



Mistakes I See in GIST Management, and Ethical Issues In Clinical Trials

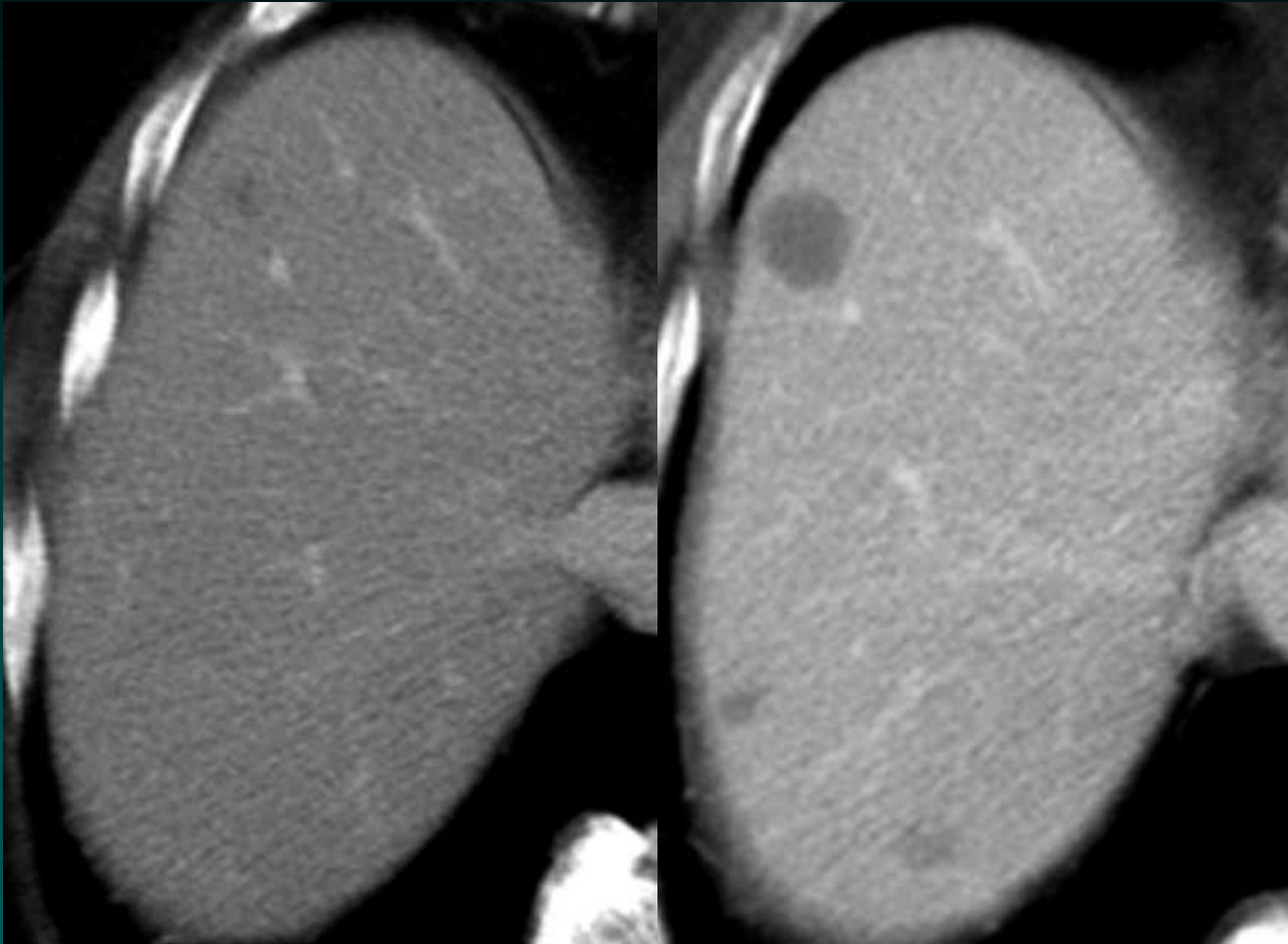
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The Connective Tissue Oncology Society



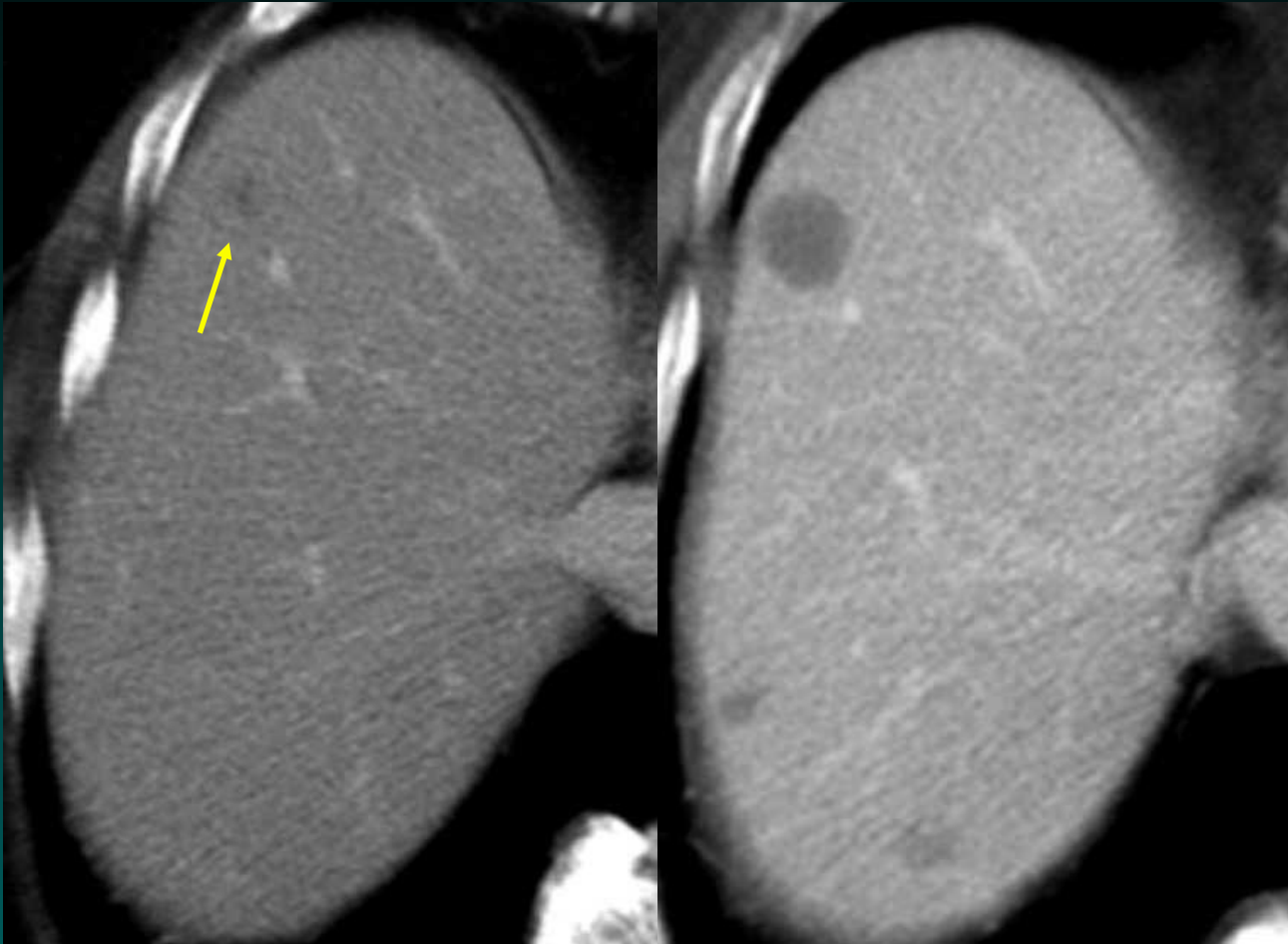
Effects of Imatinib on GIST: CT findings



