Gastrointestinal Stromal Tumor Case Presentations

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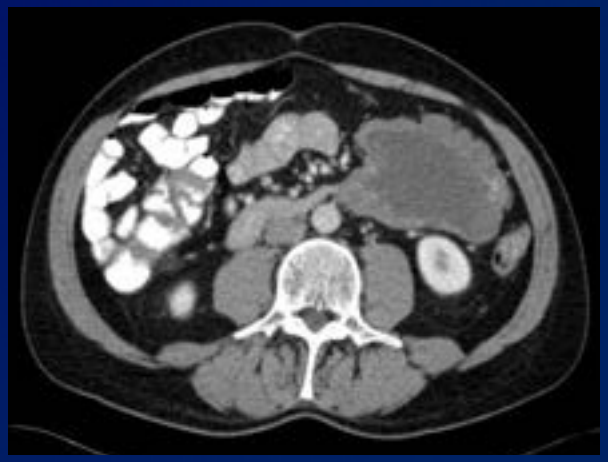
Patient number 1

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

CT Day 0

CT 12 mos

Preop CT

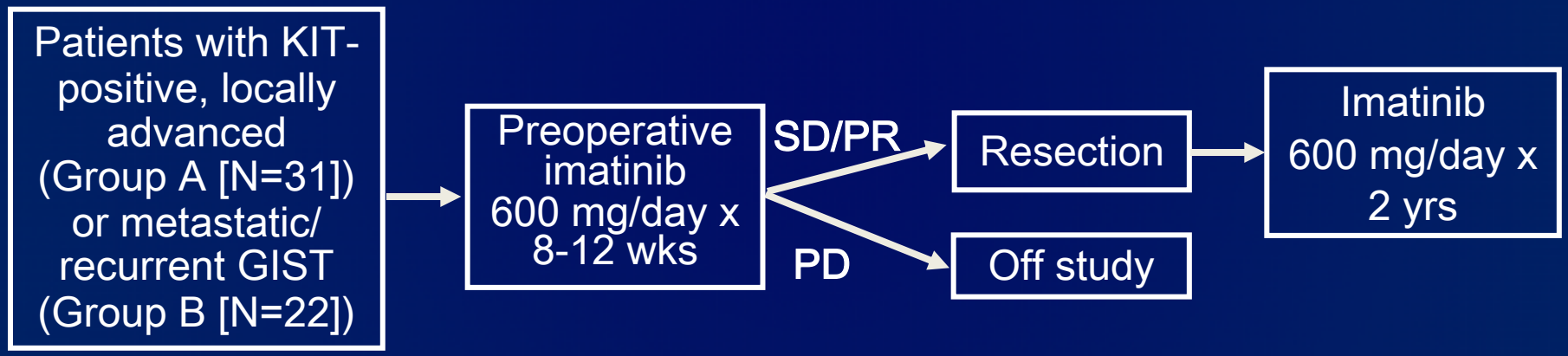


Patient number 1

- 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)

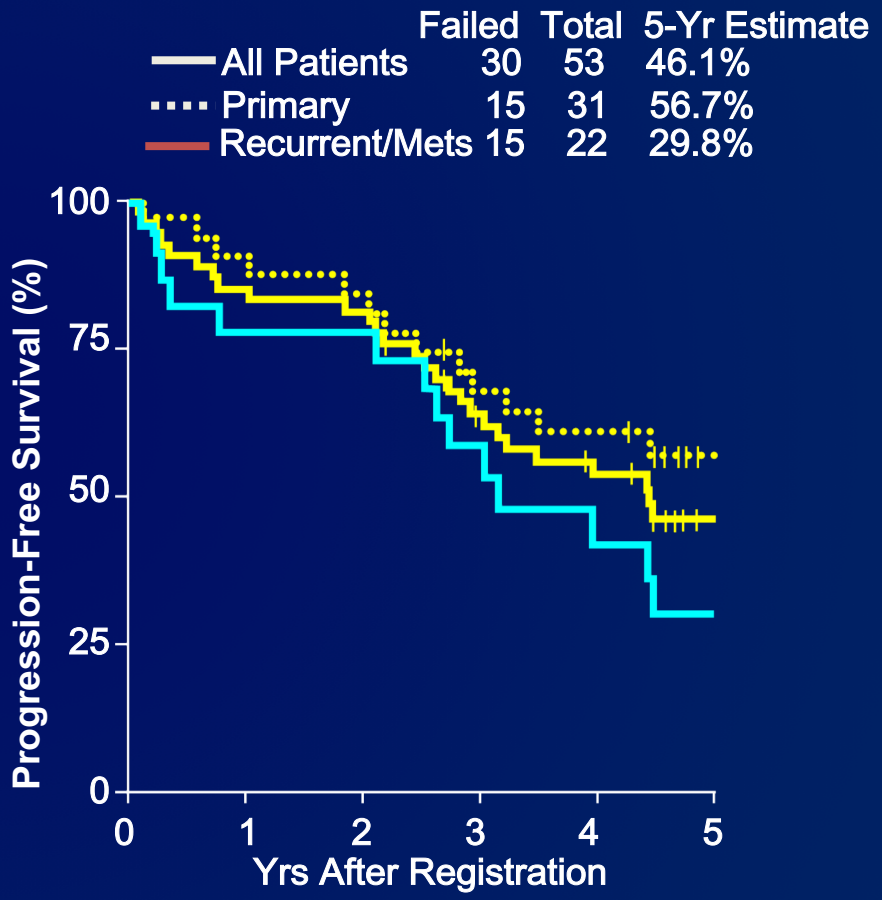


Designed as a phase II feasibility trial for neoadjuvant imatinib given 8-12 weeks before planned surgery.

