



GIST and Imatinib in 2015: Who Should Be Treated and How Long?

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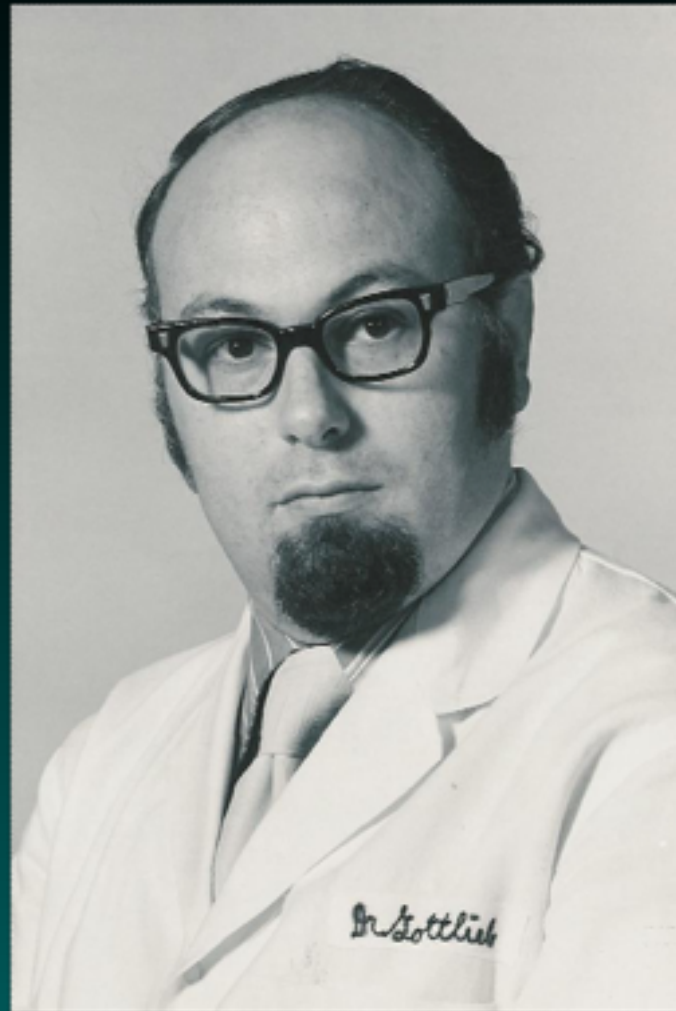


Outline

- GIST
- Treatment before Imatinib
- Imatinib
- Imaging
- Therapy Duration
- Adjuvant Therapy
- Adjuvant Therapy Duration

Jeffrey A. Gottlieb, M.D.

1940-1975



Chief of Chemotherapy, Developmental Therapeutics, MD Anderson
SWOG General Secretary
Chairman, Sarcoma Committee



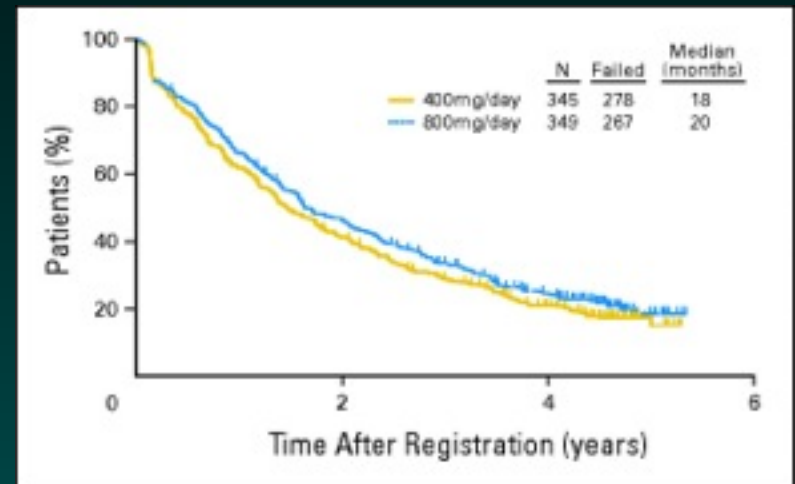
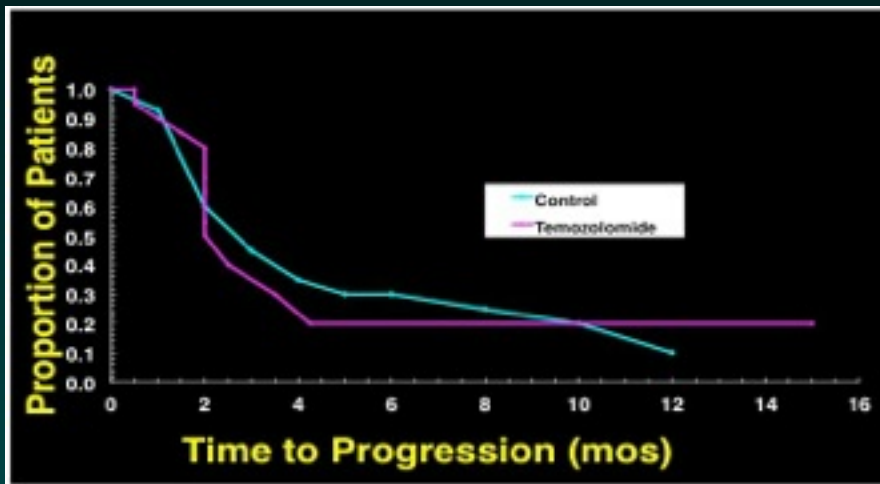
ADRIAMYCIN-DTIC IN SARCOMAS

RESPONSE BY SITE OF PRIMARY

LOCATION	# PTS.	% RESPONSE
Head & Neck	19	58
GU & Uterus	17	53
Retroperitoneum	26	50
Unk. Prim. & Misc.	35	49
Limb	40	39
Pelvis + Trunk	19	26
GI Tract	14	21
All	200	42.5

GIST

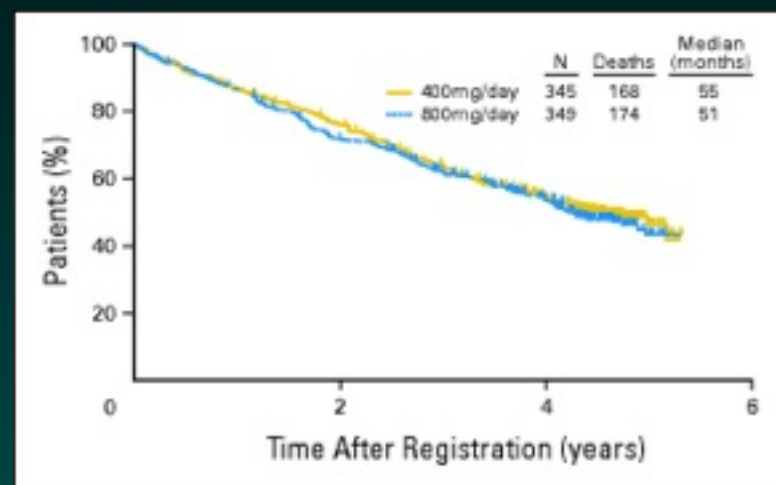
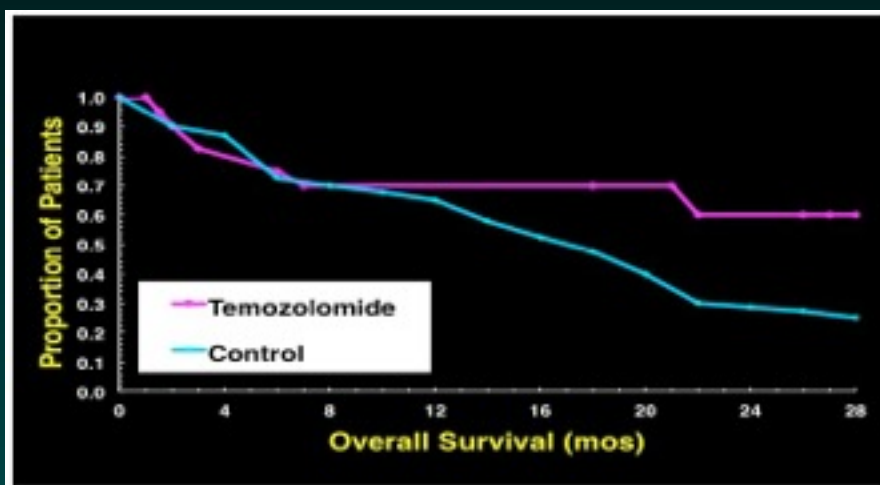
Time to Progression



