



Reflections on GIST 15 Years after Imatinib

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The Connective Tissue Oncology Society



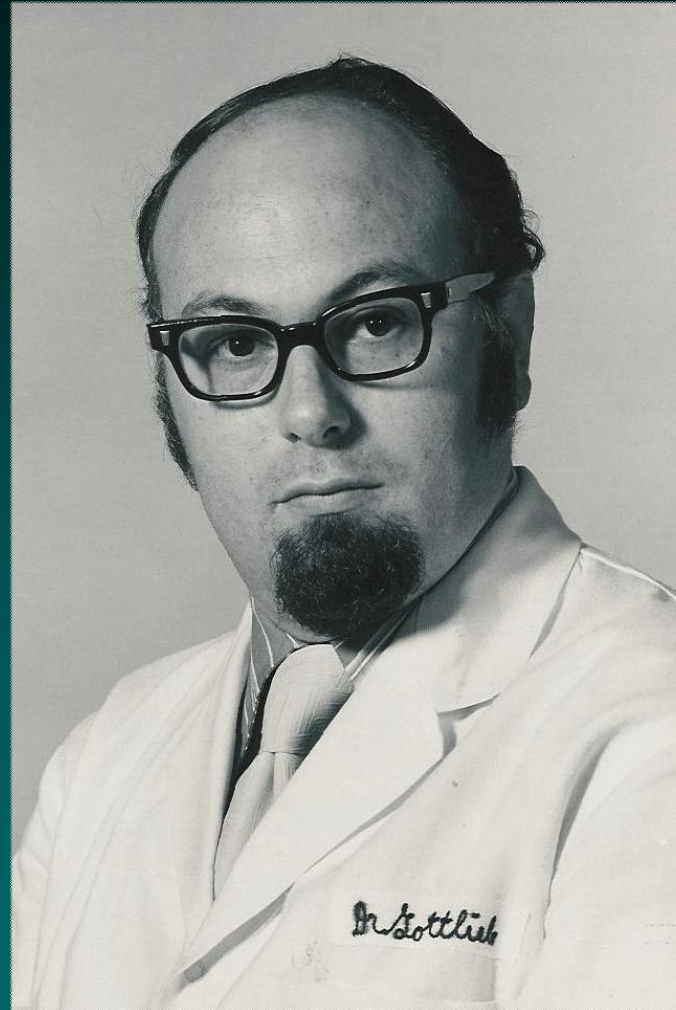


Outline

- GIST
- Treatment before Imatinib
- Imatinib
- Imaging
- Other TKIs
- Adjuvant Therapy

Jeffrey A. Gottlieb, M.D.

1940-1975



SWOG General Secretary
Chairman, Sarcoma Committee



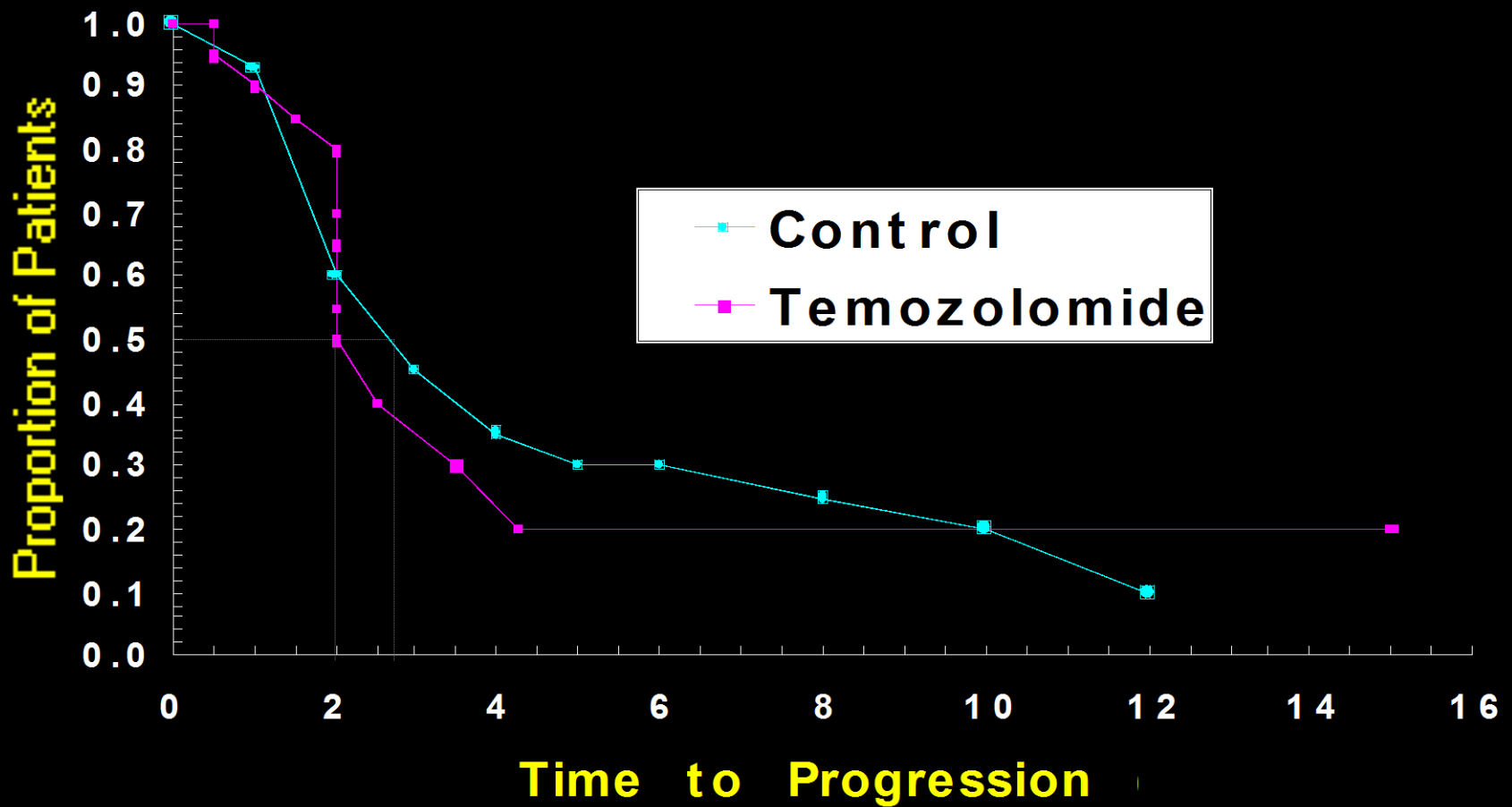
ADRIAMYCIN-DTIC IN SARCOMAS

RESPONSE BY SITE OF PRIMARY

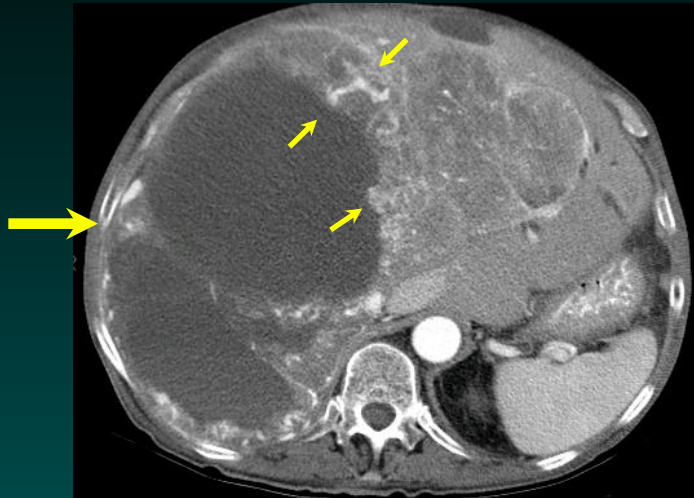
| LOCATION | # PTS. | % RESPONSE |
|--------------------|--------|------------|
| Head & Neck | 19 | 58 |
| GU & Uterus | 17 | 53 |
| Retroperitoneum | 26 | 50 |
| Unk. Prim. & Misc. | 35 | 49 |
| Limb | 40 | 39 |
| Pelvis + Trunk | 19 | 26 |
| GI Tract | 14 | 21 |
| All | 200 | 42.5 |