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3/30

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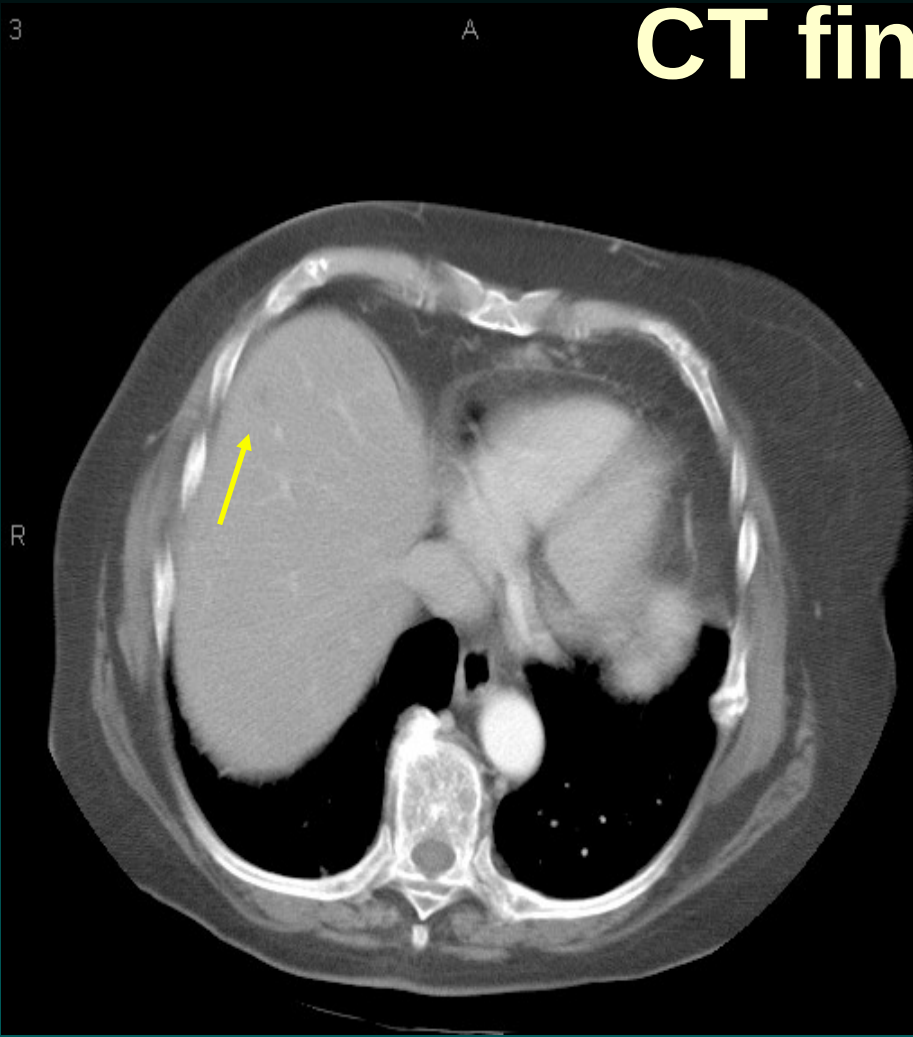