Charles D. Blanke et al. JCO 2008;26:626-632

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GIST Survival

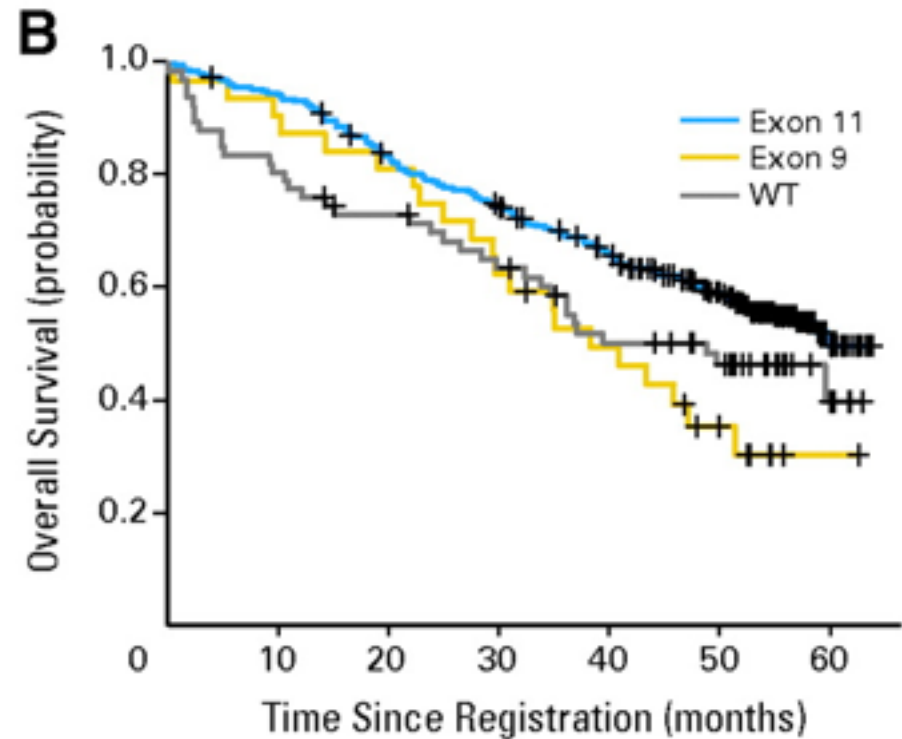
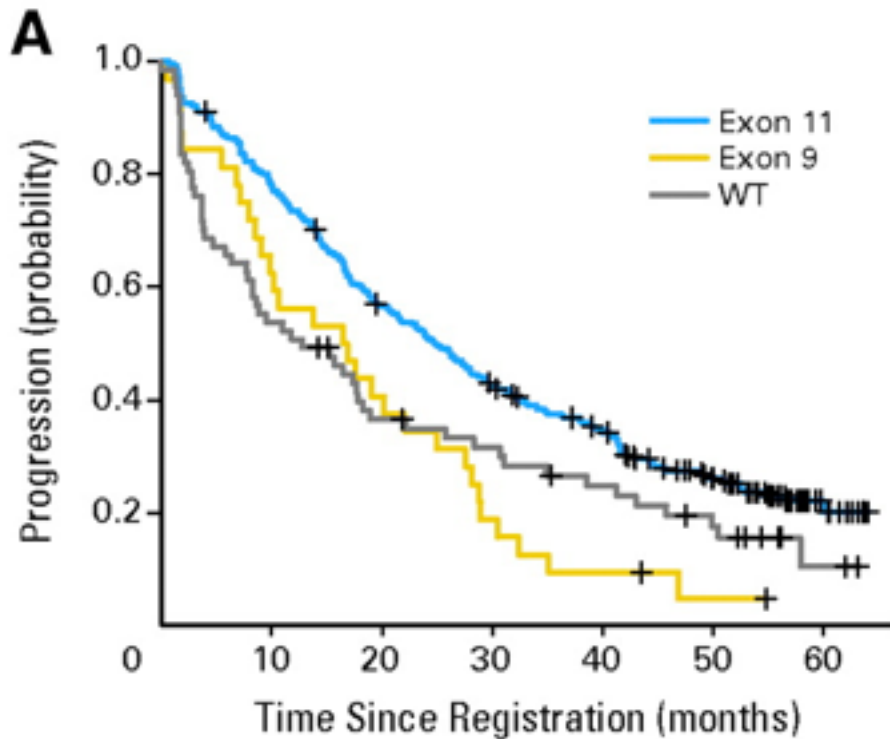


Charles D. Blanke et al. JCO 2008;26:626-632

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Time to Progression and Survival by Genotype