GIST

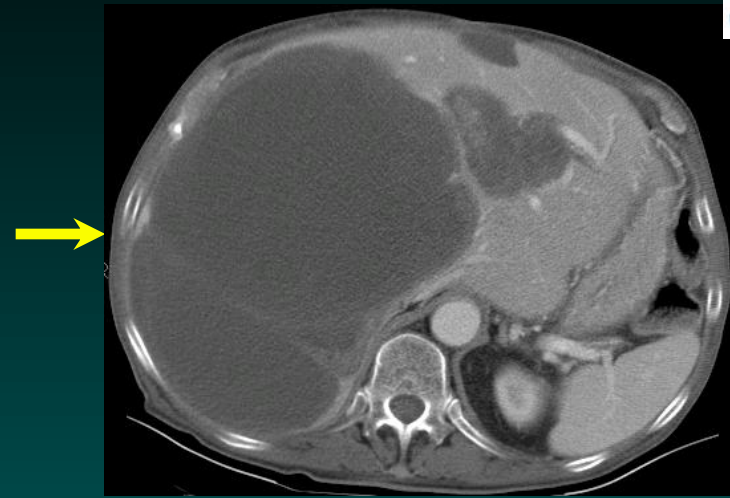
Time to Progression



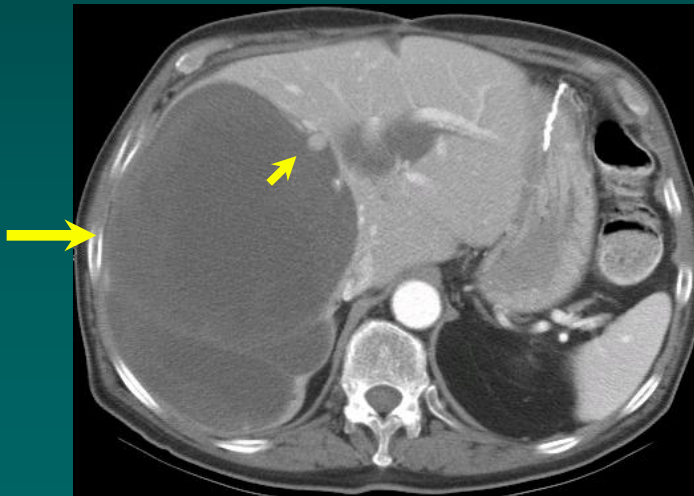
Embolization, Response, Progression



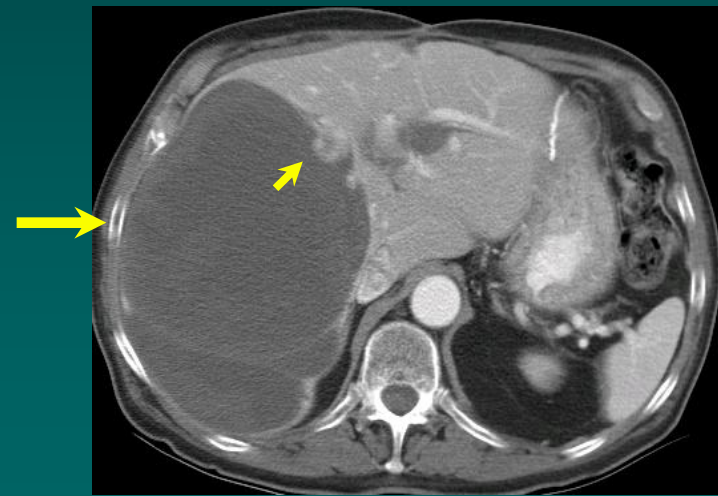
Pre-Treatment



2 Months Post-Treatment

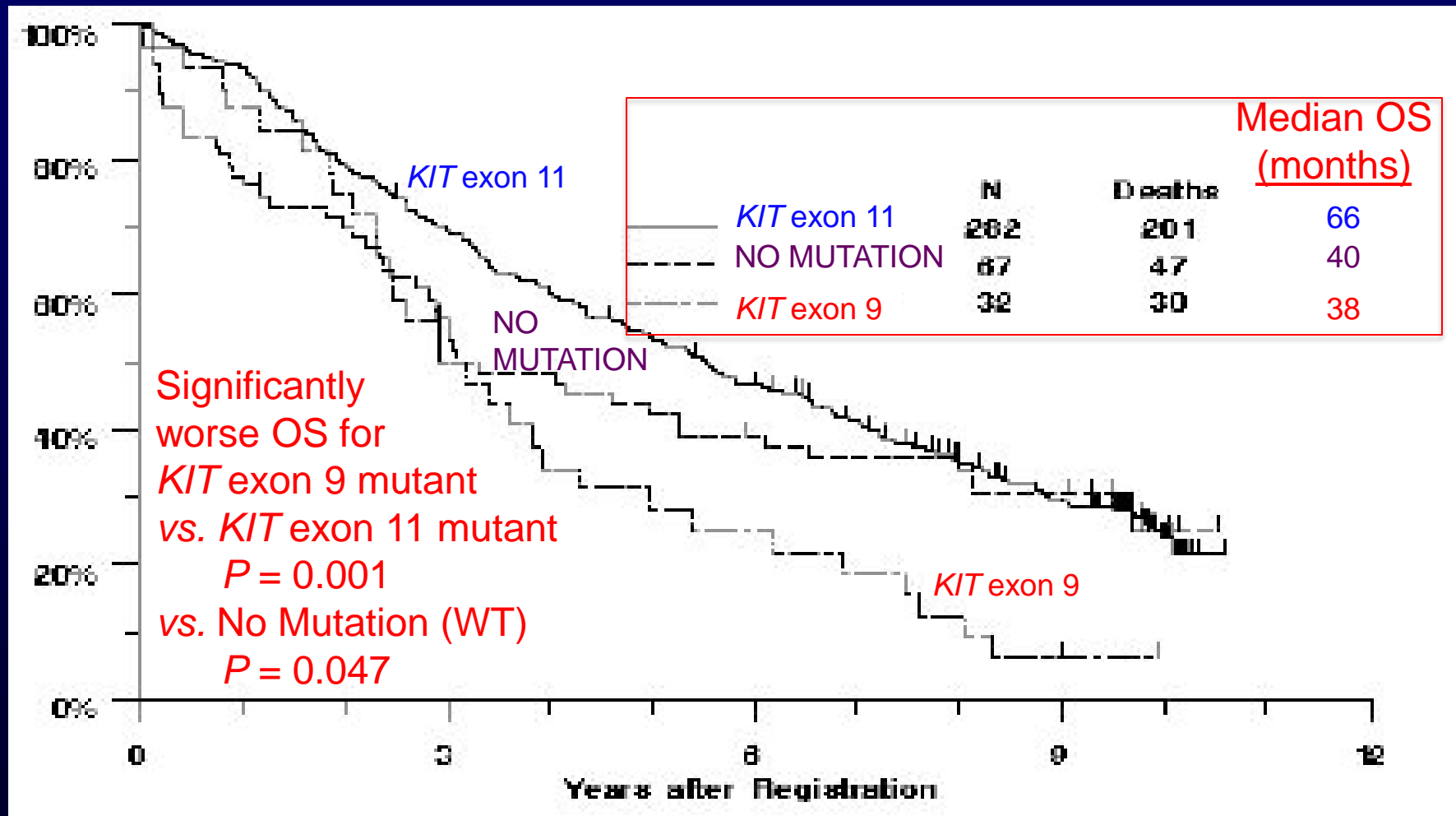