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

	Group A	Group B
Med Size	8.9cm	5.8cm
R0/R1	92%	63%
R2	8%	32%



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

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

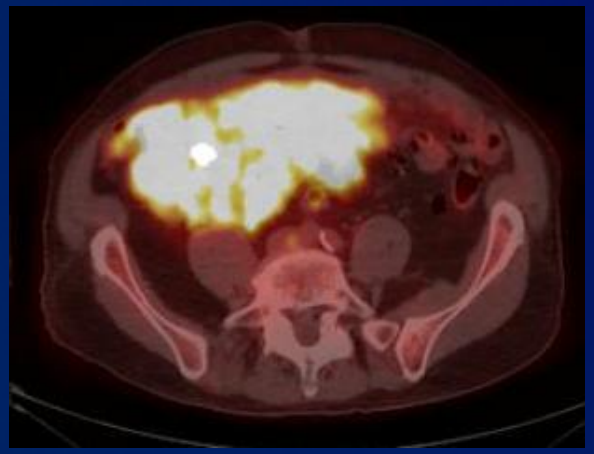
Demetri *NEJM* 2002
Antnescu *Clin Can Res* 2005
Verweij *Lancet* 2004

Metastasectomy and Debulking for Gastrointestinal Stromal Tumors

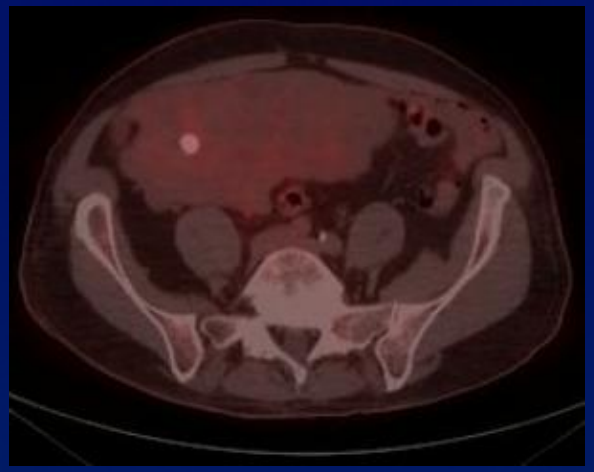
Patient number 2

- 86 yo male with right lower discomfort and fullness

PET/CT time 0



PET/CT @ 30 days



Preop CT at 6 mos

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

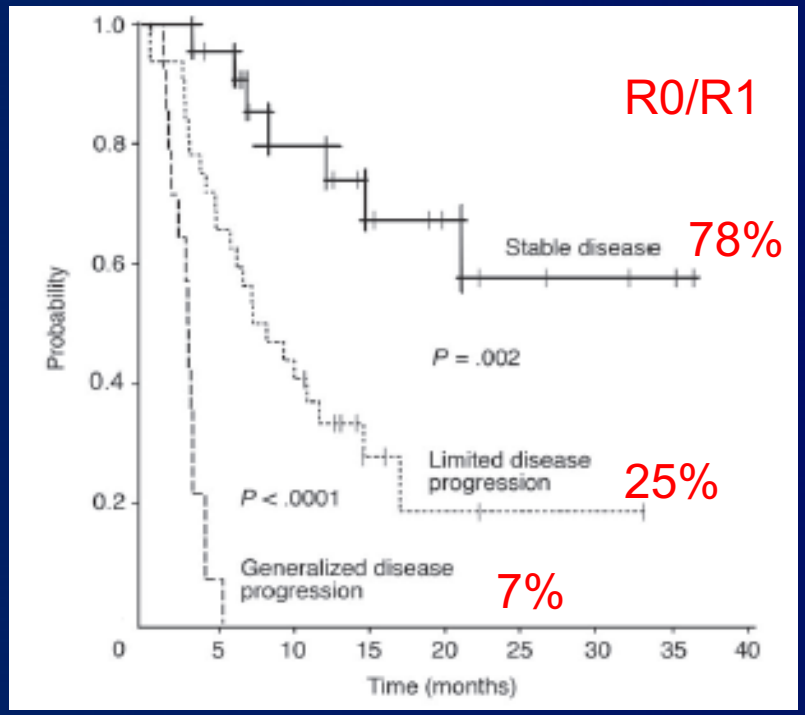
- N=69 patients with advanced GIST (45 imatinib and 25 imatinib then sunitnib)
- Median f/u 14.6 months

	NED		Min Residual		Bulky Residual		
	No	**%**	**No**	**%**	**No**	**%**	**Total**
Stable disease	18	78	4	17.5	1	4.5	23
Limited progression	8	25	19	59	5	16	32
Generalized progression	1	7	7	50	6	43	14
Total	27		30		12		69

