Patient number 1

- 64 yo male with upper abdominal pain and palpable mass
- Biopsy consistent with C-KIT (+), DOG-1 (+) spindle cell neoplasm.
Patient number 1

- Exploratory laparotomy, resection of 4th portion of duodenum and primary duodenojejunostomy
Phase II Trial of Neoadjuvant/Adjuvant Imatinib Mesylate (IM) for Advanced Primary and Metastatic/Recurrent Operable Gastrointestinal Stromal Tumor (GIST): Early Results of RTOG 0132/ACRIN 6665

N= 30 primary patients (Group A)
N= 22 recurrent/metastatic patients (Group B)

Patients with KIT-positive, locally advanced (Group A [N=31]) or metastatic/recurrent GIST (Group B [N=22])

Preoperative imatinib 600 mg/day x 8-12 wks

SD/PR
Resection

PD
Off study

Imatinib 600 mg/day x 2 yrs

Designed as a phase II feasibility trial for neoadjuvant imatinib given 8-12 weeks before planned surgery.

Eisenberg J Surg Oncol 2009
Phase II Trial of Neoadjuvant/Adjuvant Imatinib Mesylate (IM) for Advanced Primary and Metastatic/Recurrent Operable Gastrointestinal Stromal Tumor (GIST): Early Results of RTOG 0132/ACRIN 6665

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Med Size</td>
<td>8.9cm</td>
<td>5.8cm</td>
</tr>
<tr>
<td>R0/R1</td>
<td>92%</td>
<td>63%</td>
</tr>
<tr>
<td>R2</td>
<td>8%</td>
<td>32%</td>
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</tbody>
</table>

Concluded: Neoadjuvant imatinib is safe and feasible; requires multidisciplinary review and is not associated with post-op complications.

Failed Total 5-Yr Estimate

- All Patients: 30 53 46.1%
- Primary: 15 31 56.7%
- Recurrent/Mets: 15 22 29.8%

Progression-Free Survival (%)

Yrs After Registration

5
4
3
2
1
0
0 1 2 3 4 5

All Patients Primary Recurrent/Mets
Neoadjuvant therapy: when?

• May decrease the complexity of the procedure (adjacent organ involvement and tumor rupture/bleeding)

• 80% of patients benefit from imatinib, but CR’s are very low

• Responses are frequent, yet metabolically inactive tumors harbor viable cells

• Surgery is planned usually within 9-12 months

Demetri NEJM 2002
Antnescu Clin Can Res 2005
Verweij Lancet 2004
Metastasectomy and Debulking for Gastrointestinal Stromal Tumors
Patient number 2

- 86 yo male with right lower discomfort and fullness
Patient number 2

- Exploratory laparotomy, resection of jejunal GIST, and 2 peritoneal implants, no tumor rupture
Surgical Management of Advanced Gastrointestinal Stromal Tumors After Treatment With Targeted Systemic Therapy Using Kinase Inhibitors

- N=69 patients with advanced GIST (45 imatinib and 25 imatinib then sunitinib)
- Median f/u 14.6 months

<table>
<thead>
<tr>
<th></th>
<th>NED</th>
<th>Min Residual</th>
<th>Bulky Residual</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td>Stable disease</td>
<td>18</td>
<td>78</td>
<td>4</td>
</tr>
<tr>
<td>Limited progression</td>
<td>8</td>
<td>25</td>
<td>19</td>
</tr>
<tr>
<td>Generalized progression</td>
<td>1</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>7</td>
<td>30</td>
</tr>
</tbody>
</table>

Raut, JCO 2006
Surgical Management of Advanced Gastrointestinal Stromal Tumors After Treatment With Targeted Systemic Therapy Using Kinase Inhibitors

- Concluded that patients with advanced or metastatic disease and stable or limited progression benefit from surgery

Raut JCO 2006
Patient 3

- 70 yo male with a remote history of small bowel resection for a “benign lesion.”
- Upper abdominal pain
Treated to maximal Response

- Imatinib for 2 years
- Then referred to our Moffitt Cancer Center after progression noted
- Sunitinib started
Extended Right Hepatectomy

Post-op  2 years later
Therapy by Type of Progression

• Limited or Nodular Progression
  – Surgical Resection
  – Hepatic Artery Chemoembolization
  – Hepatic Radio-frequency Catheter Ablation

• Widespread progression
  – Increase Imatinib to 800 mg daily
  – Sunitinib
  – Regorafenib
  – Clinical Trial
Hepatic Artery Embolization

Pre-embolization

Post-embolization
Hepatic Arterial Embolization

Radiographic Response Rates

- 14 patients with imatinib-resistant GIST and progressive liver metastases
  - Treated with hepatic arterial embolization or chemoembolization
  - 13 patients evaluable for radiologic response

<table>
<thead>
<tr>
<th>RESPONSE</th>
<th>BEST RESPONSE (Choi Criteria)</th>
<th>BEST RESPONSE (RECIST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>54%</td>
<td>8%</td>
</tr>
<tr>
<td>Complete</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Partial</td>
<td>54%</td>
<td>8%</td>
</tr>
<tr>
<td>Stable</td>
<td>46%</td>
<td>92%</td>
</tr>
<tr>
<td>Progression</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Hepatic Arterial Embolization
Progression-Free Survival

Regional Therapies for Sarcoma

Jonathan Zager, MD
Director of Regional Therapy
Hepatic Perfusion

- Started out as Isolated hepatic perfusion (IHP) in 1980’s and 1990’s at NCI
- Alexander, Bartlett and colleagues

Retro Hepatic Cava

Supra Hepatic Cava

Portal Dissection/ Isolation
Chemosaturation/PHP

Isolation of Liver for Regional Tx

Saturation of Liver with Melphalan

Extracorporeal Filtration and Veno-Veno Bypass
Leiomyosarcoma
Debulking Surgery

- Three retrospective studies have demonstrated a prolonged PFS in patients with response/stable disease and focal progression.
- Surgery in metastatic GIST patients in the absence of MPD on imatinib is associated with outcomes at least comparable with second-line sunitinib and may be considered in select patients.
- With generalized progression surgery may be considered for palliative intent.
- Metastasectomy may enhance the effectiveness of TKI therapy in responders or stable disease.
Gastrointestinal Stromal Tumor
Case Presentations

Ricardo J. Gonzalez, MD
Professor of Surgery
Chair, Sarcoma Department
Chief of Surgery
Moffitt Cancer Center
Thank you!!