24 Months Post-Treatment

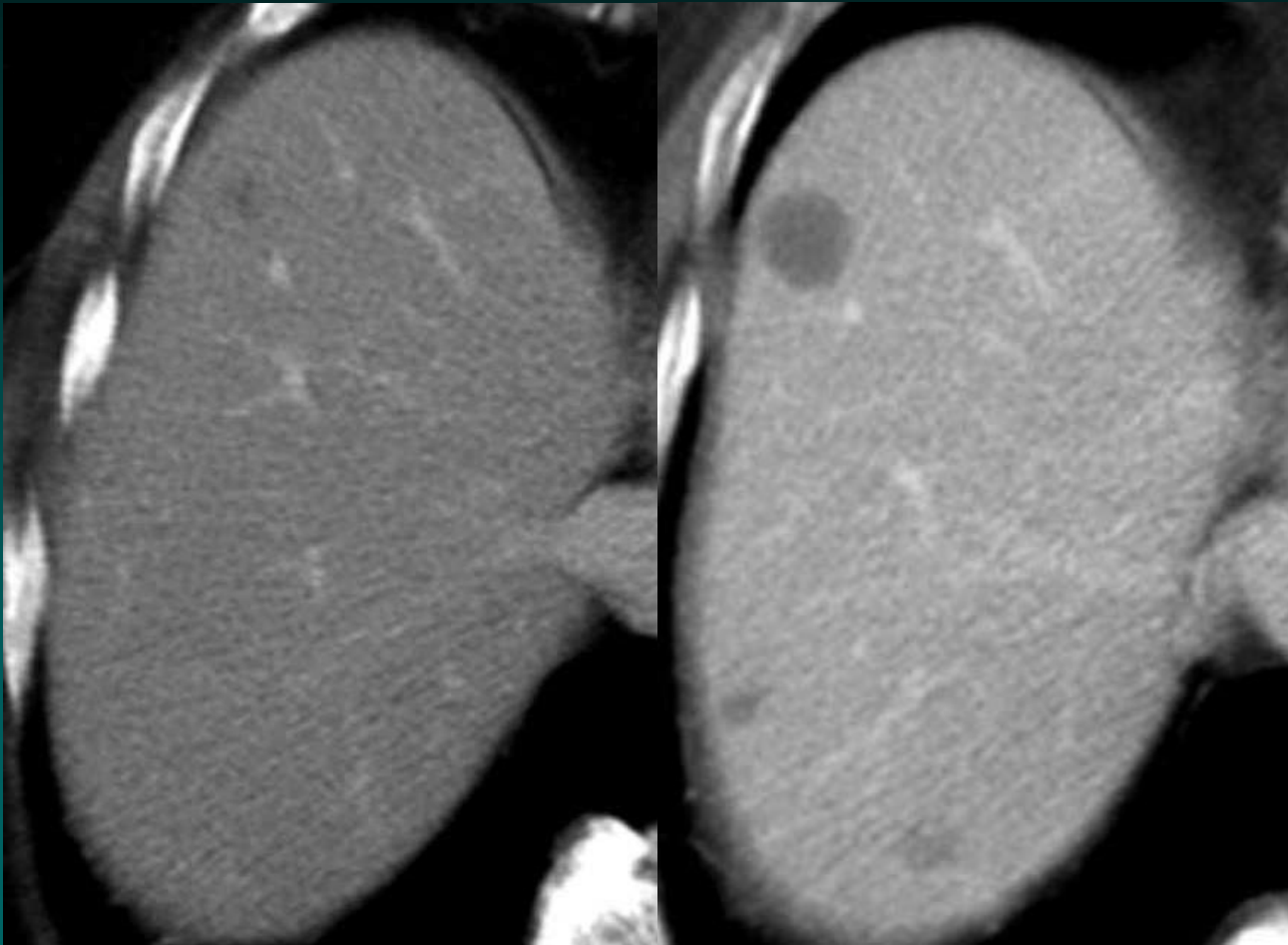


27 Months Post-Treatment

S0033 Overall Survival by GIST Genotype – 2014 data



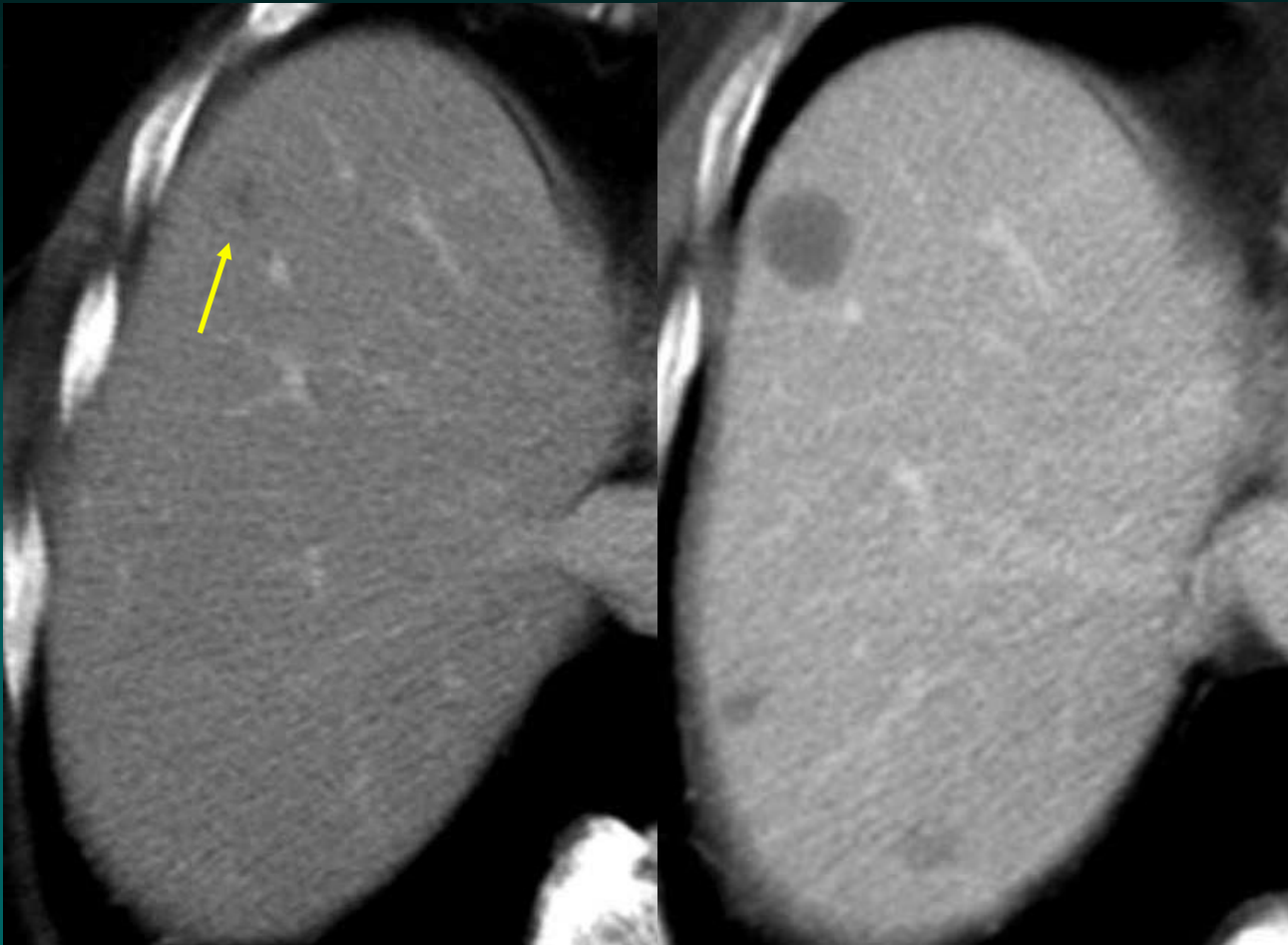
Effects of Imatinib on GIST: CT findings