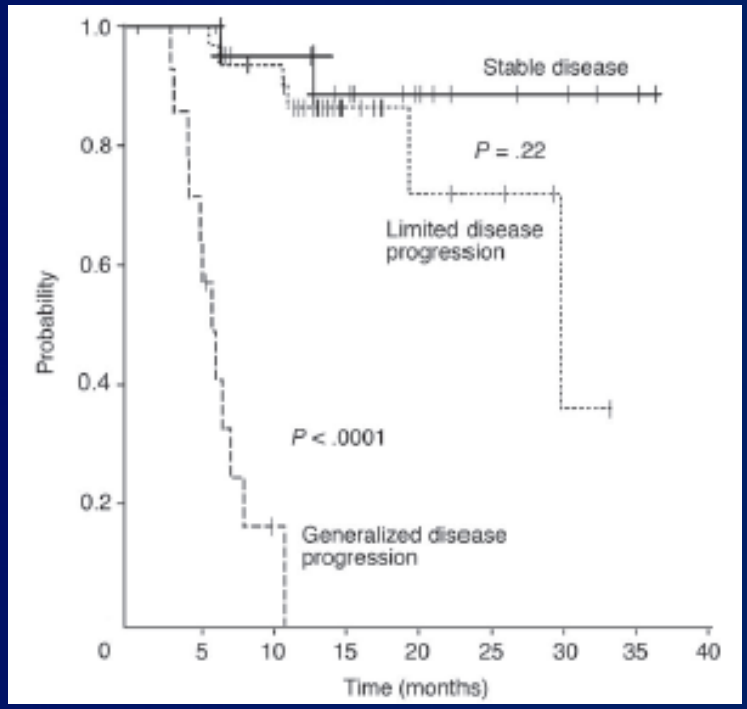
Raut JCO 2006

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

Progression Free Survival



Overall Survival

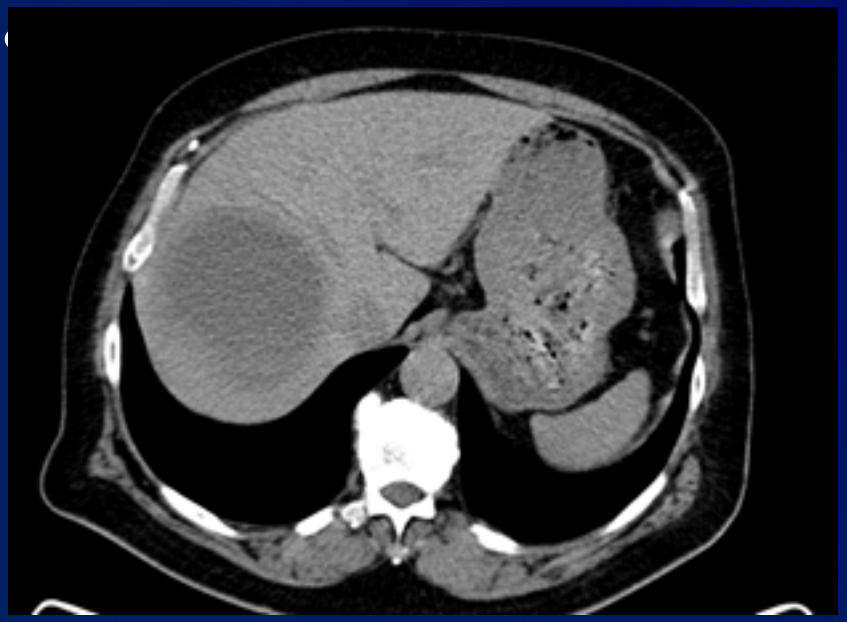


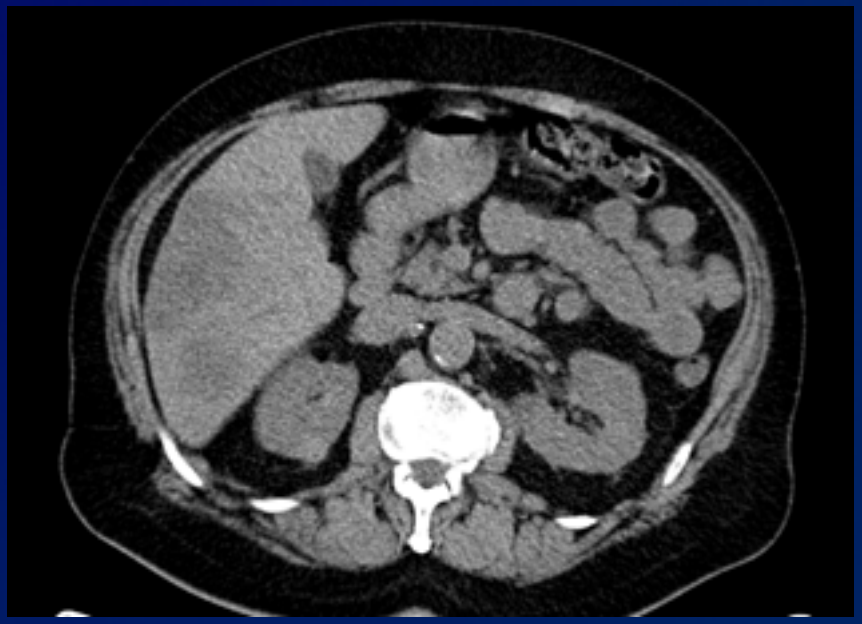
- Concluded that patients with advanced or metastatic disease and stable or limited progression benefit from surgery