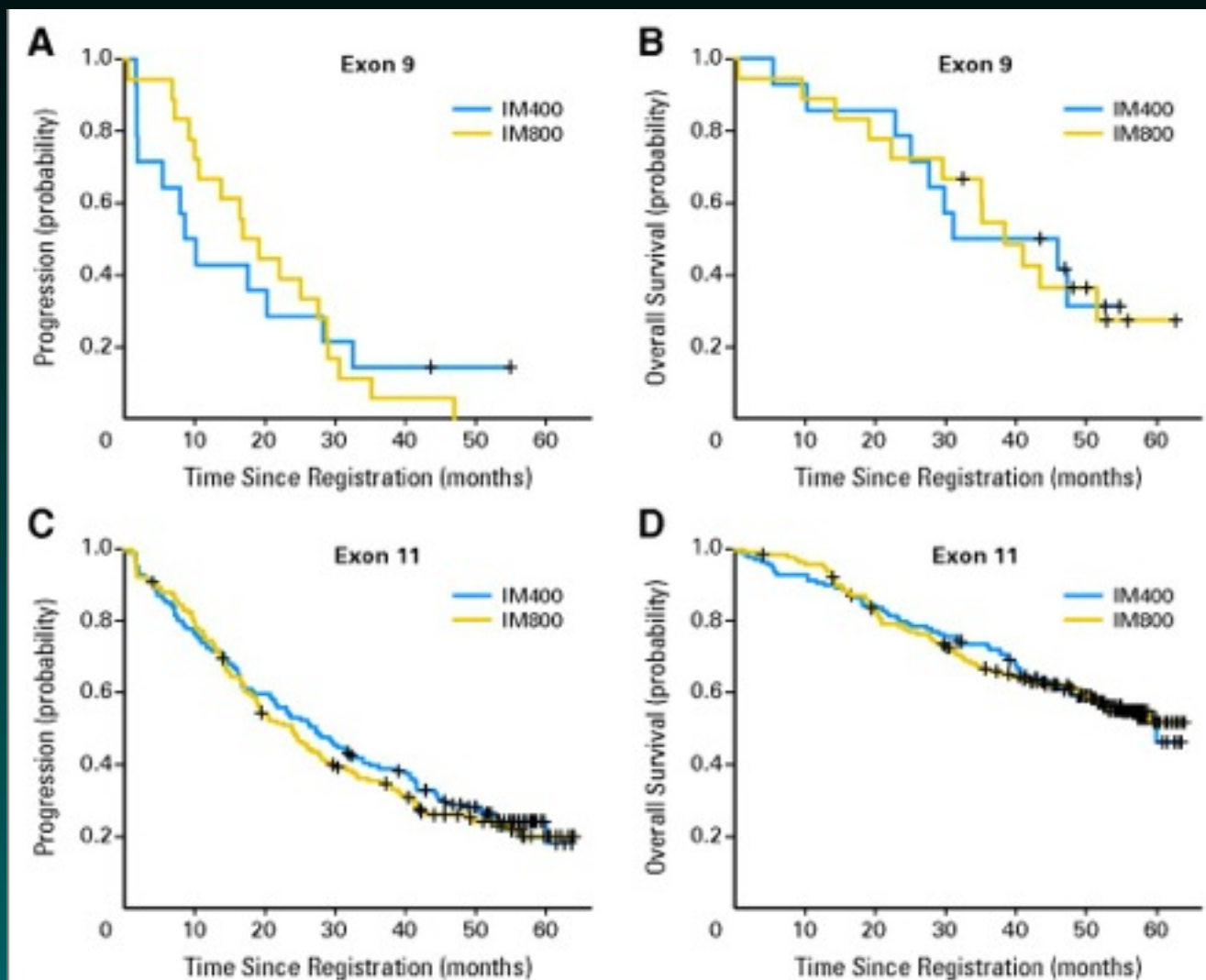


Michael C. Heinrich et al. JCO 2008;26:5360-5367

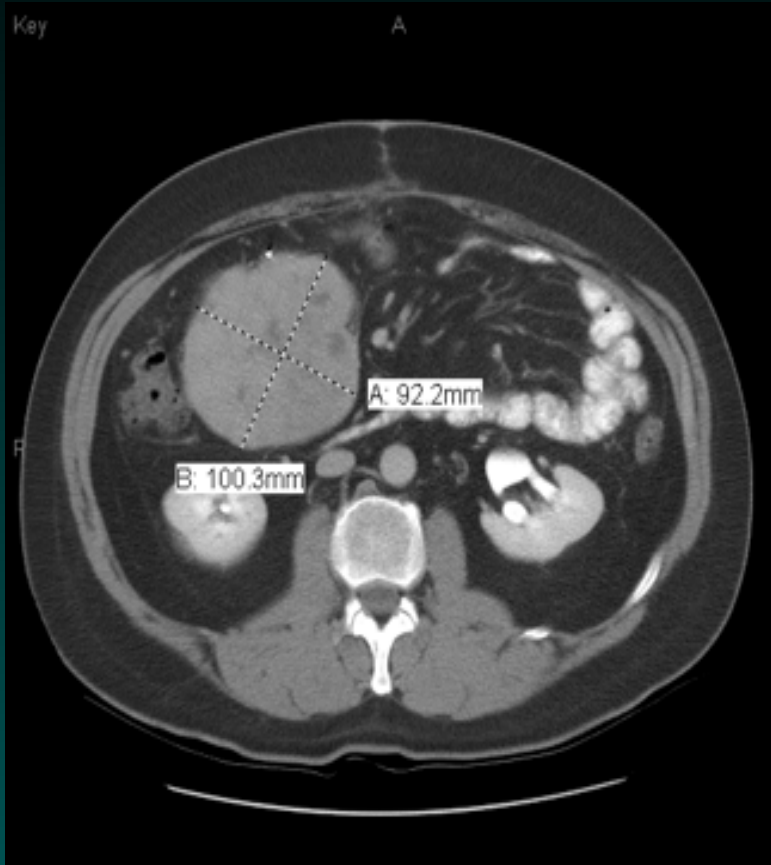


GIST

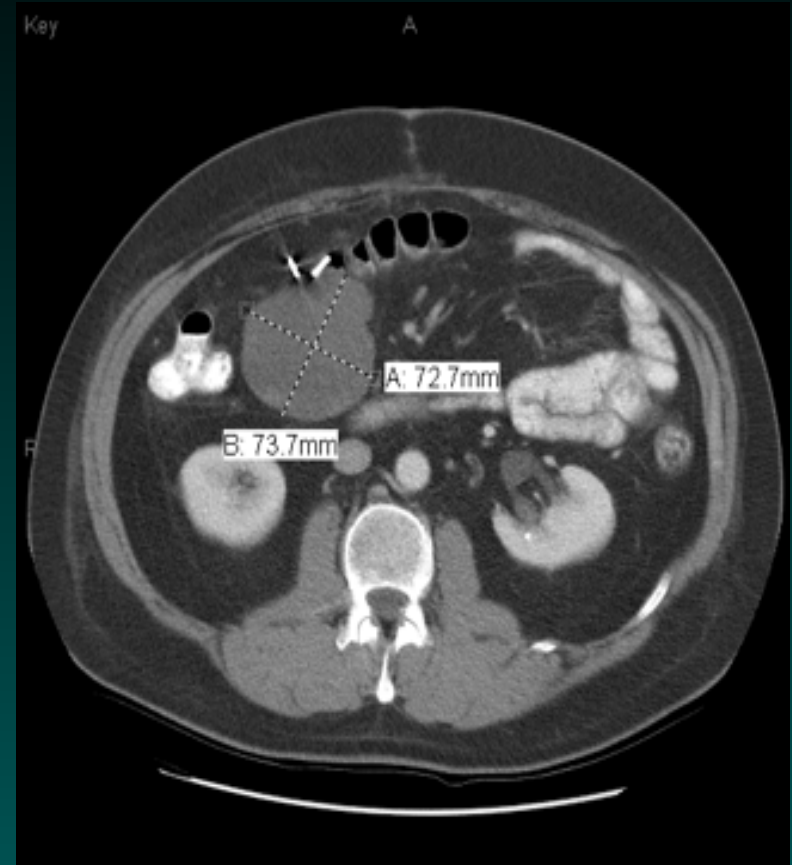
Time to Progression and Survival by Genotype and Dose