1/12

3/30

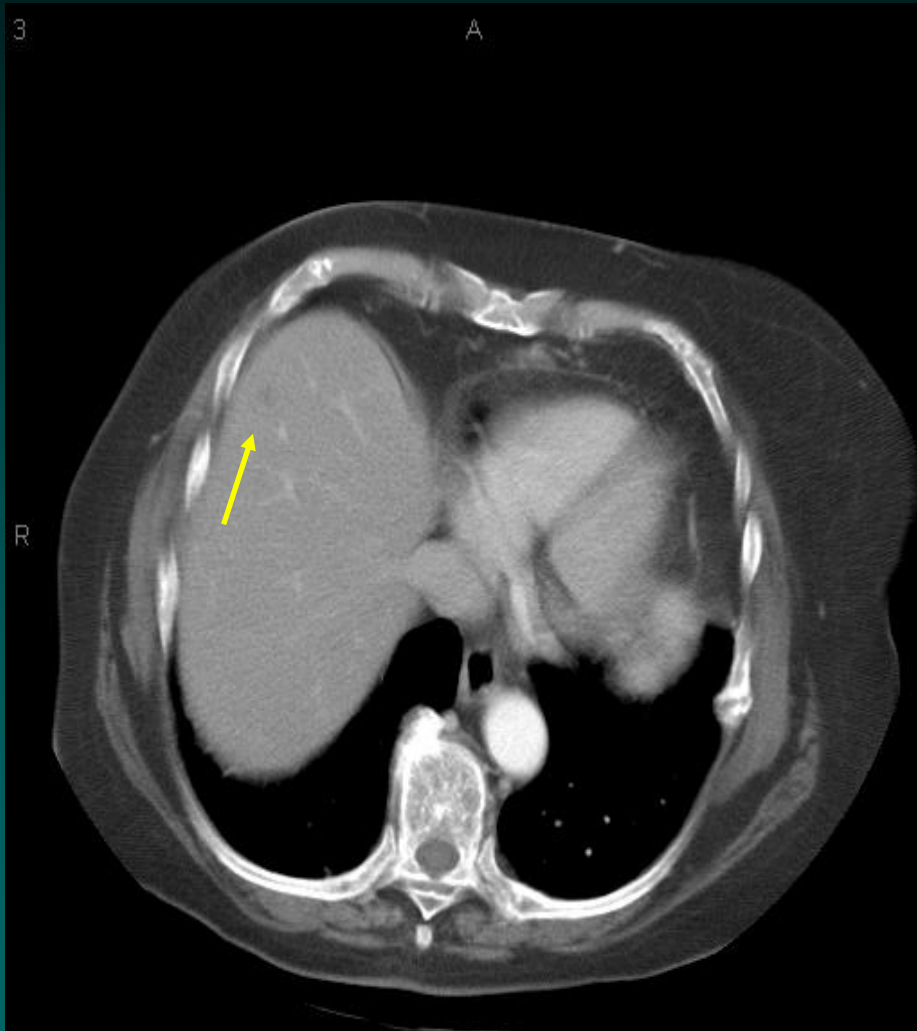
Effects of Imatinib on GIST: CT findings



1/12

3/30

Effects of Imatinib on GIST: CT findings

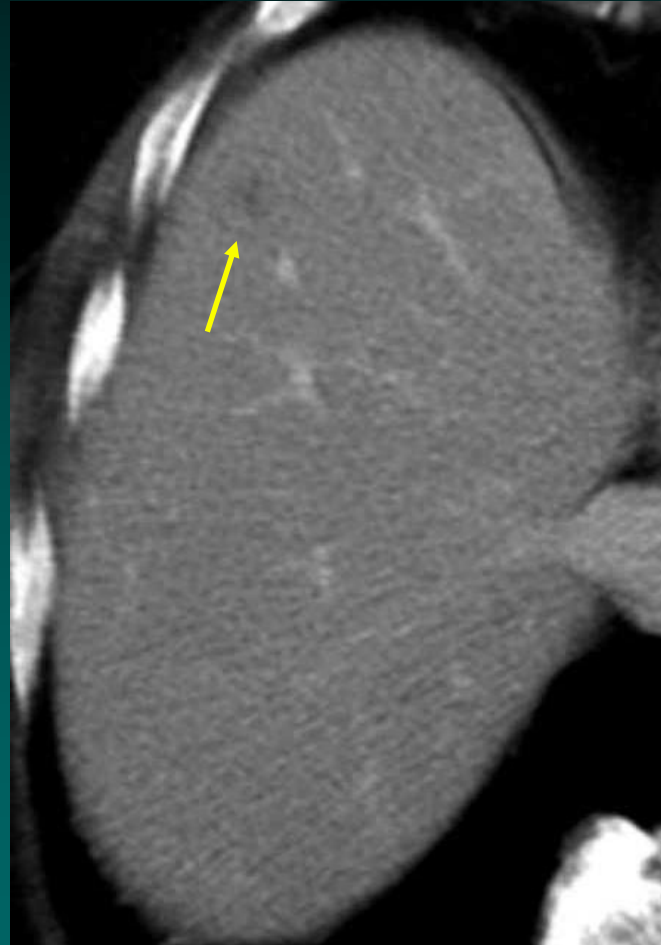


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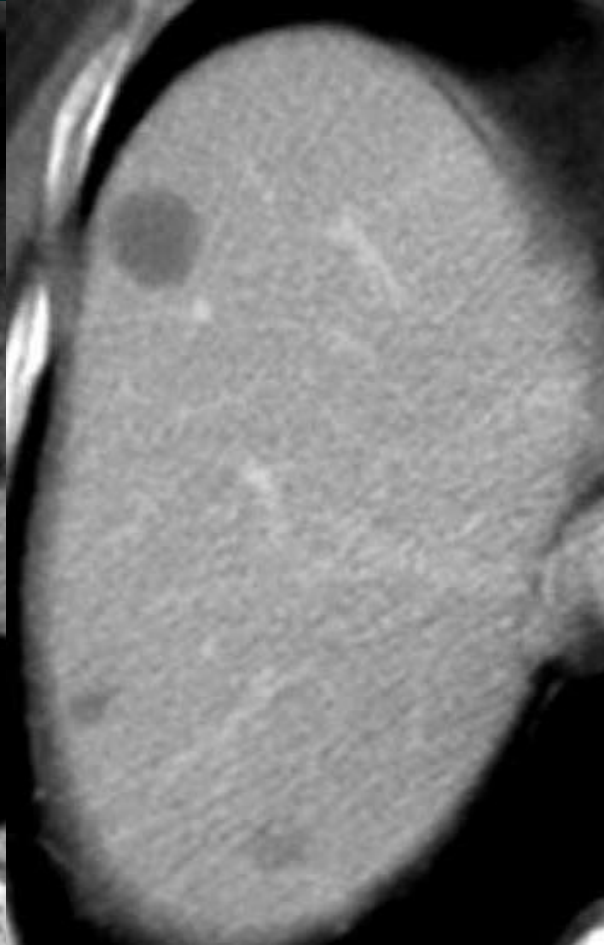


1/12

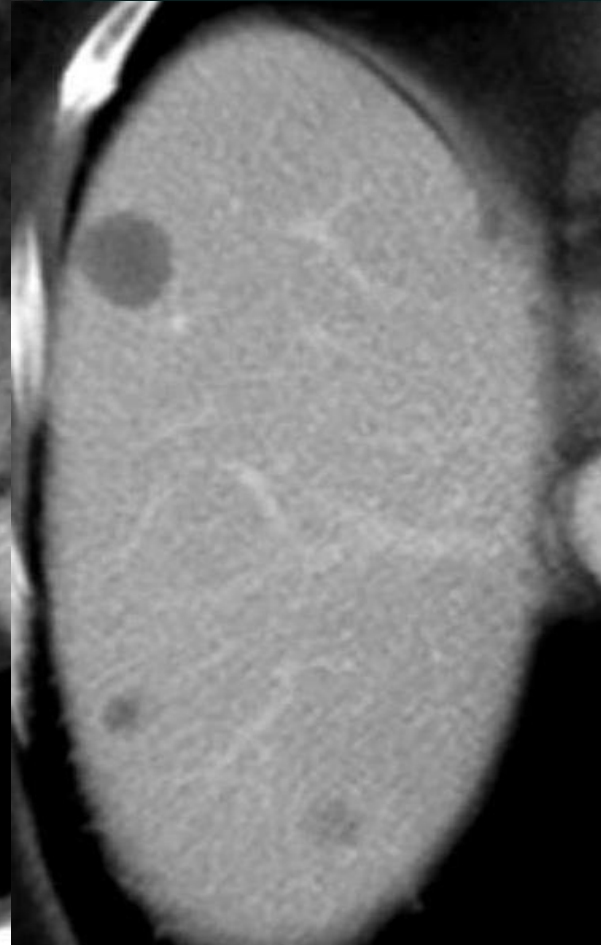
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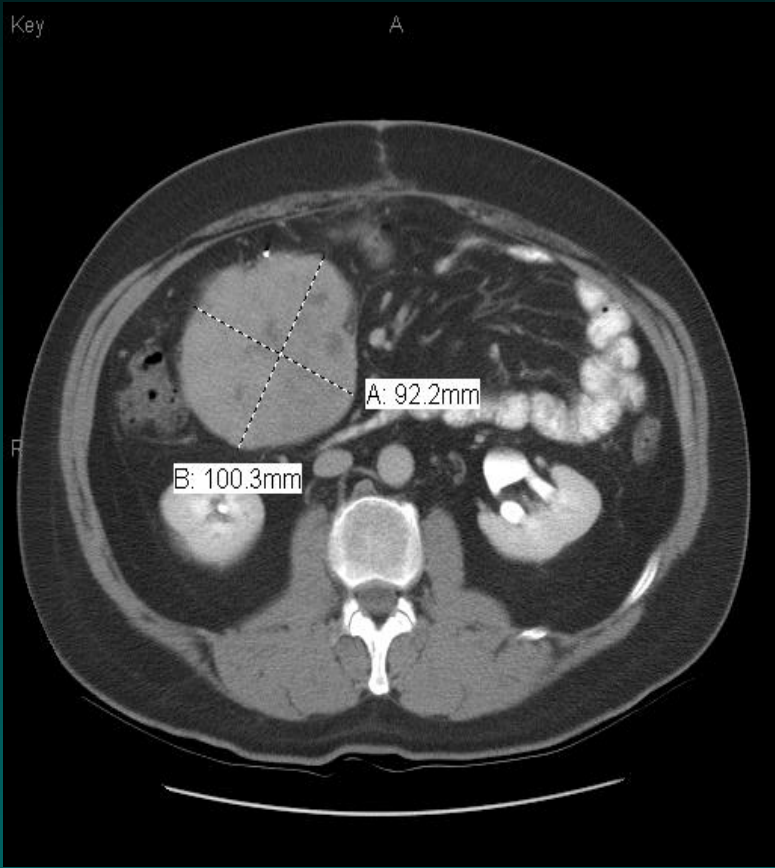