Raut JCO 2006

Patient 3

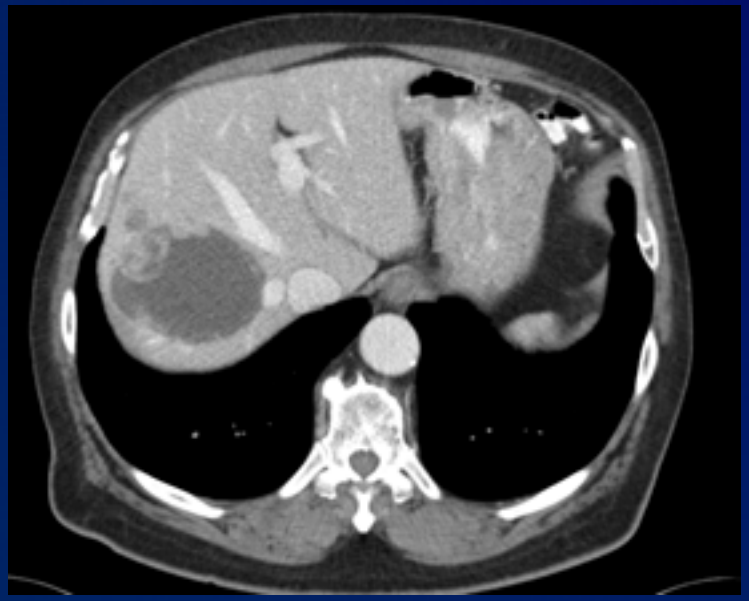
- 70 yo male with a remote history of small bowel resection for a “benign lesion.”
- Upper abdominal pain



