248 ?
Effect of Octreotide on Carcinoid Syndrome Survival

- Prior to 1988: Mean 5 year survival → 18%
- By 1996: Mean 5 year survival → 67%
- By 2003: Octreotide plus other treatment modalities (surgery, HACE, RFA, alpha interferon and chemotherapy)

Mean 5 year survival → 84%
Take Home Message

The best management for carcinoid is case-customized, sequential multimodality treatment.
CARCINOID CANCER FOUNDATION, Inc.

http://www.carcinoid.org