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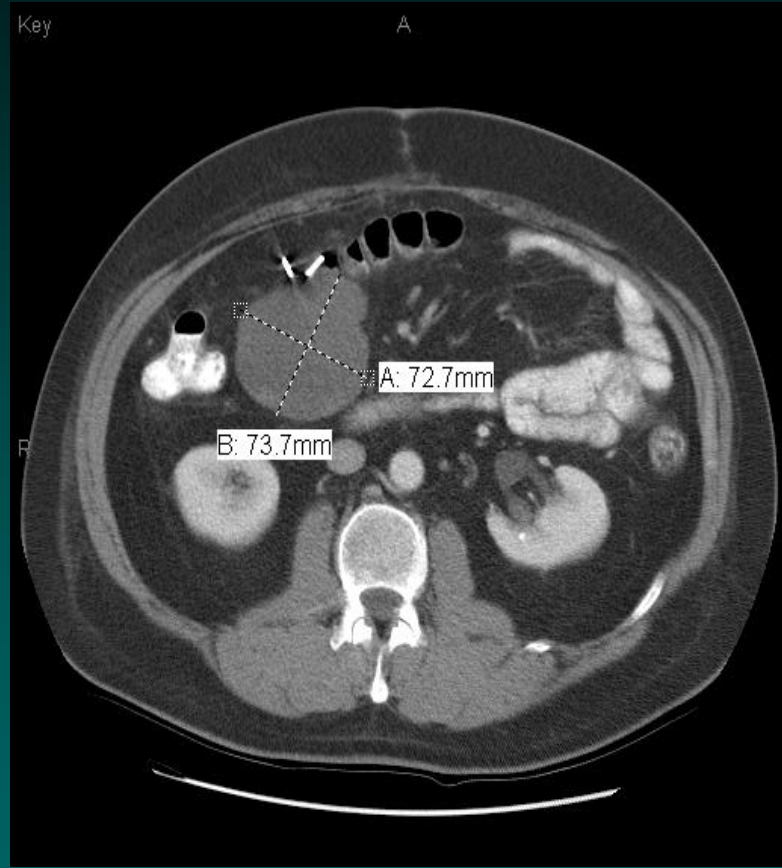


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Effects of Imatinib on GIST: CT findings - Size