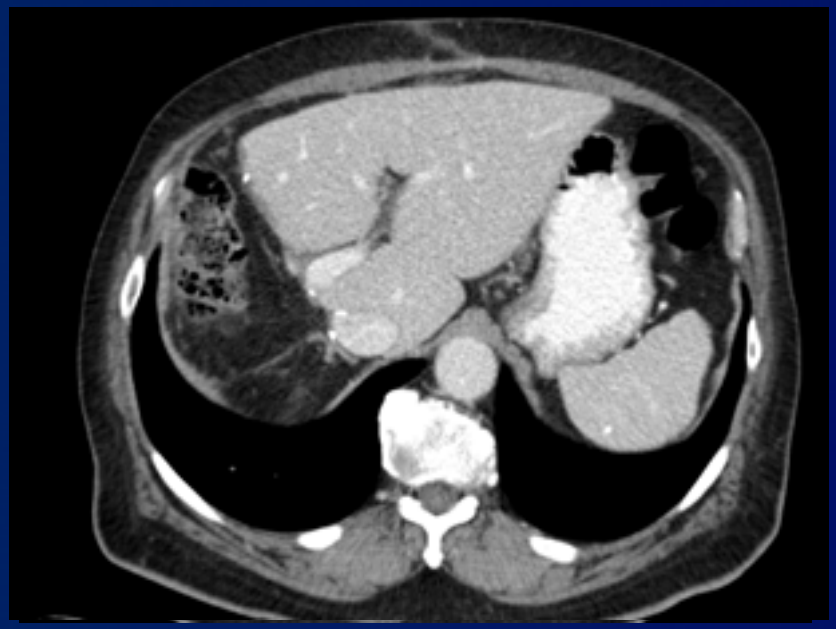


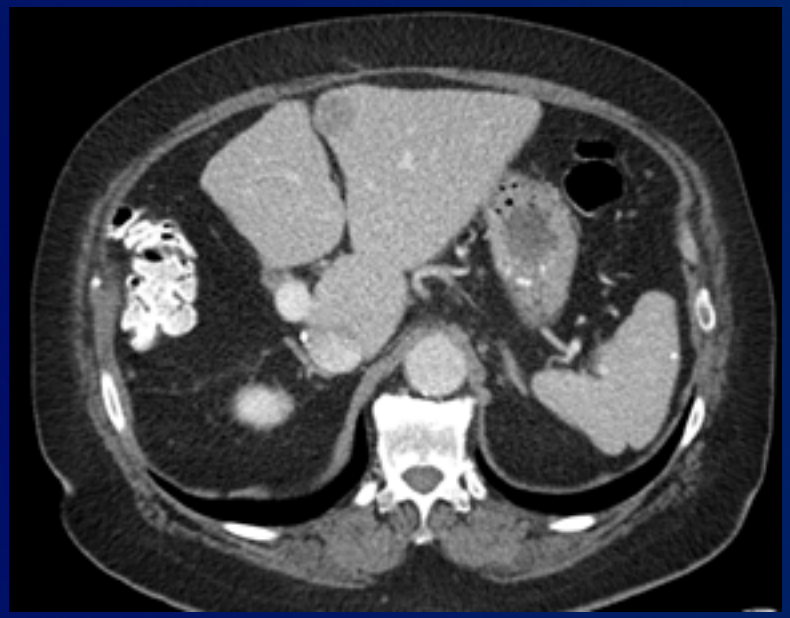
Treated to maximal Response

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



Extended Right Hepatectomy





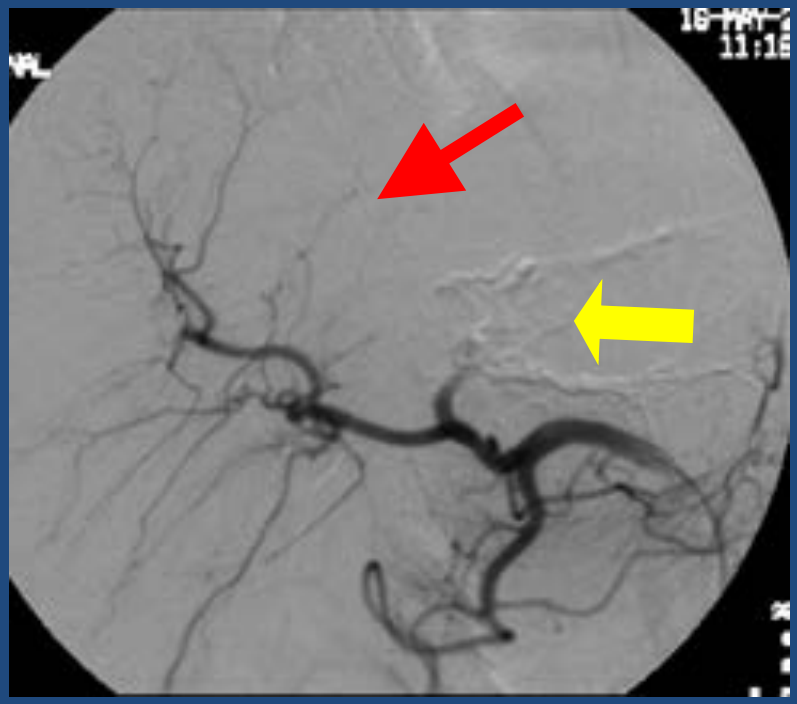
Post-op **2 years later**

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

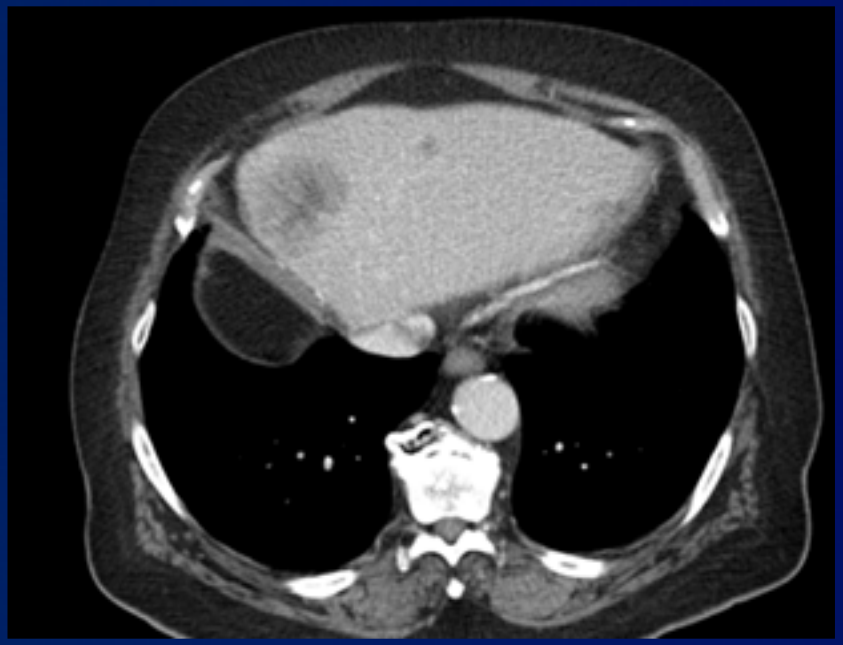
Hepatic Artery Embolization

Pre-embolization

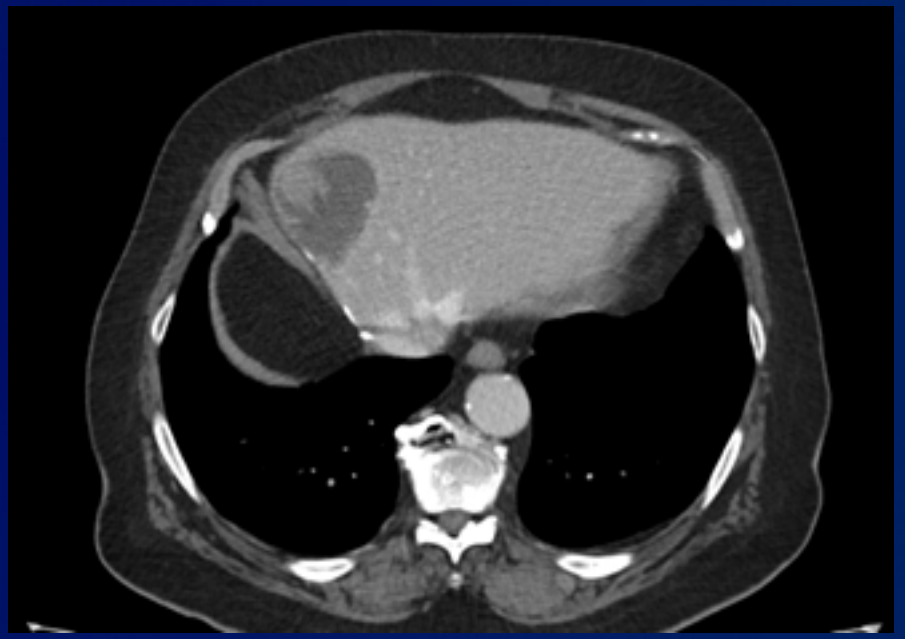


Post-embolization

Pre-embolization