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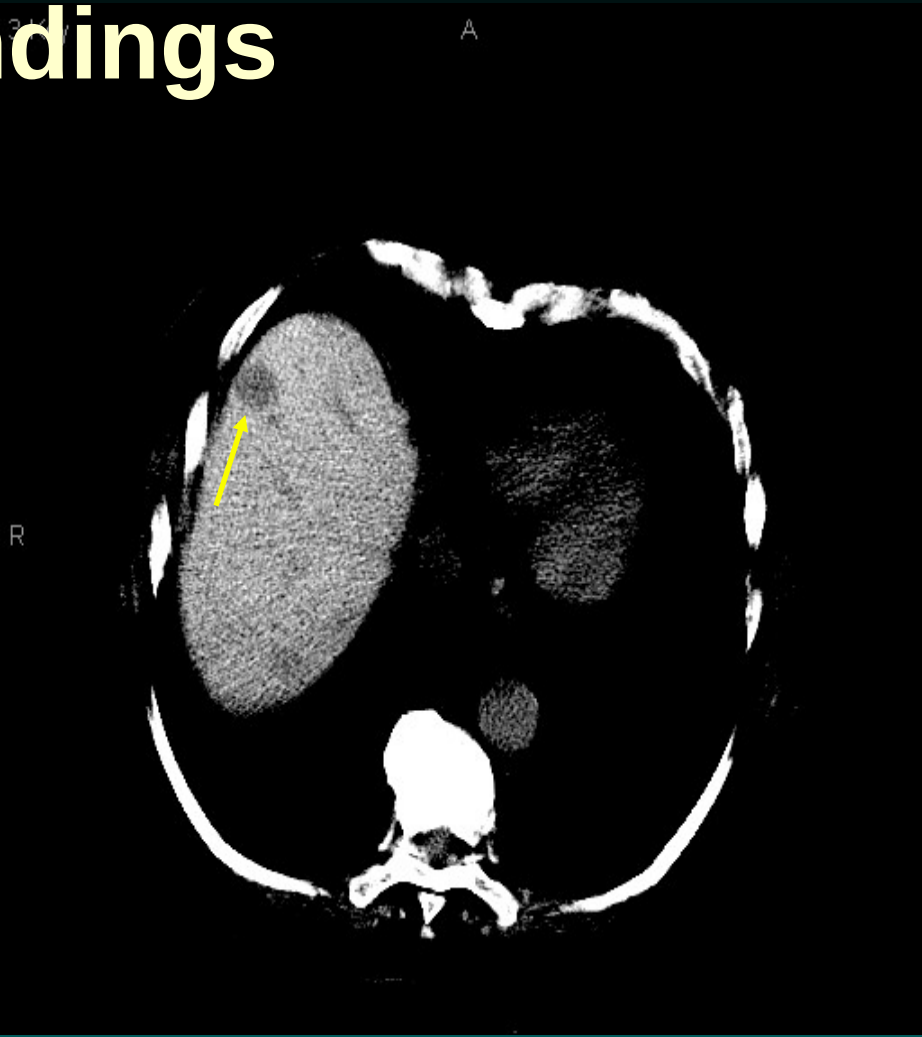
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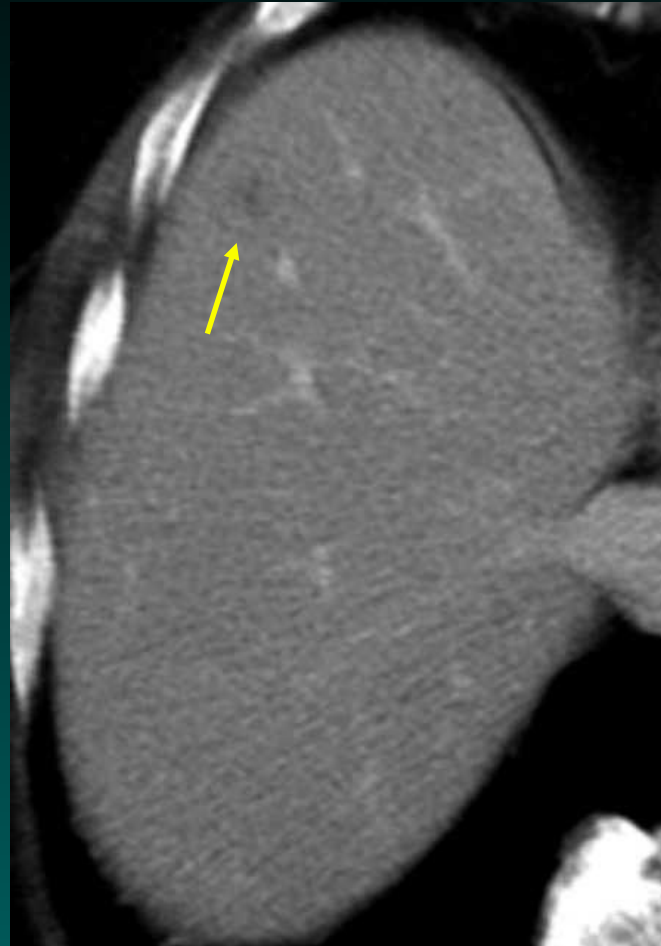


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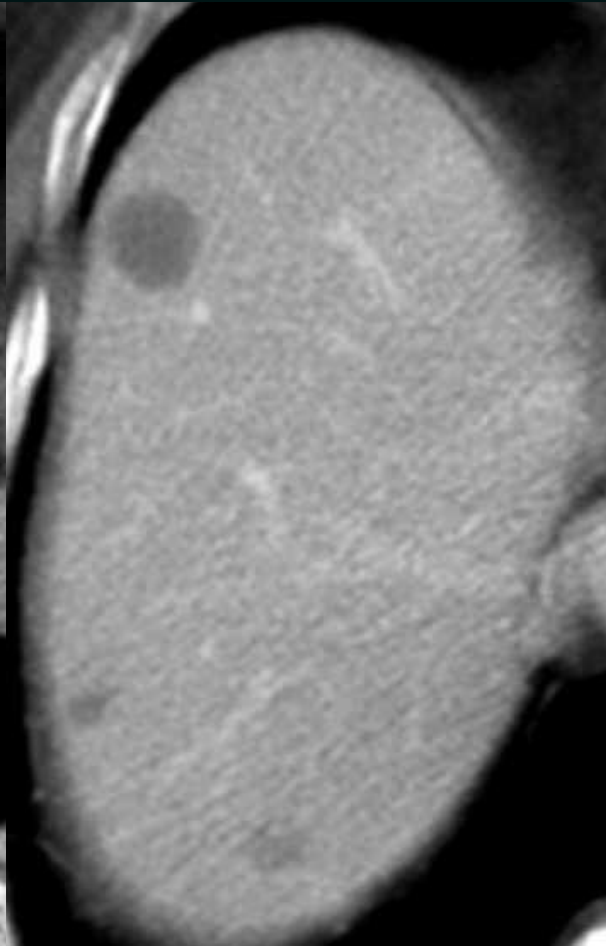


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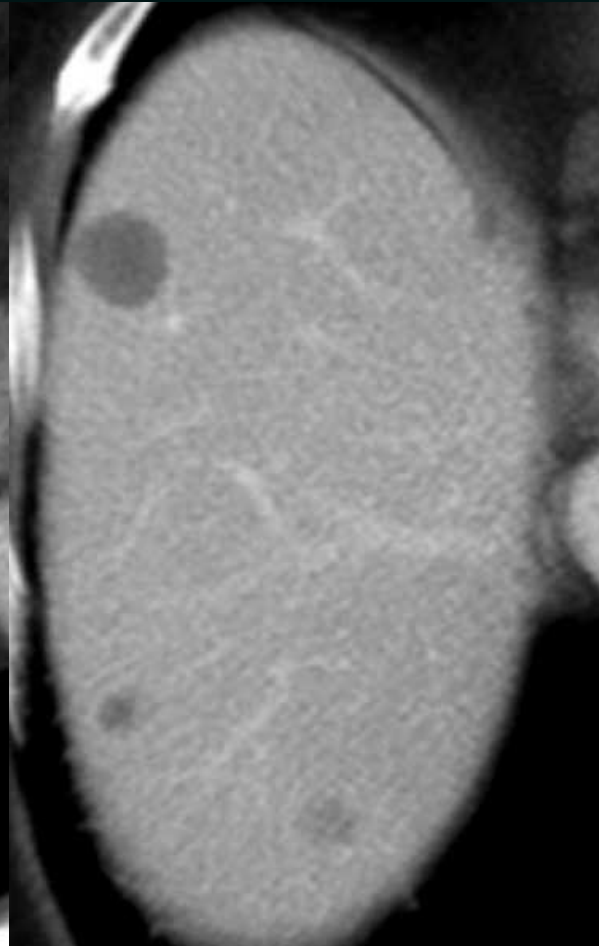
Effects of Imatinib on GIST: CT findings