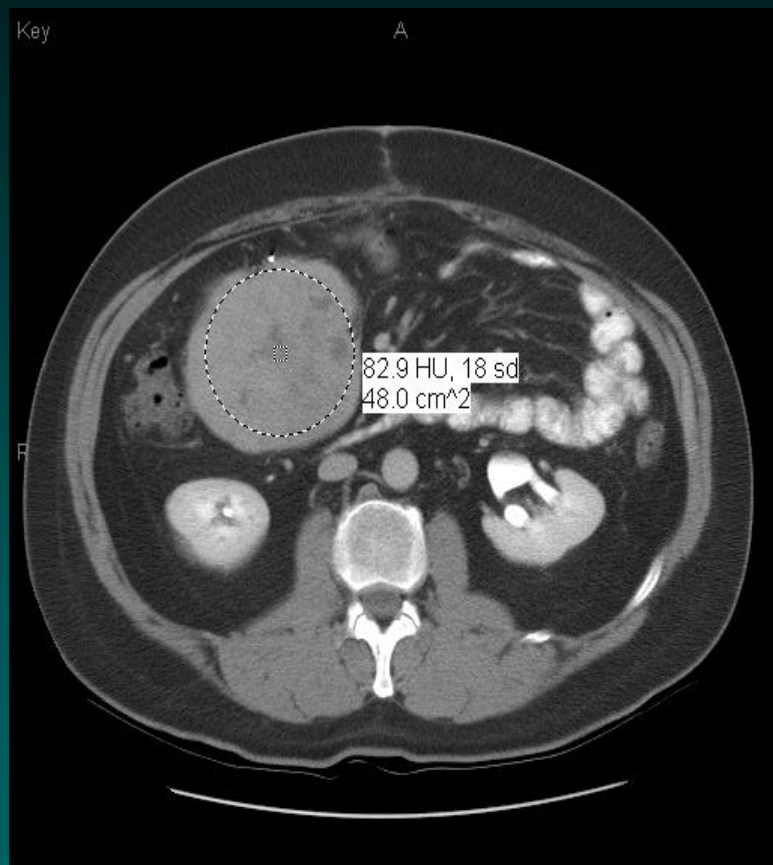


Baseline

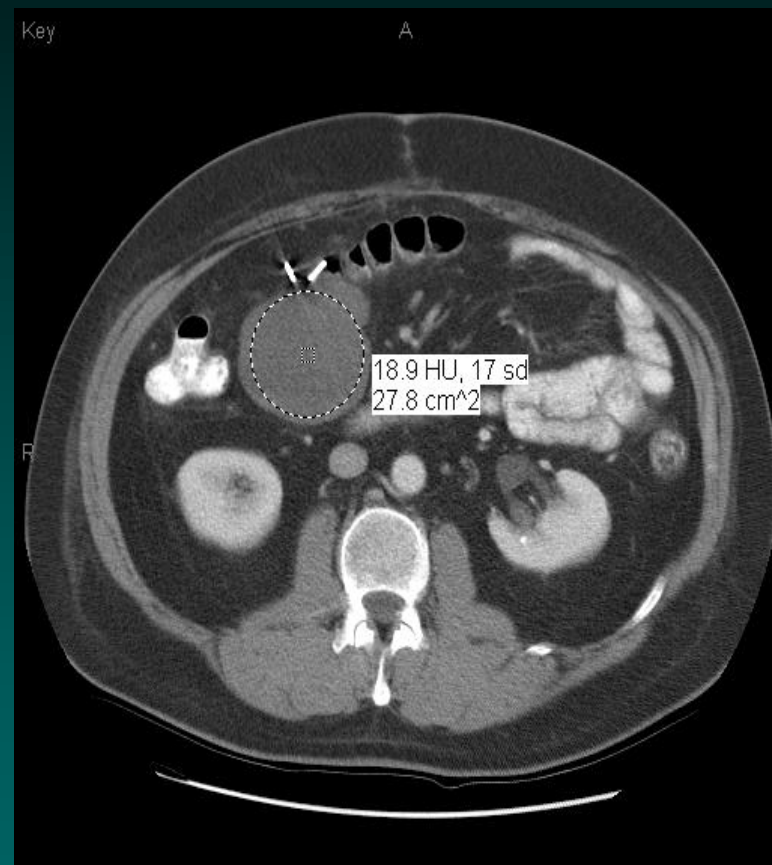


8 Weeks

Effects of Imatinib on GIST: CT findings - Density



**Baseline with
Density Measurement**



**8 weeks with
Density Measurement**



We Should Desist Using RECIST at Least in GIST



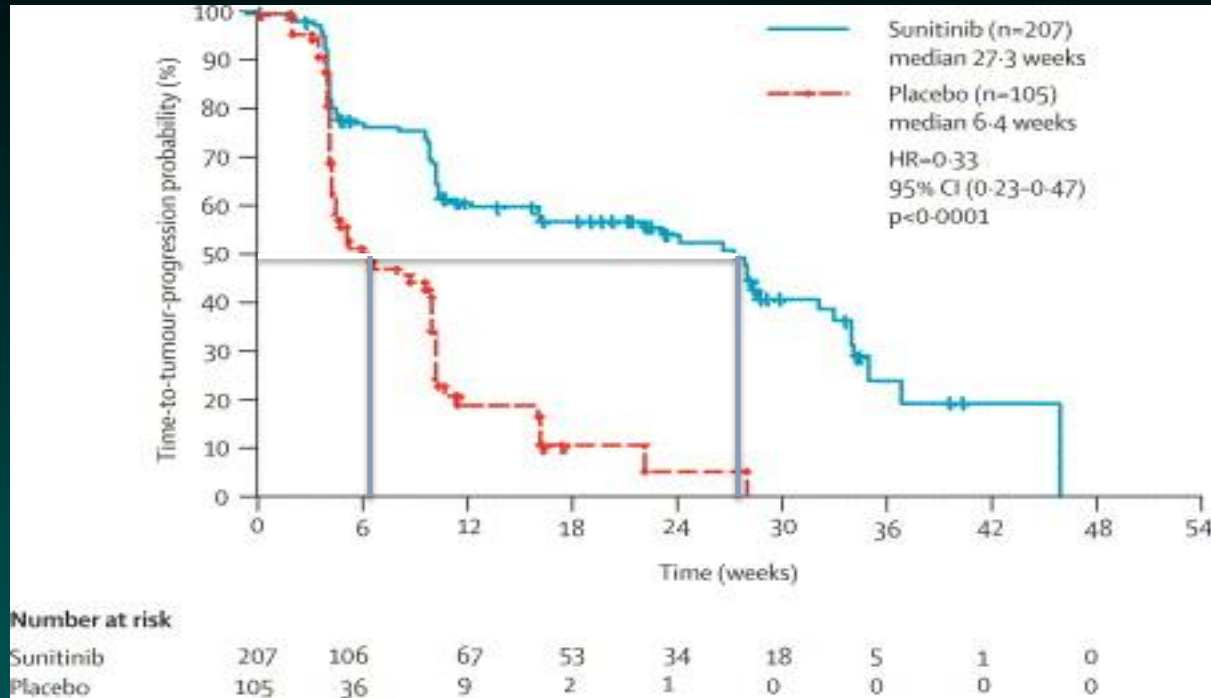


Figure 2 Kaplan-Meier estimates of time to tumour progression Results represent central radiology assessment of ITT population.

George D Demetri , Allan T van Oosterom , Christopher R Garrett , Martin E Blackstein , Manisha H Shah , Jaap Verw...

Efficacy and safety of sunitinib in patients with advanced gastrointestinal stromal tumour after failure of imatinib: a randomised controlled trial

The Lancet Volume 368, Issue 9544 2006 1329 - 1338

[http://dx.doi.org/10.1016/S0140-6736\(06\)69446-4](http://dx.doi.org/10.1016/S0140-6736(06)69446-4)