Post-embolization



Hepatic Arterial Embolization

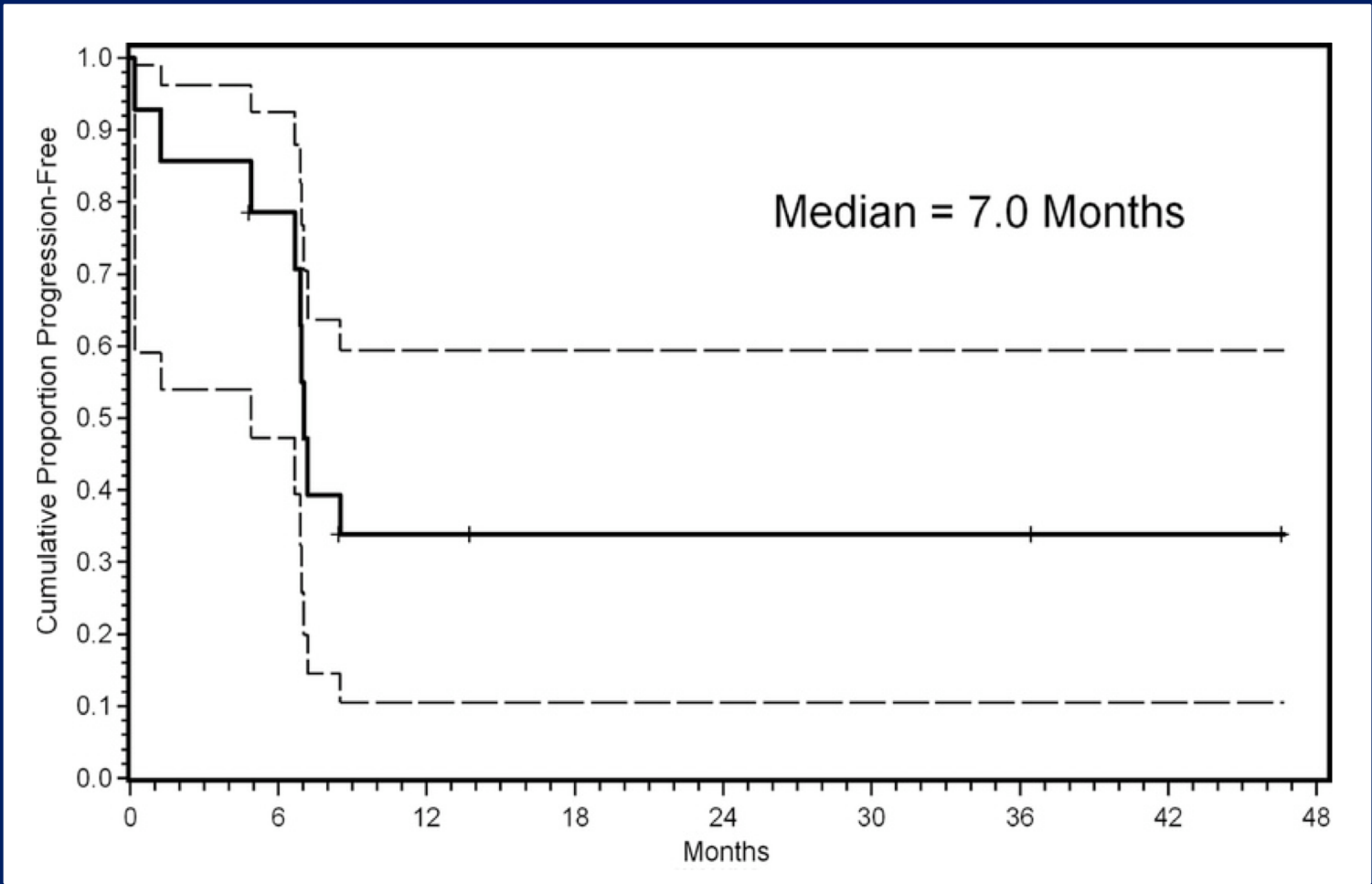
Radiographic Response Rates

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

RESPONSE	BEST RESPONSE (Choi Criteria)	BEST RESPONSE (RECIST)
Overall	54%	8%
Complete	0%	0%
Partial	54%	8%
Stable	46%	92%
Progression	0%	0%

Kobayashi, K, et al. *Am J Clin Oncol.* 2009;32:574-581.

Hepatic Arterial Embolization
Progression-Free Survival



Kobayashi, K, et al. *Am J Clin Oncol.* 2009;32:574-581.