Effects of Imatinib on GIST: CT findings - Size



Baseline

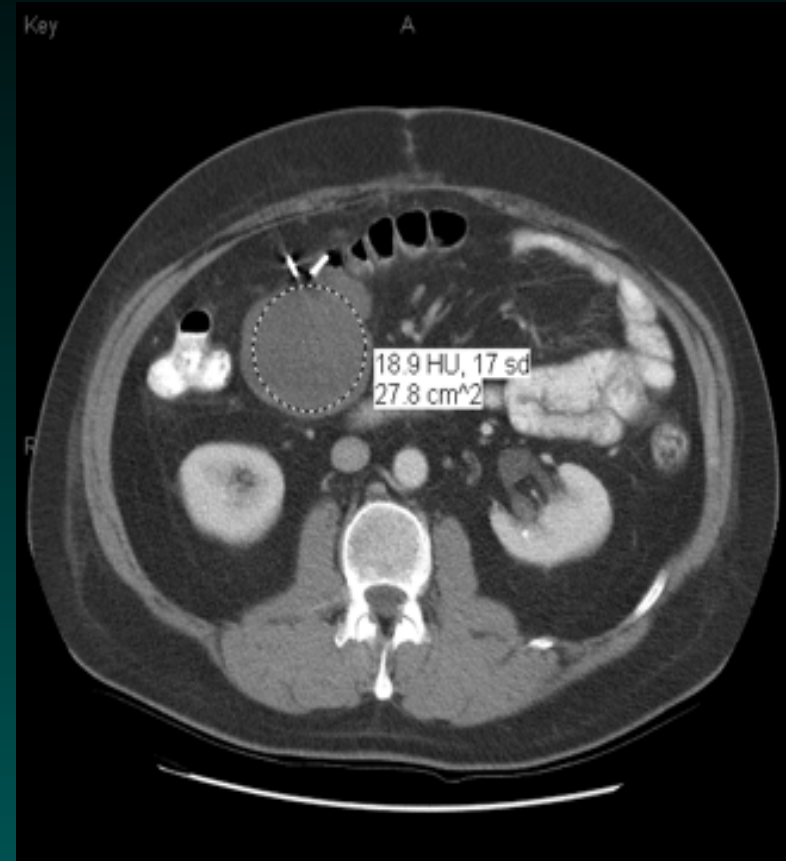


8 Weeks

Effects of Imatinib on GIST: CT findings - Density

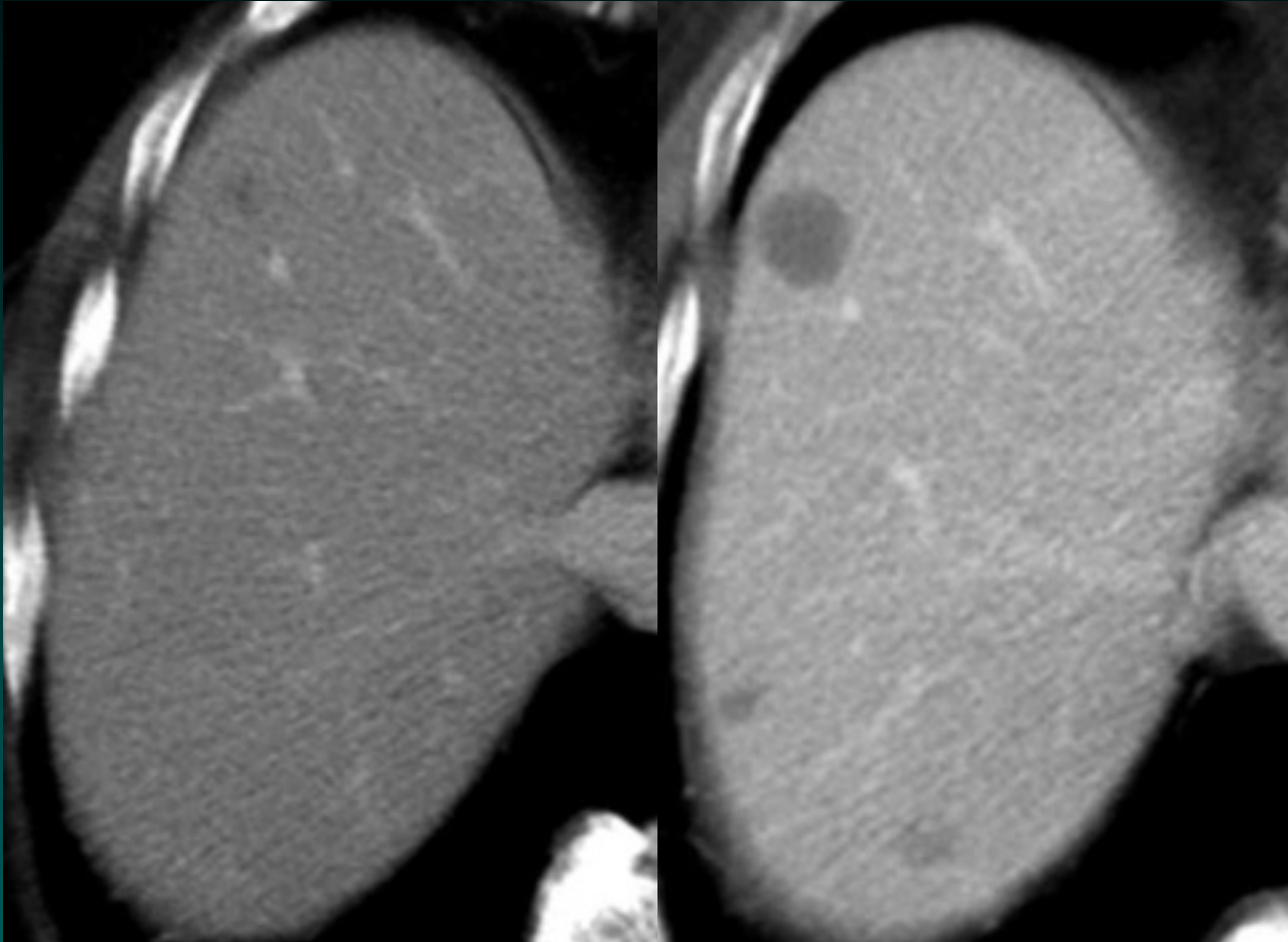


**Baseline with
Density Measurement**



**8 weeks with
Density Measurement**

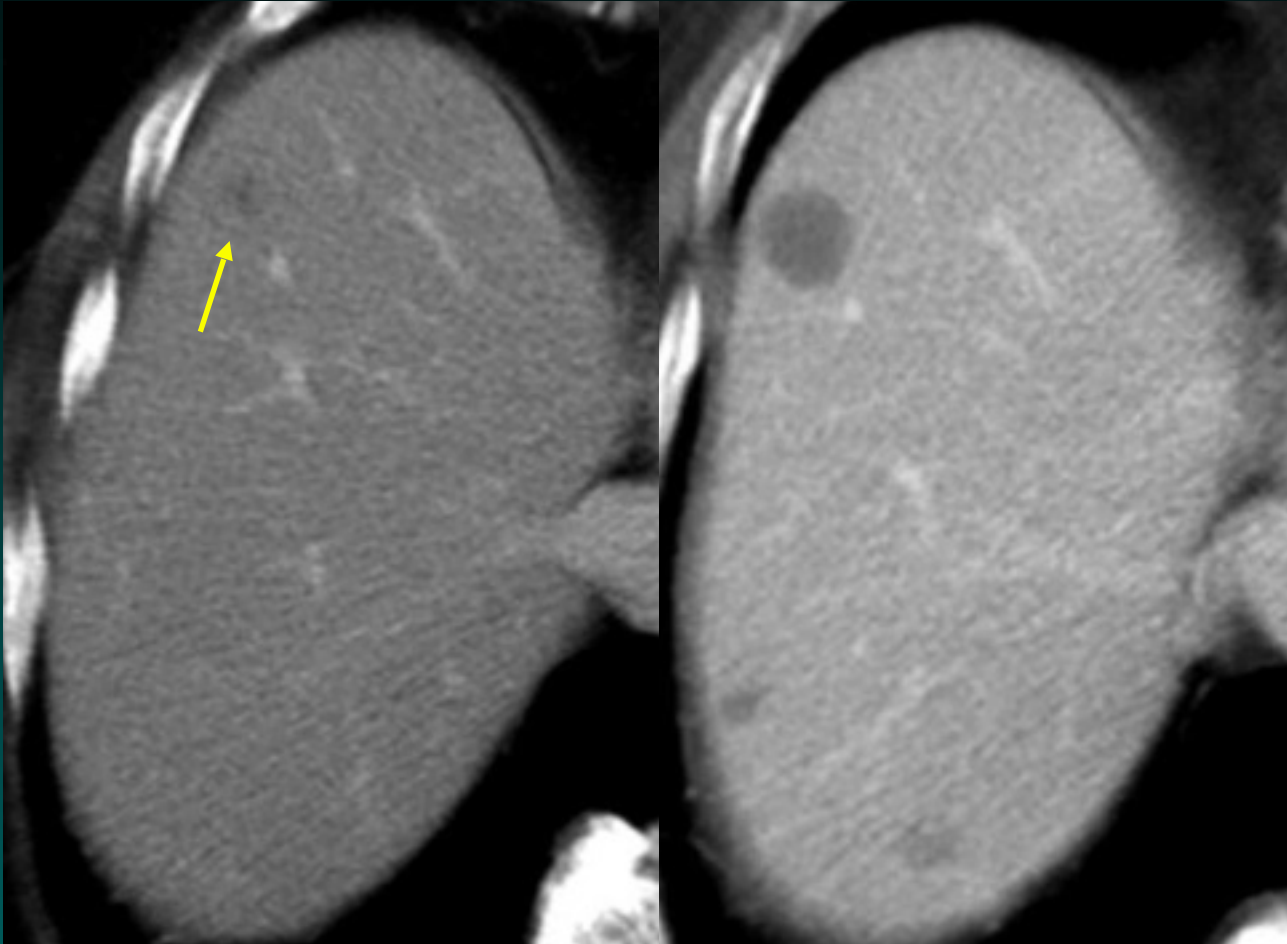
Effects of Imatinib on GIST: CT findings