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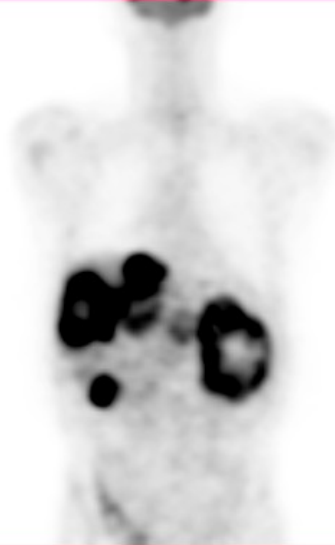


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**THE UNIVERSITY OF TEXAS
M.D. ANDERSON CANCER CENTER
HOUSTON, TEXAS**

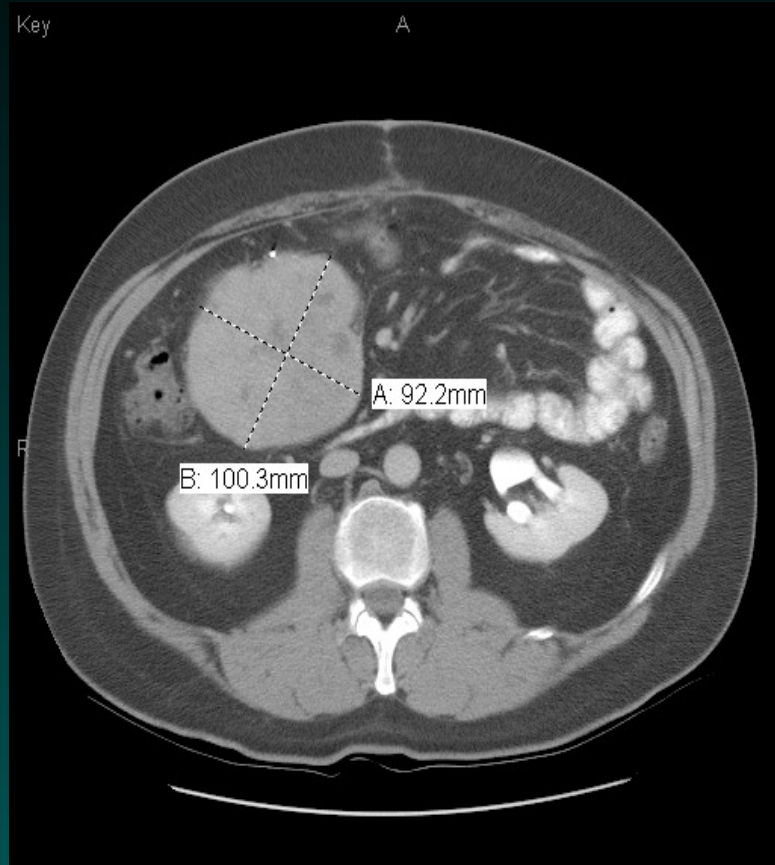
Section of Positron Emission Tomography

Now you see it

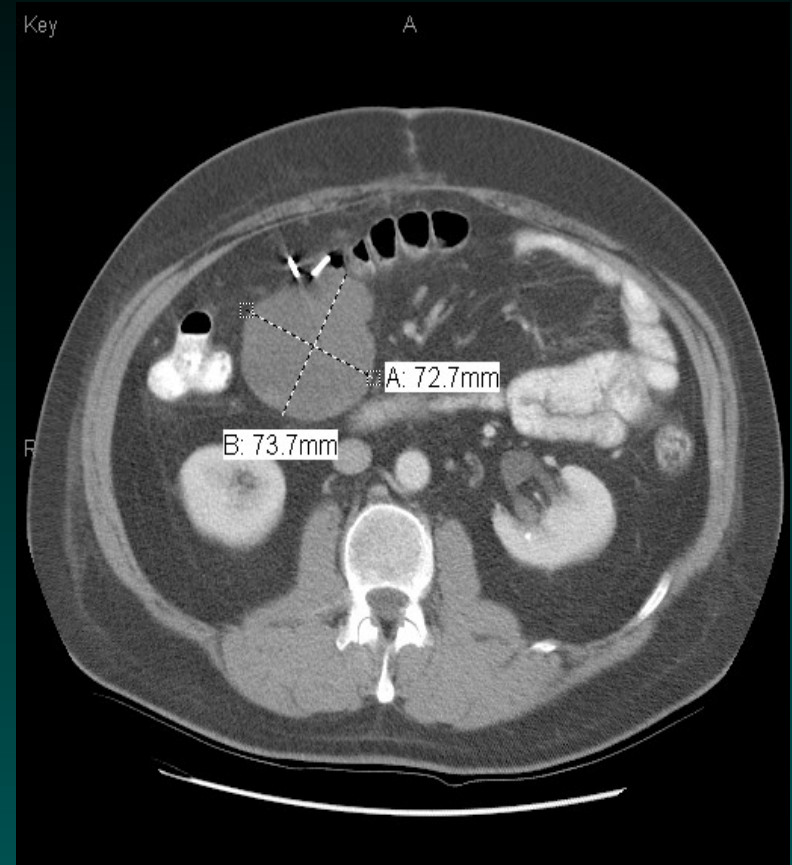


Now you don't

Effects of Imatinib on GIST: CT findings - Size