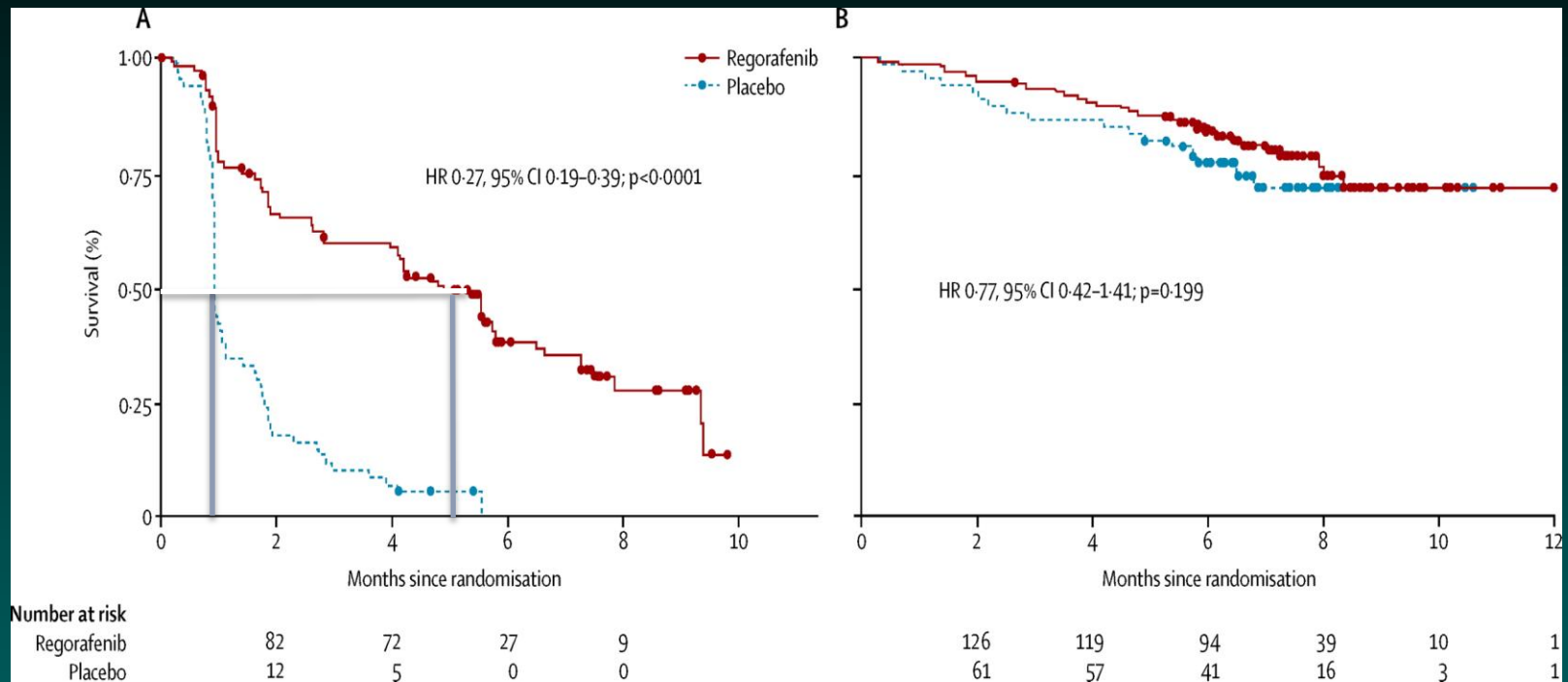


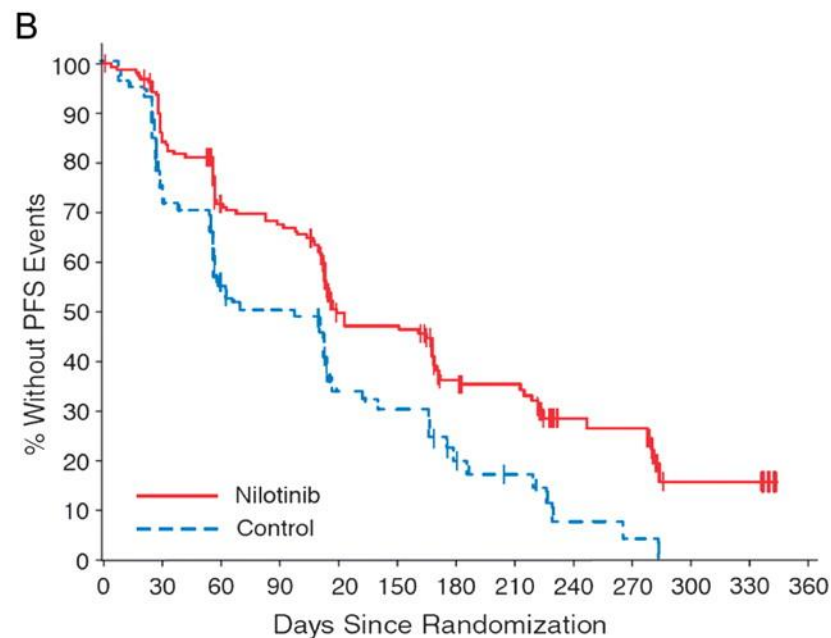
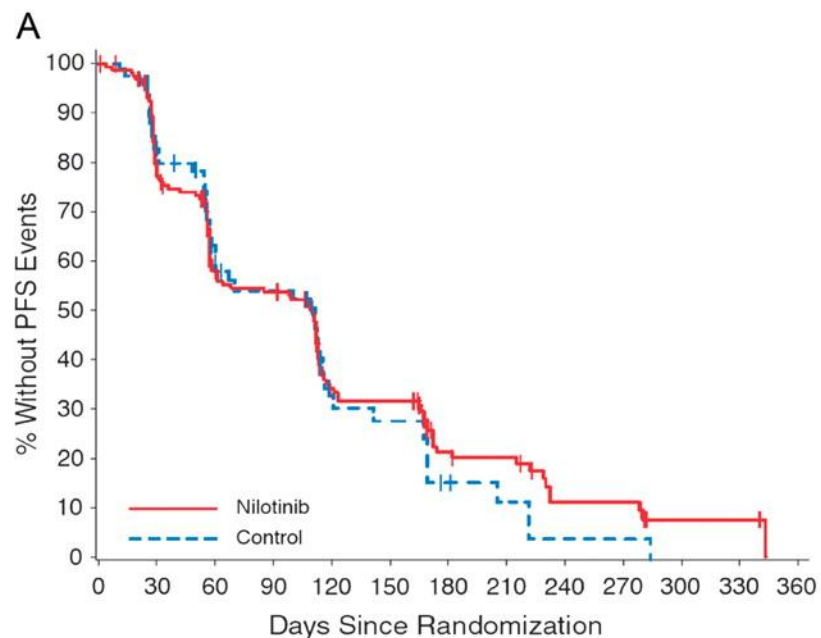
Figure 2 Kaplan-Meier survival analysis after treatment with regorafenib or placebo (A) Progression-free survival, per central review (primary endpoint, final analysis). (B) Overall survival (interim analysis). HR=hazard ratio.

George D Demetri , Peter Reichardt , Yoon-Koo Kang , Jean-Yves Blay , Piotr Rutkowski , Hans Gelderblom , Peter H...

Efficacy and safety of regorafenib for advanced gastrointestinal stromal tumours after failure of imatinib and sunitinib (GRID): an international, multicentre, randomised, placebo-controlled, phase 3 trial

The Lancet Volume 381, Issue 9863 2013 295 - 302

PFS based on central (A) and local (B) radiological review (intent-to-treat population).



Reichardt P et al. *Ann Oncol* 2012;23:1680-1687

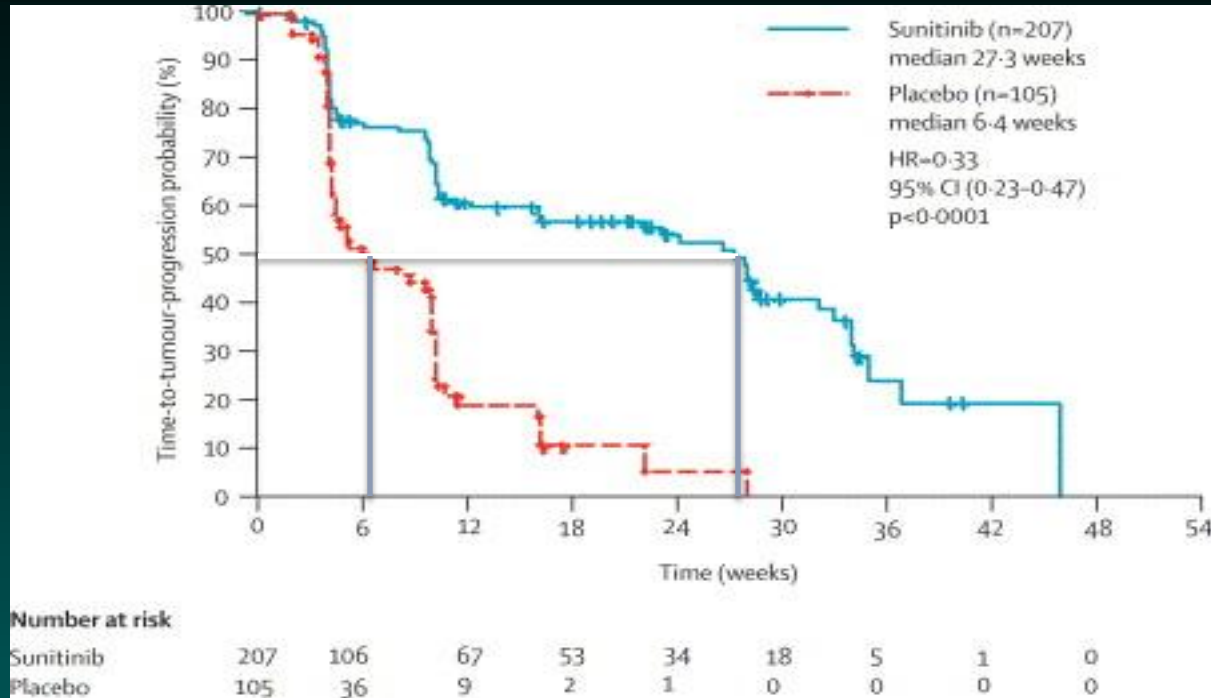


Figure 2 Kaplan-Meier estimates of time to tumour progression Results represent central radiology assessment of ITT population.