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3/30

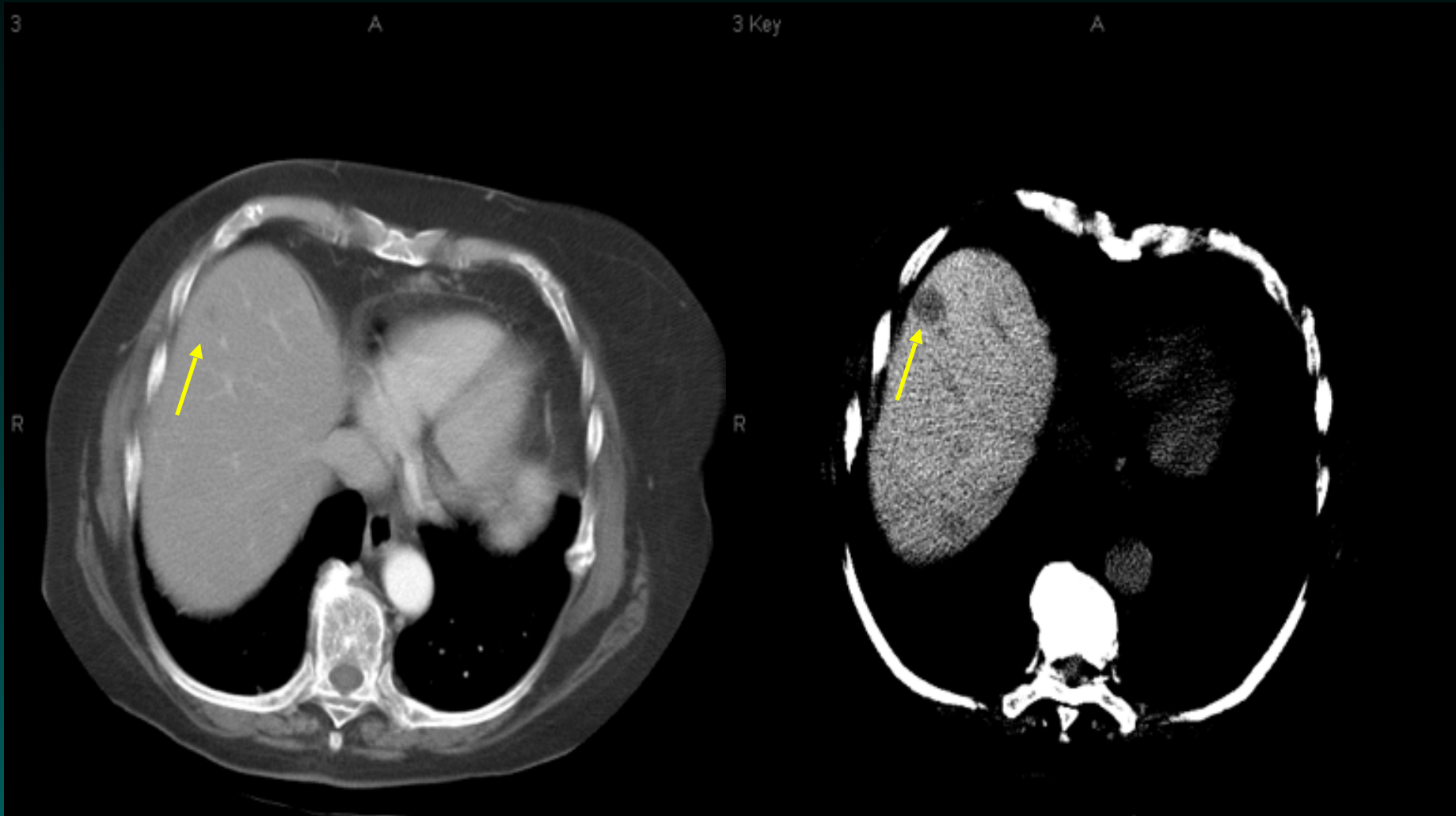
Effects of Imatinib on GIST: CT findings



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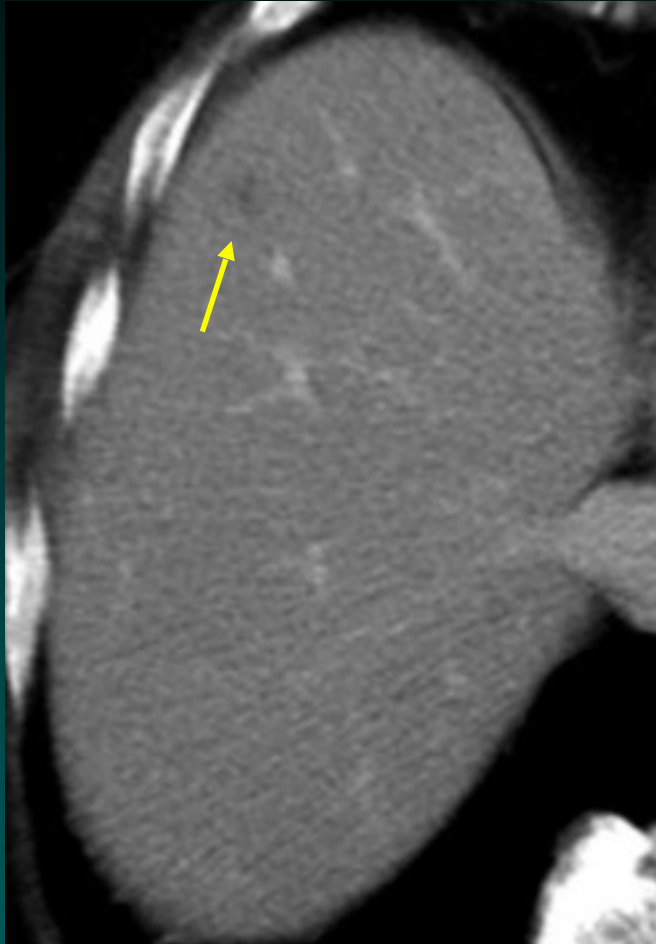
Effects of Imatinib on GIST: CT findings



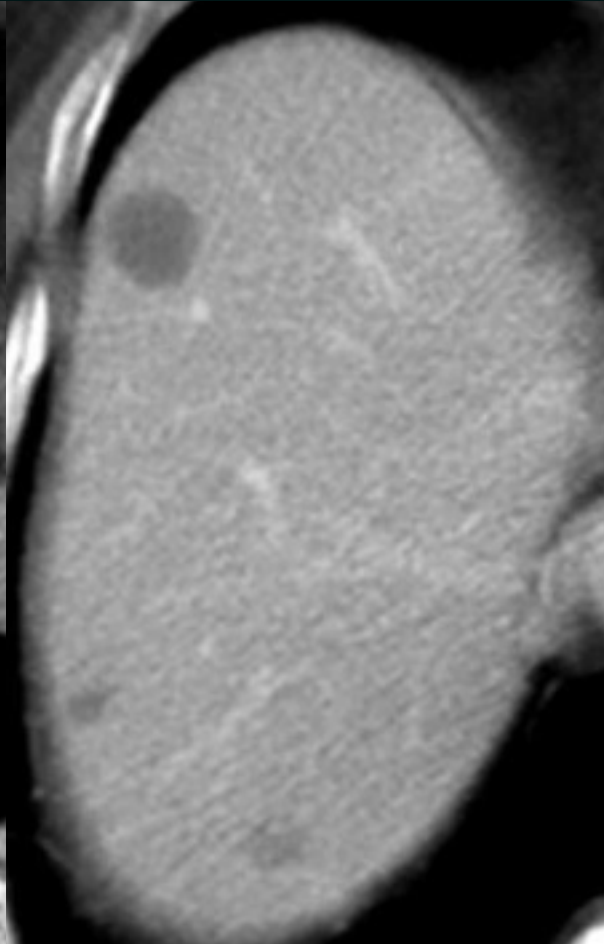
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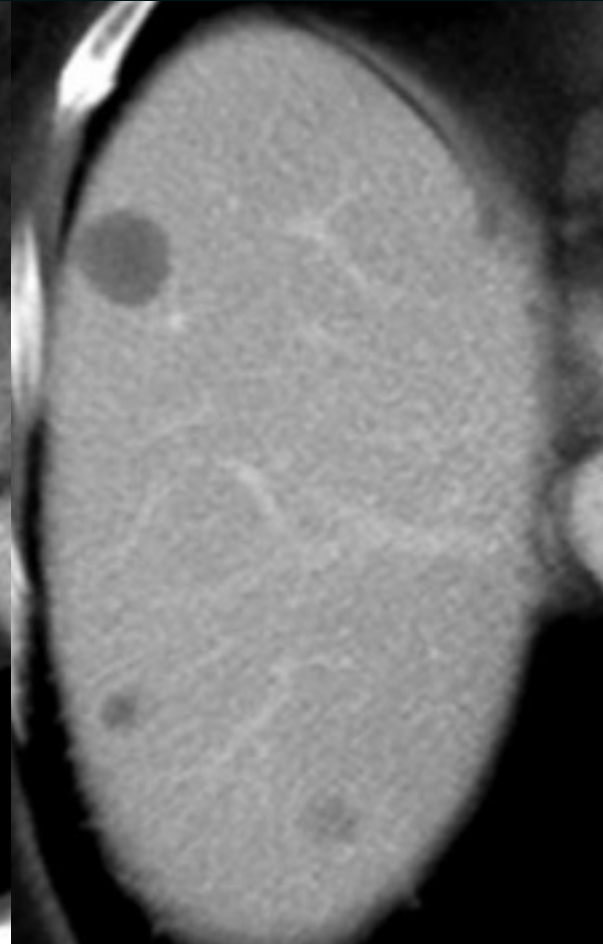
Effects of Imatinib on GIST: CT findings