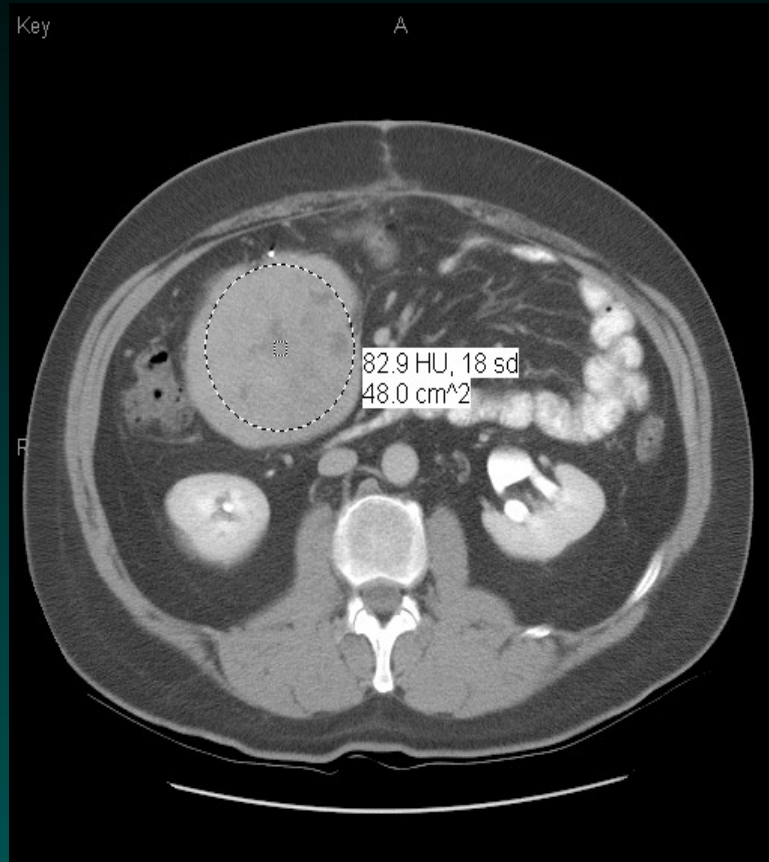


Baseline

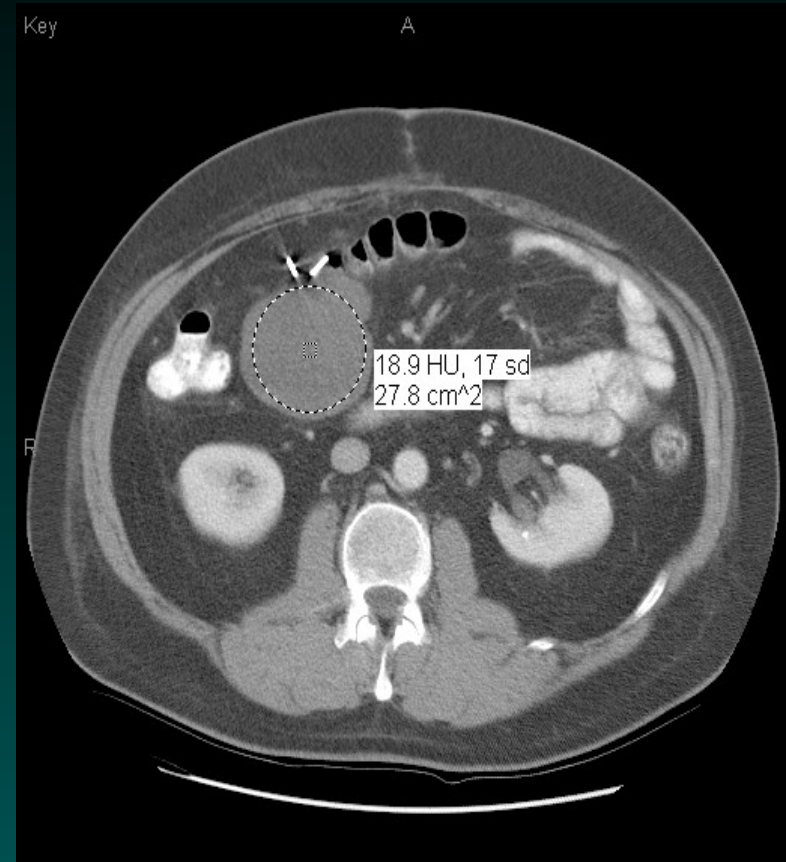


8 Weeks

Effects of Imatinib on GIST: CT findings - Density

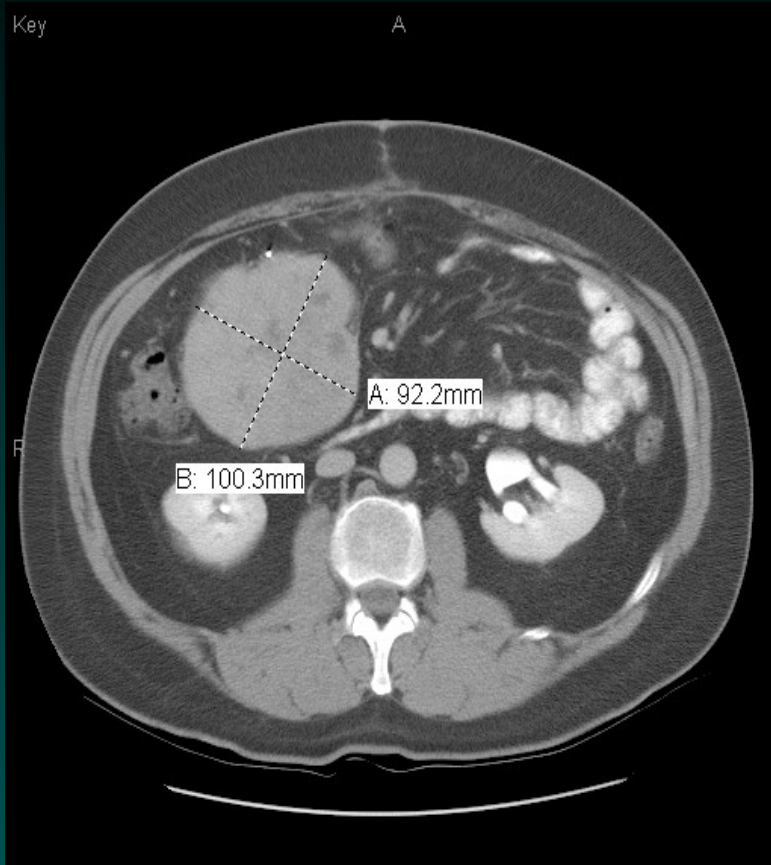


**Baseline with
Density Measurement**

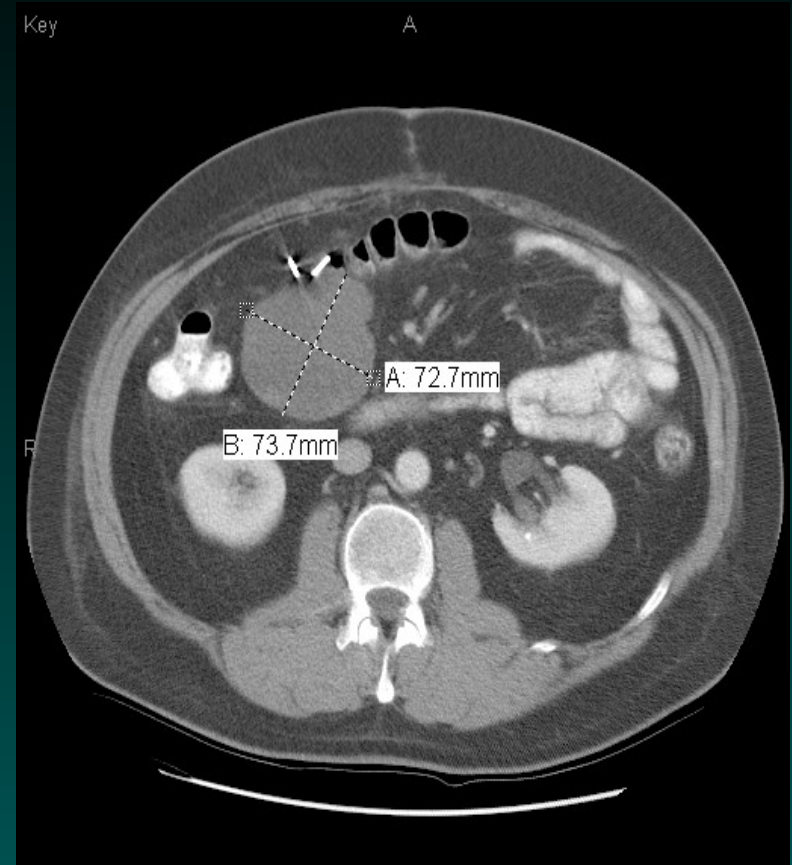


**8 weeks with
Density Measurement**

Effects of Imatinib on GIST: CT findings - Size