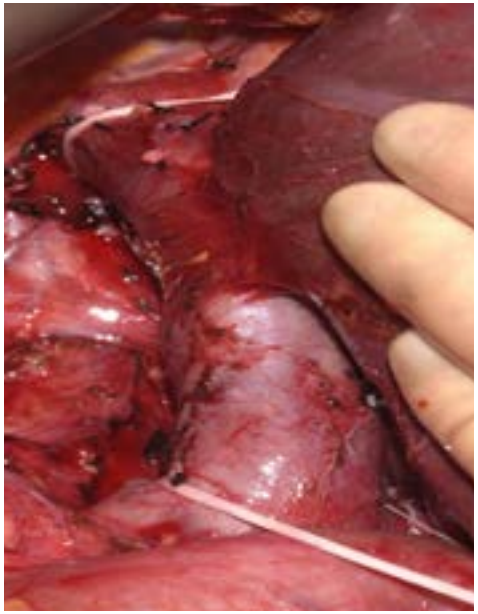
Regional Therapies for Sarcoma

Jonathan Zager, MD

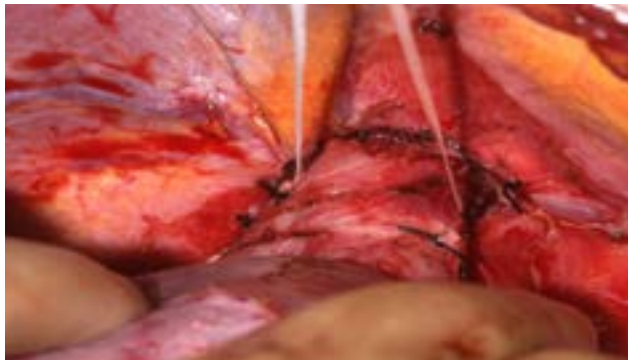
Director of Regional Therapy

Hepatic Perfusion

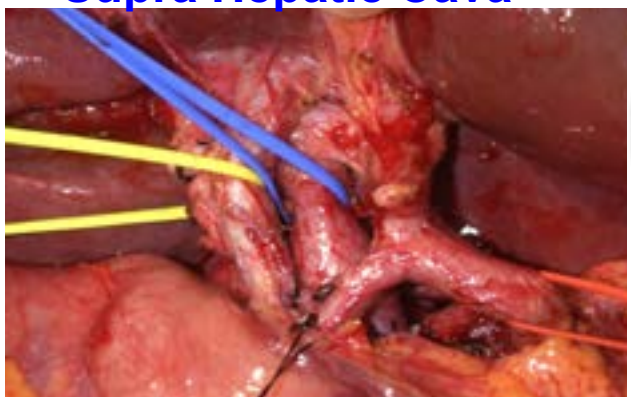
- Started out as Isolated hepatic perfusion (IHP) in 1980's and 1990's at NCI
- Alexander, Bartlett and colleagues