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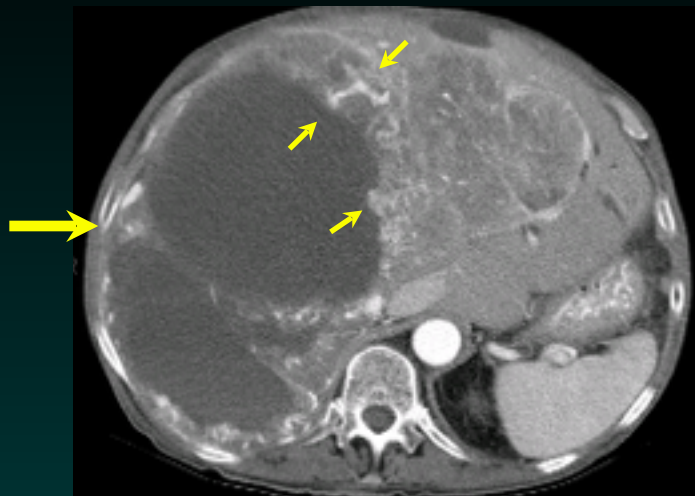


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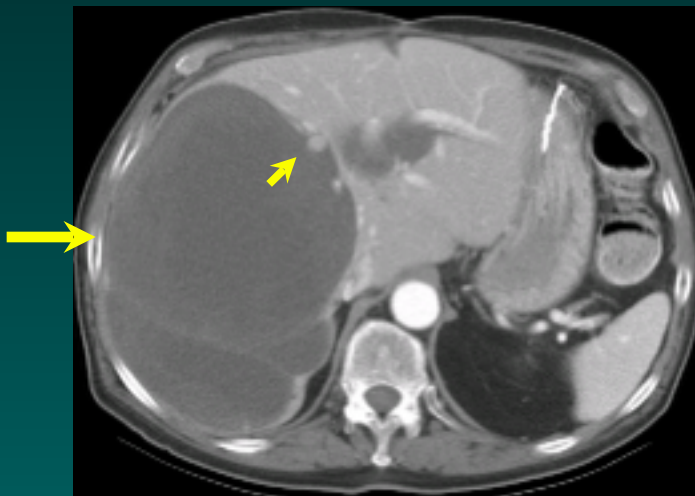
Embolization, Response, Progression