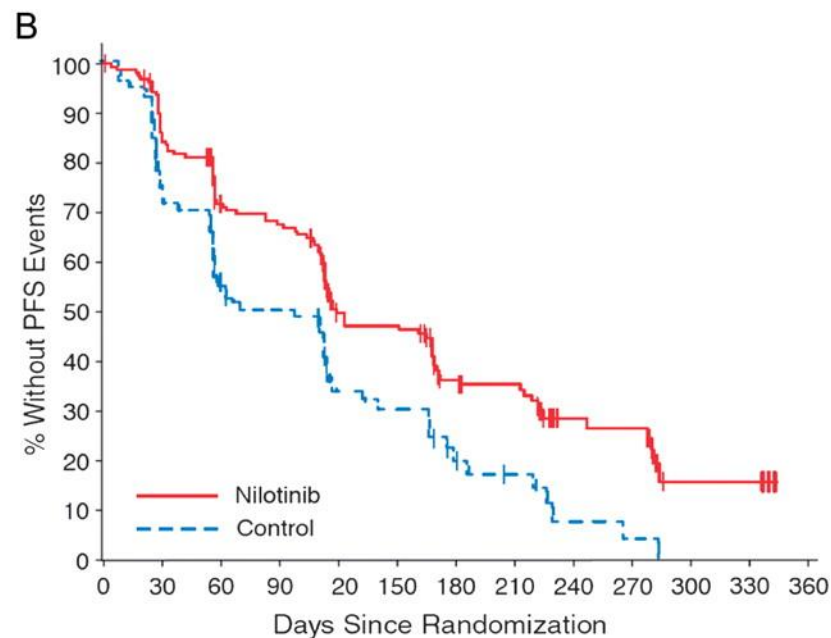
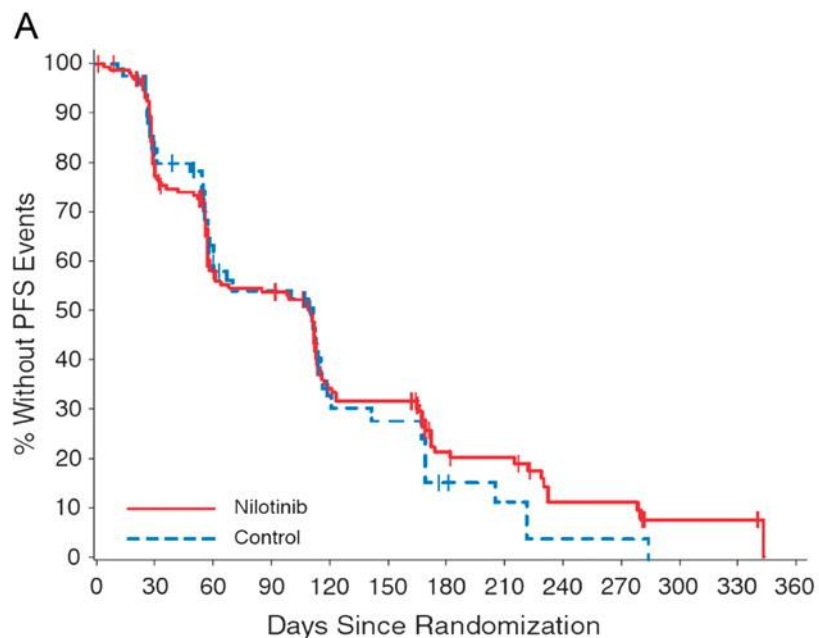
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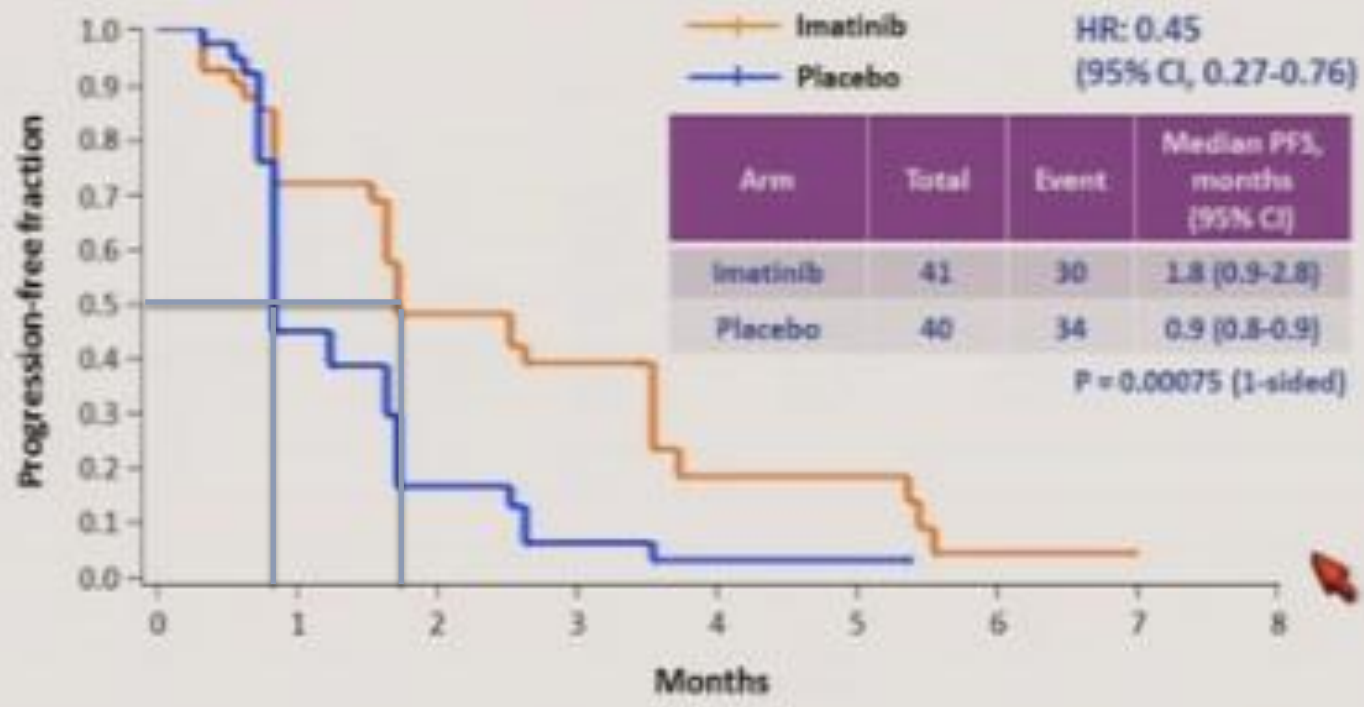


Reichardt P et al. Ann Oncol 2012;23:1680-1687

RIGHT Trial

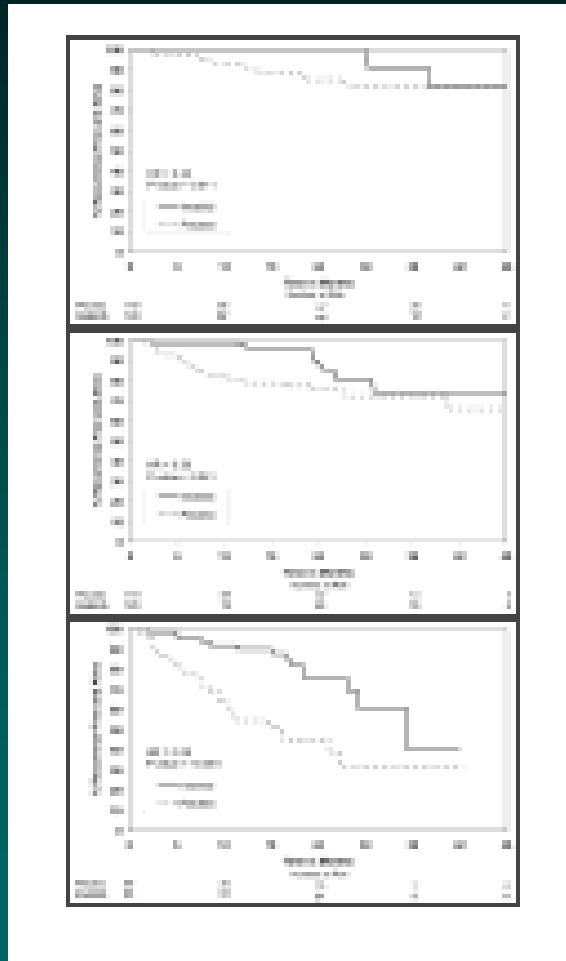


Progression-Free Survival (Primary endpoint per blinded external review)





De Matteo Adjuvant GIST



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

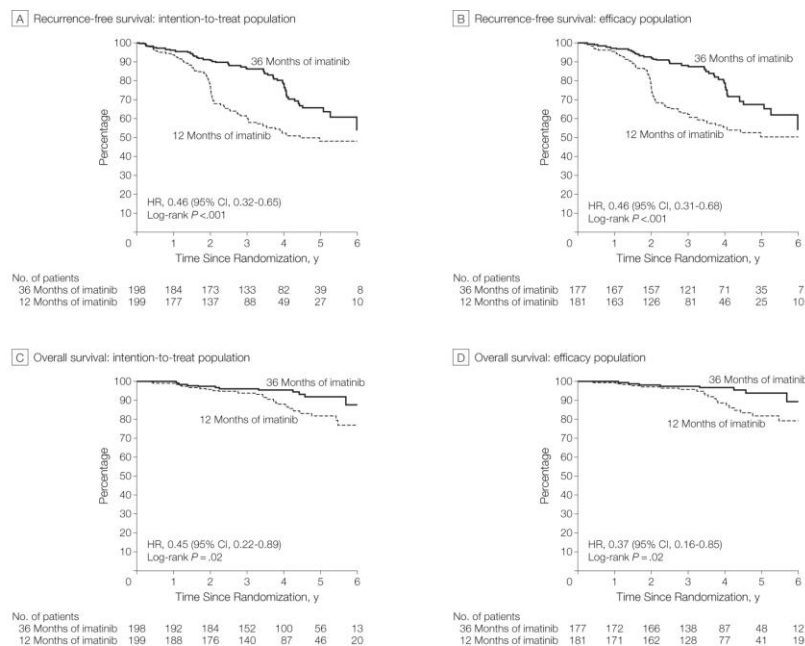


Figure Legend:

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).



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