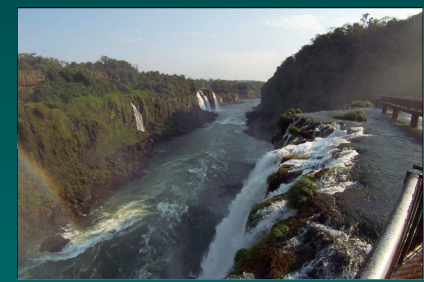
Baseline



8 Weeks



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





SU11248 in Advanced GIST

Sunitinib Malate, Sutent
Stop
Imatinib
4 weeks



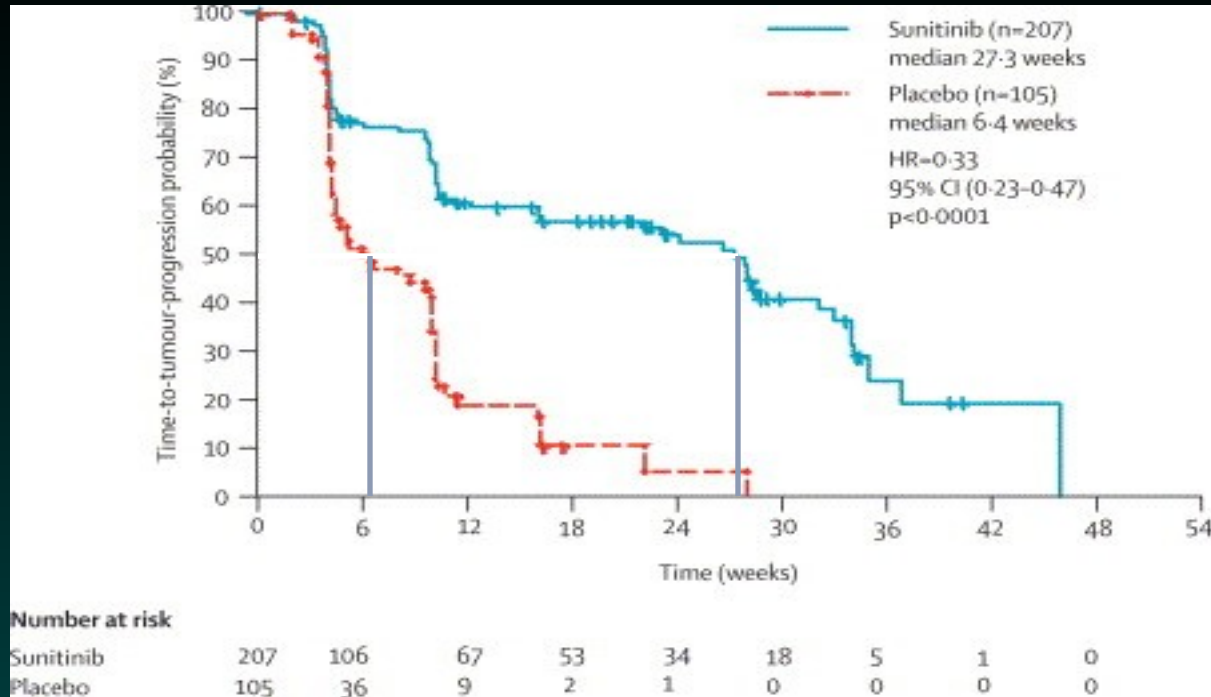


Figure 2 Kaplan-Meier estimates of time to tumour progression Results represent central radiology assessment of ITT population.

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)