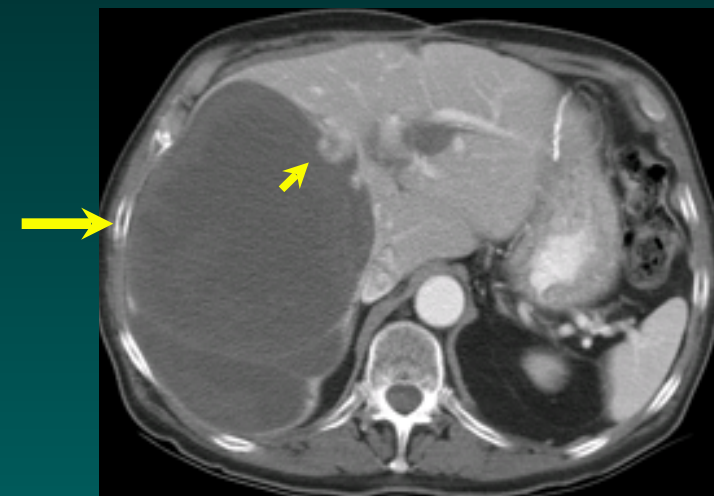
Pre-Treatment



2 Months Post-Treatment



24 Months Post-Treatment



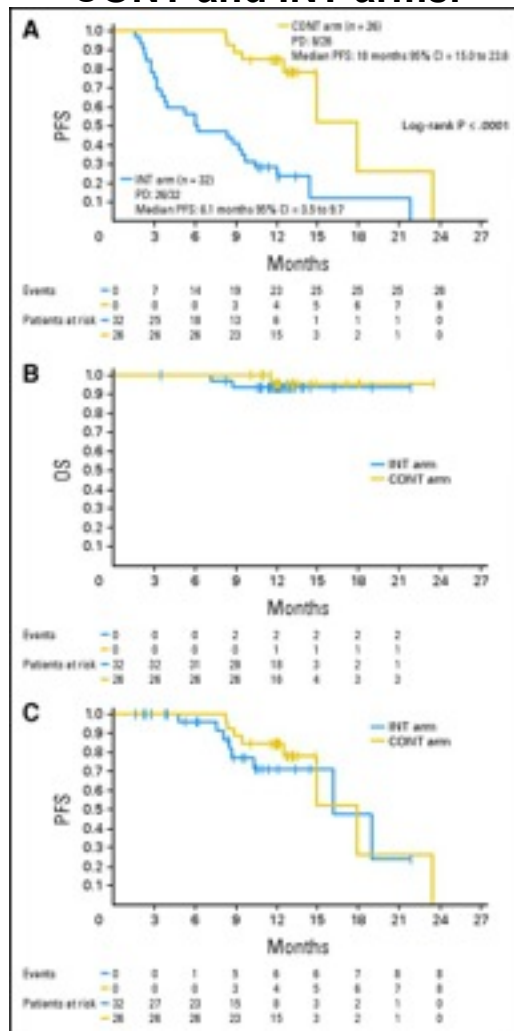
27 Months Post-Treatment



We Should Desist Using RECIST **at Least** in GIST

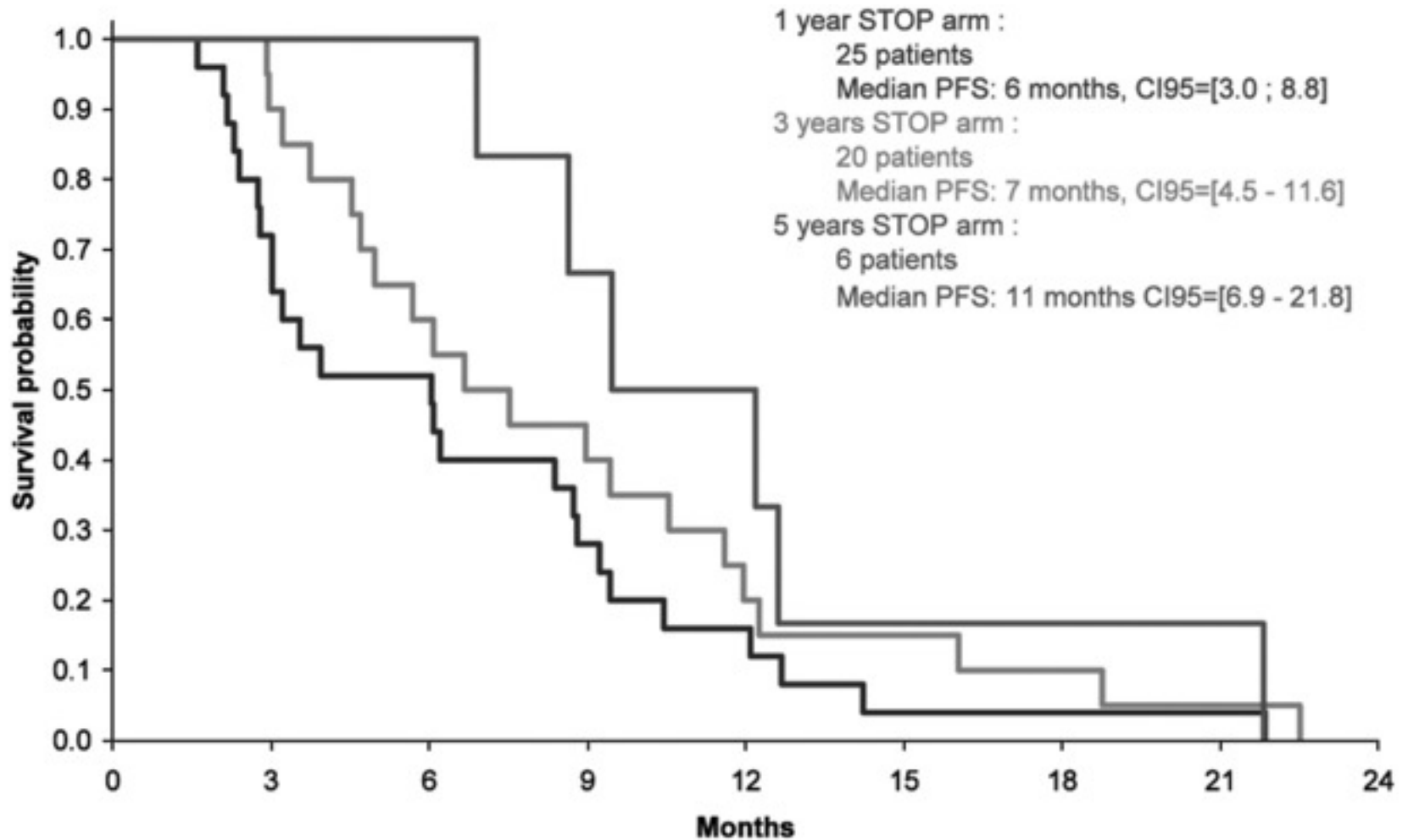


(A) Progression-free survival (PFS) in randomly assigned patients, (B) overall survival (OS) in the continuous (CONT) and interrupted (INT) arms, and (C) imatinib-resistant PFS in the CONT and INT arms.



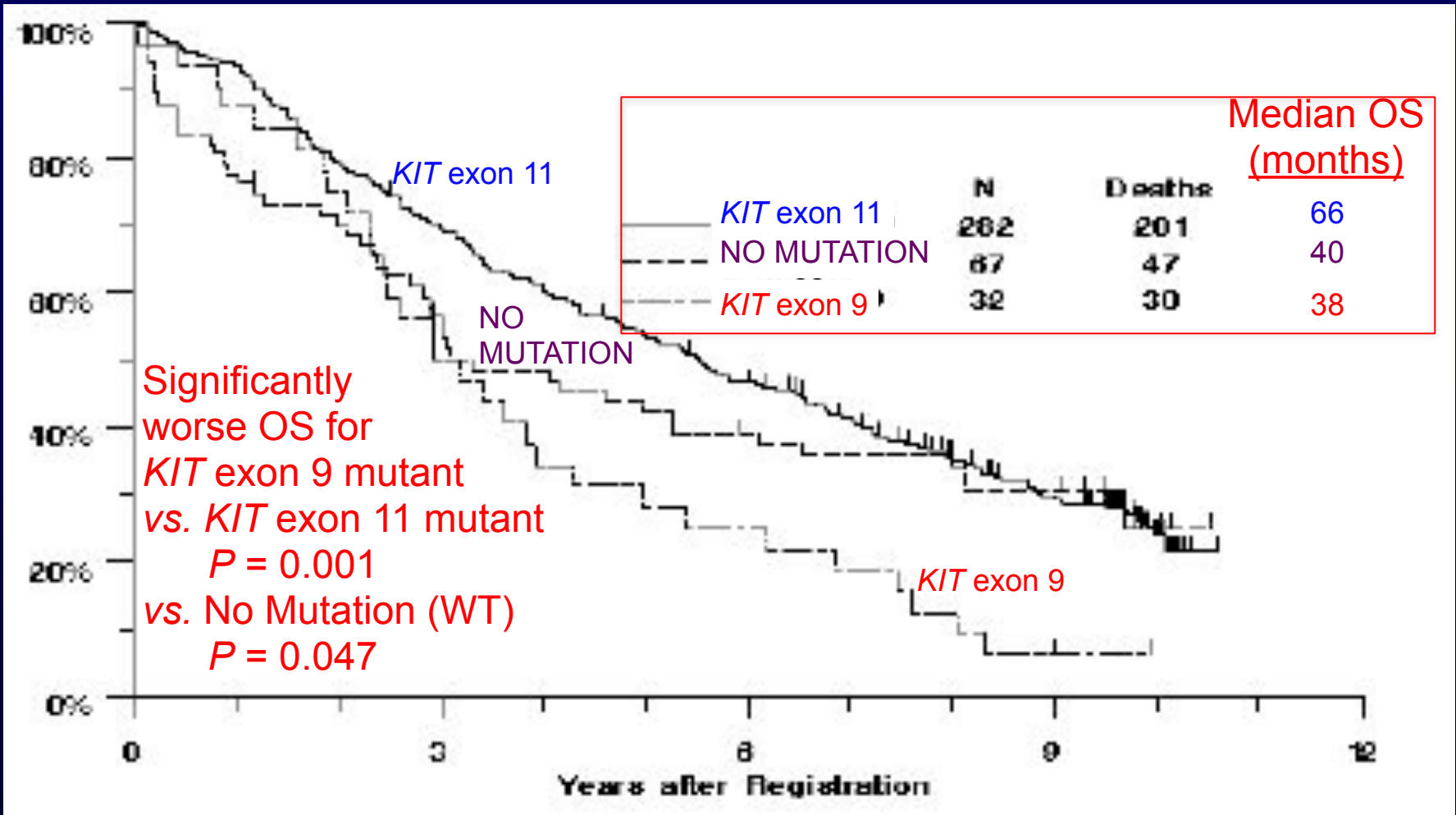
Jean-Yves Blay et al. JCO 2007;25:1107-1113

PFS among patients randomised in the interruption arms after 1, 3 and 5 years of treatment with imatinib.