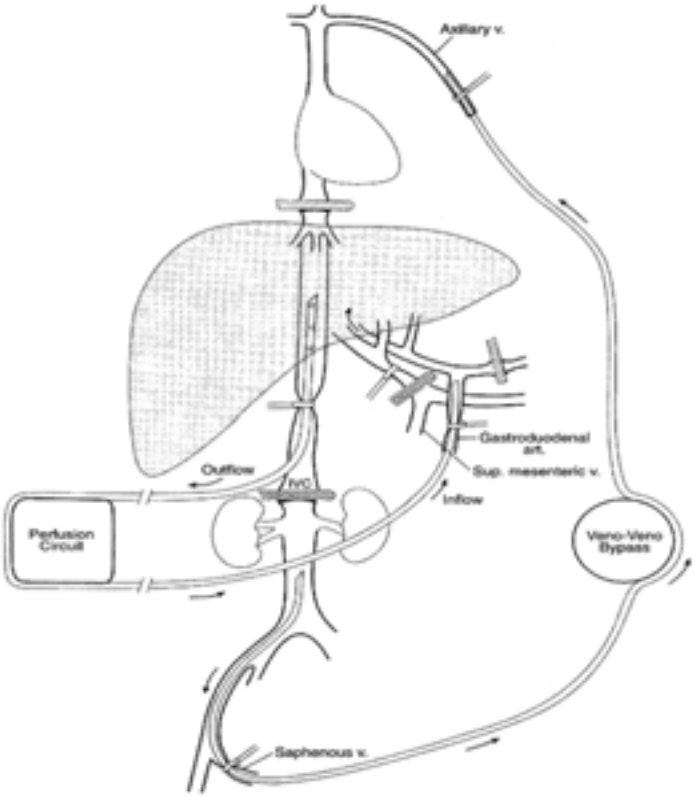
Retro Hepatic Cava



Supra Hepatic Cava

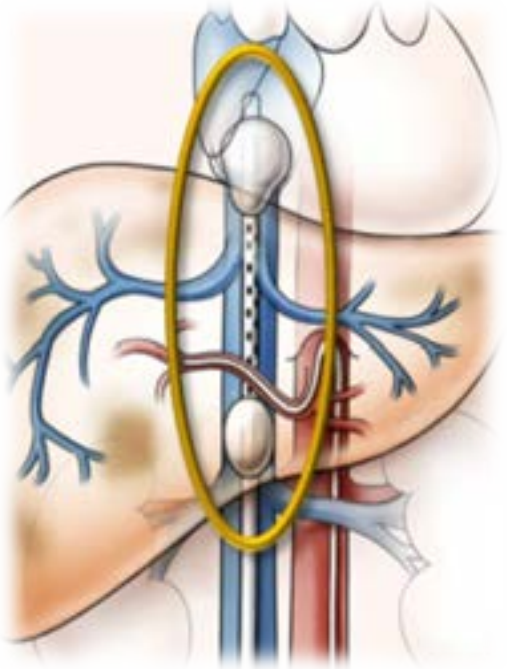


Portal Dissection/ Isolation

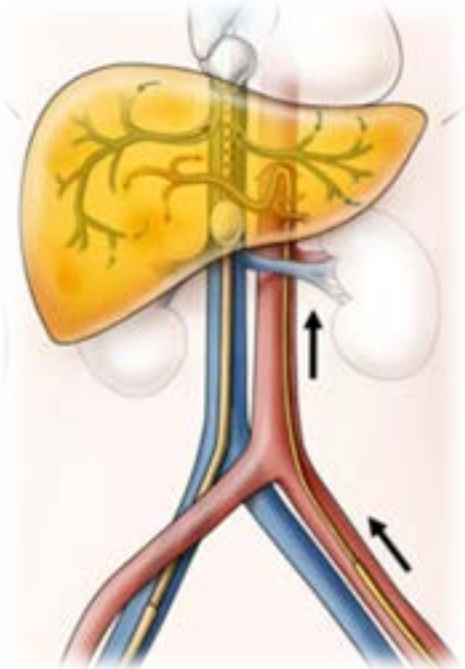


Chemosaturation/PHP

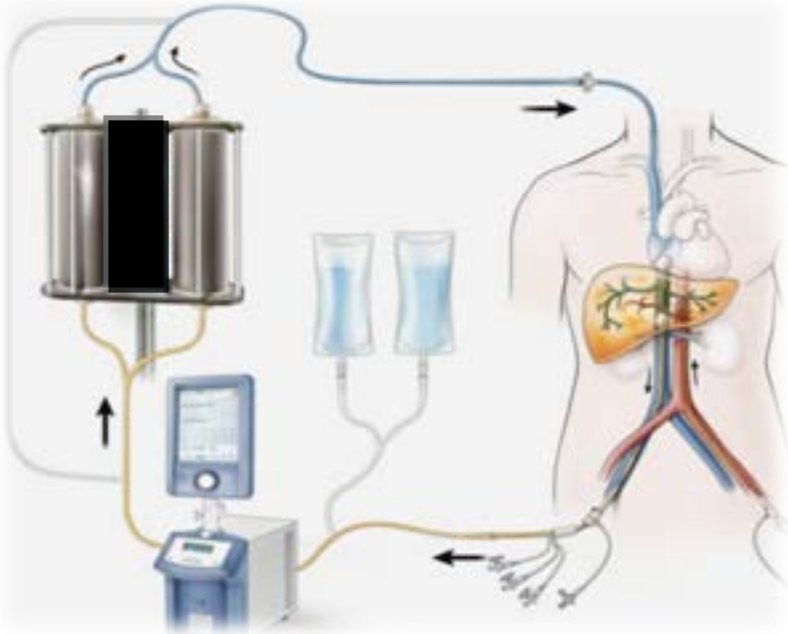
Isolation of Liver for Regional Tx



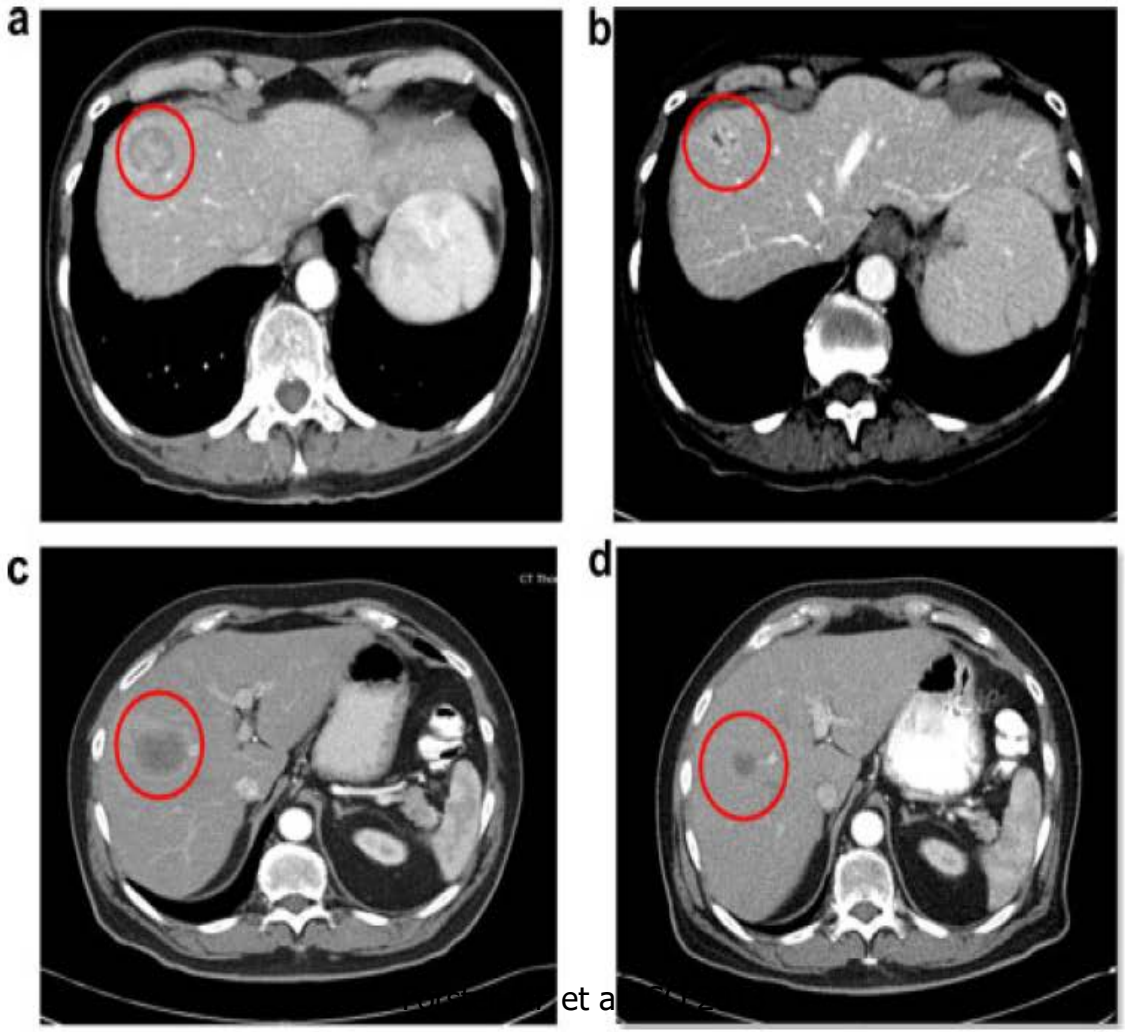
Saturation of Liver with Melphalan



Extracorporeal Filtration and Veno-Veno Bypass



Leiomyosarcoma



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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

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Thank you!!