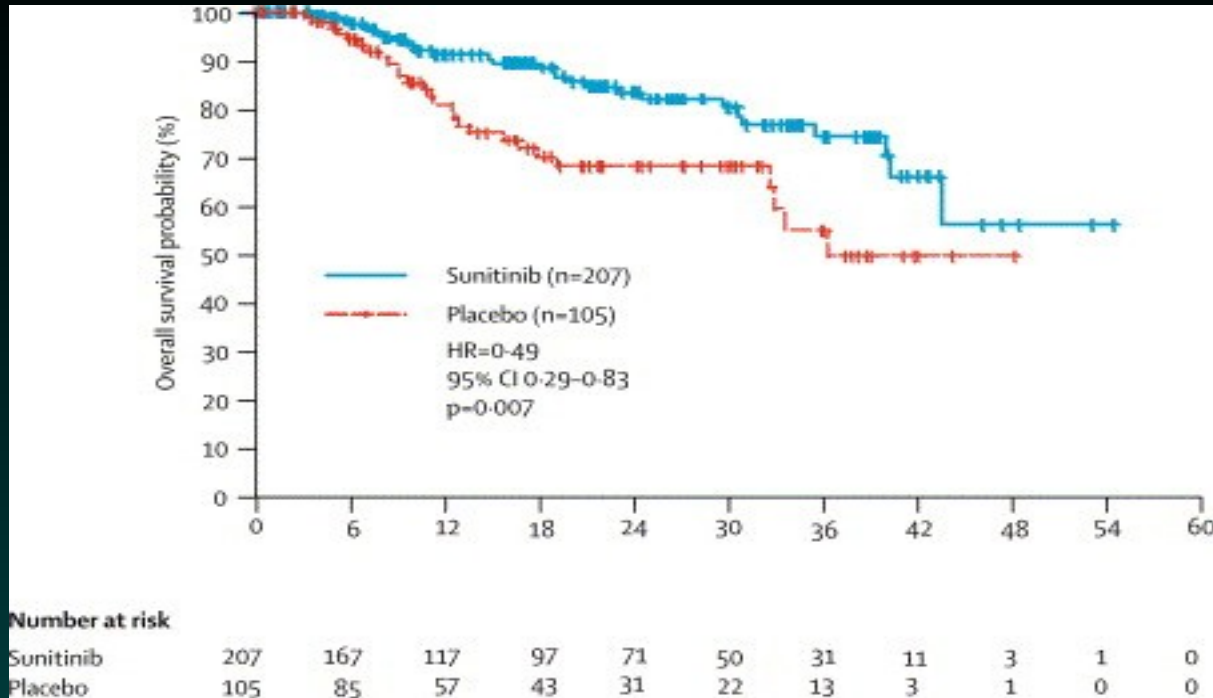


Figure 4 Kaplan-Meier estimates of overall survival. Results represent central radiology assessment of ITT population and include open-label treatment subsequent to crossover after progression.

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

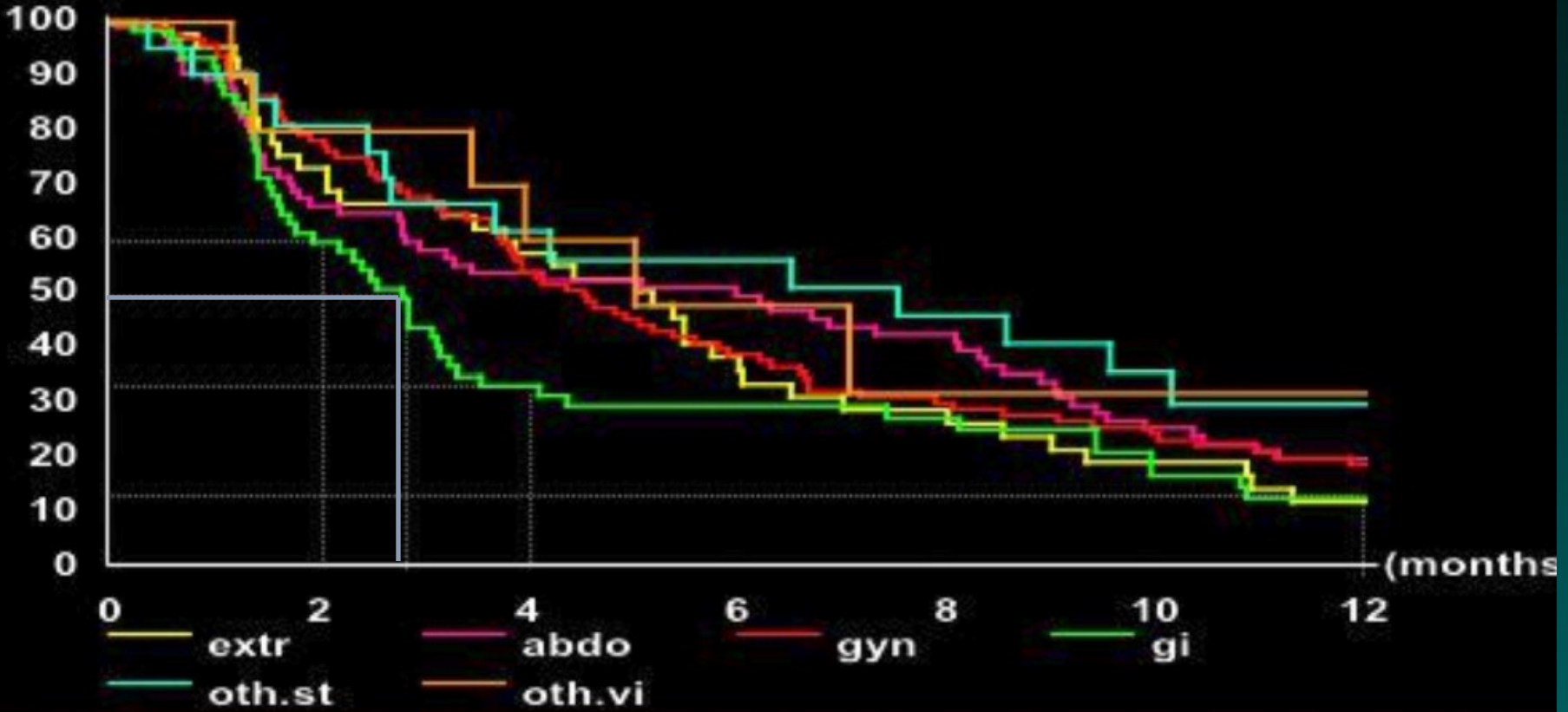
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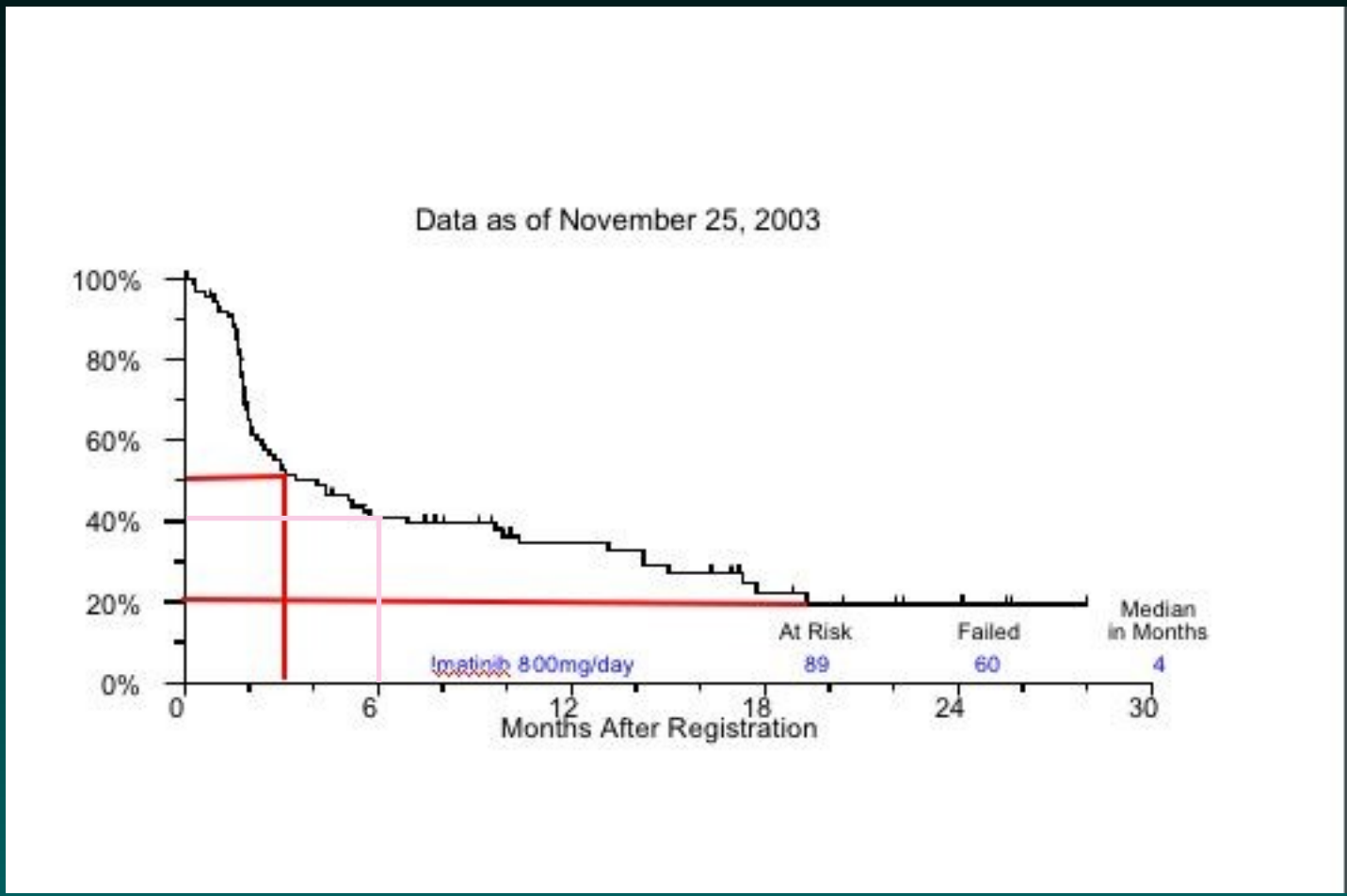
EORTC 1st Line Chemotherapy: Active Single Agents or Combinations