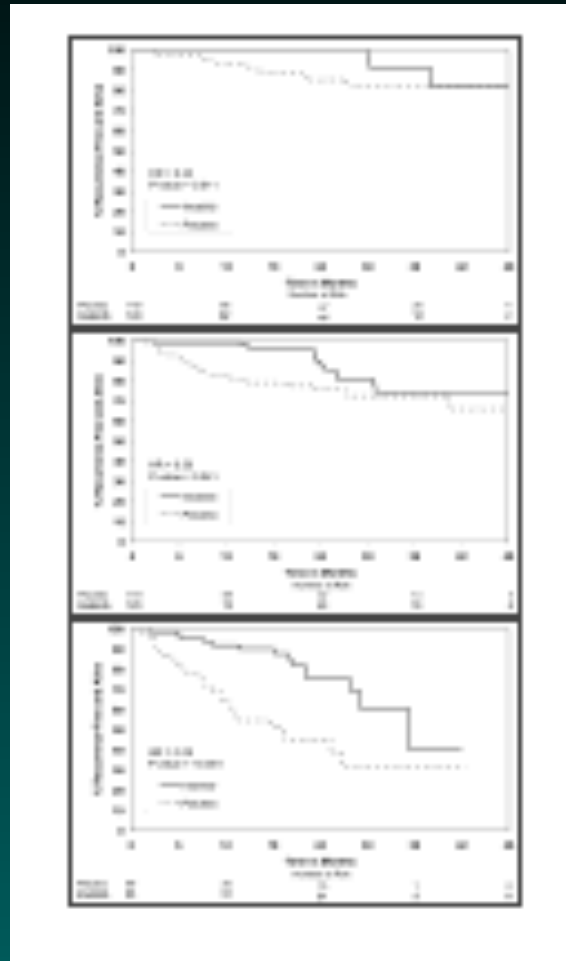
A. Patrikidou et al. Ann Oncol 2013;24:1087-1093

S0033 Overall Survival by GIST Genotype – 2014 data





De Matteo Adjuvant GIST





GIST Risk of Recurrence Modified Consensus Criteria

Table 1.

Risk of Relapse after Resection of GIST (from Joensuu et al.⁵)

Risk category	Tumor size (cm)	Mitotic index (per 50 HPFs)	Primary tumor site
Very low risk	<2.0	≤5	Any
Low risk	2.1-5.0	≤5	Any
Intermediate risk	2.1-5.0	>5	Gastric
	5.1-10.0	≤5	Gastric
High risk	Any	Any	Tumor rupture
	>10 cm	Any	Any
	Any	>10	Any
	>5.0	>5	Any
	2.1-5.0	>5	Nongastric
	5.1-10.0	≤5	Nongastric

From: One vs Three Years of Adjuvant Imatinib for Operable Gastrointestinal Stromal Tumor: A Randomized Trial

JAMA. 2012;307(12):1265-1272. doi:10.1001/jama.2012.347

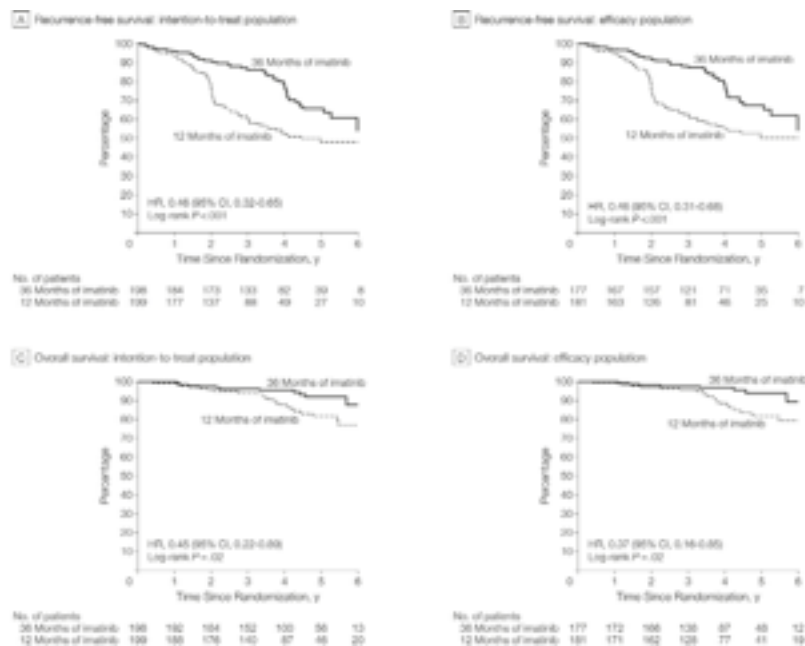


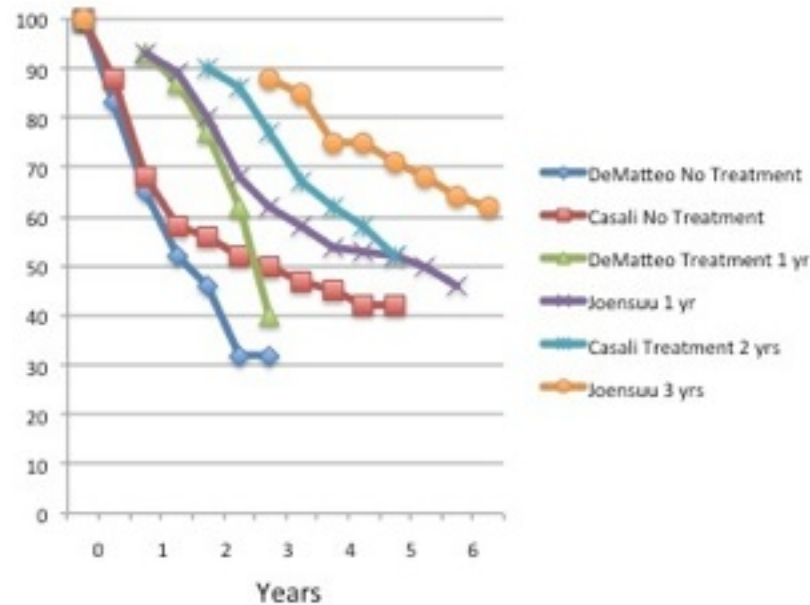
Figure Legend:

Comparison of recurrence-free survival in the modified intention-to-treat population (A) and the efficacy population (B). Comparison of overall survival in the modified intention-to-treat population (C) and the efficacy population (D). The 3-year survival rates of patients assigned to 36 months of imatinib and those assigned to 12 months of imatinib are 86.6% vs 60.1% (A), 88.1% vs 62.1% (B), 96.3% vs 94.0% (C), and 97.6% vs 95.8% (D), respectively, and the 5-year survival rates, 65.6% vs 47.9% (A), 67.4% vs 50.3% (B), 92.0% vs 81.7% (C), and 93.9% vs 81.7% (D).



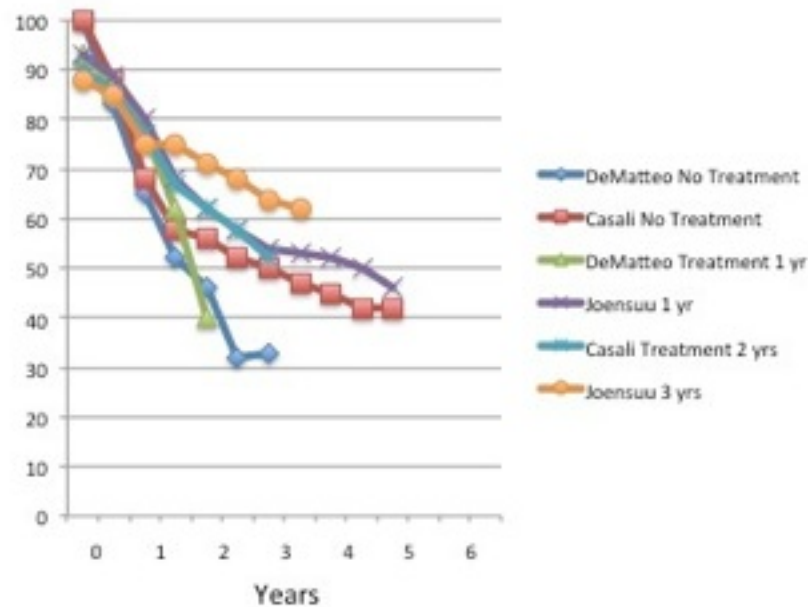
High-Risk GIST Progression-Free Survival

From Start of Therapy





High-Risk GIST Progression-Free Survival From End of Therapy





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