**Time to progression
1st line - leiomyosarcoma**



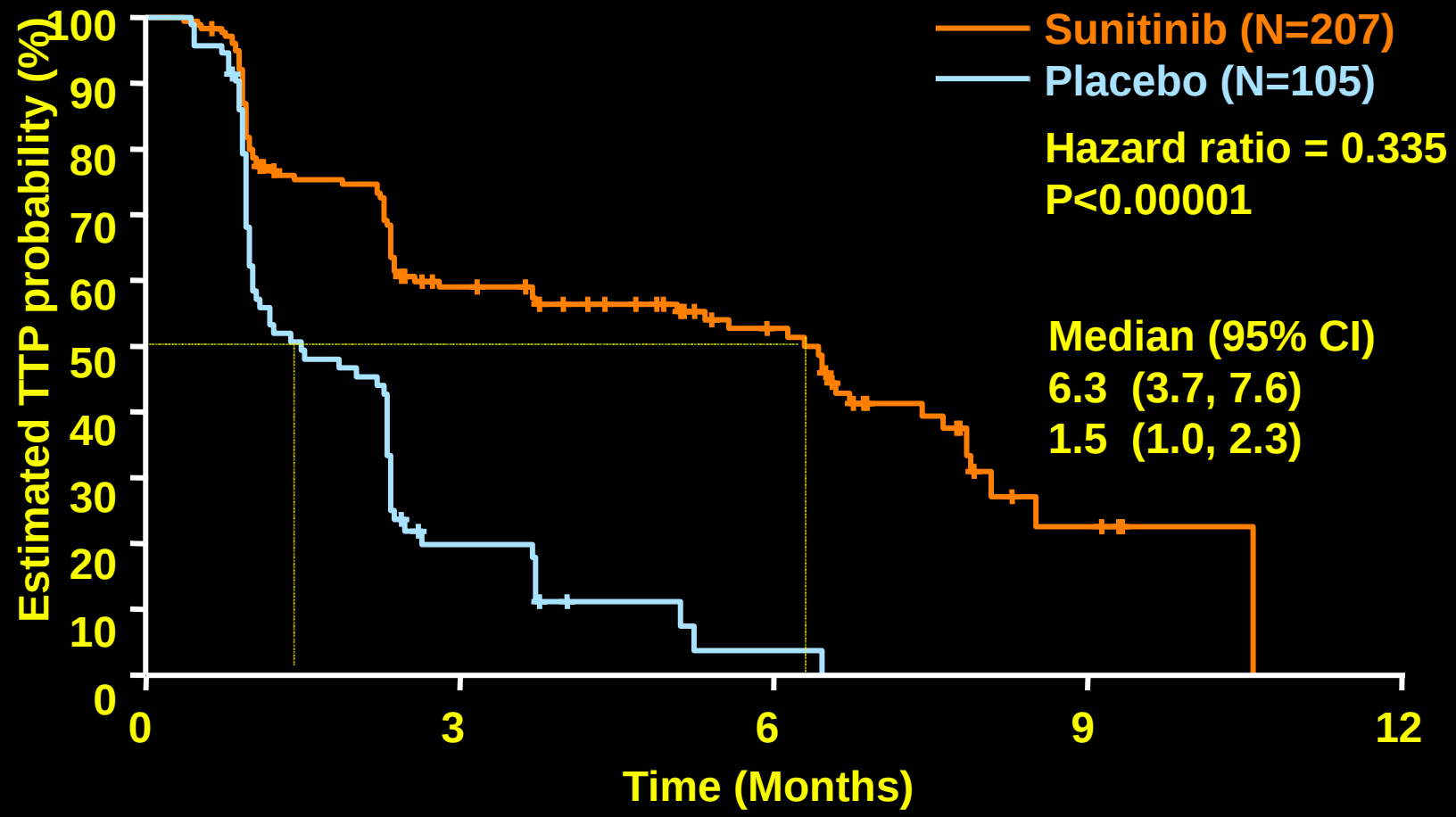


Phase III Trial: US Intergroup S0033: Time to Progression on Crossover



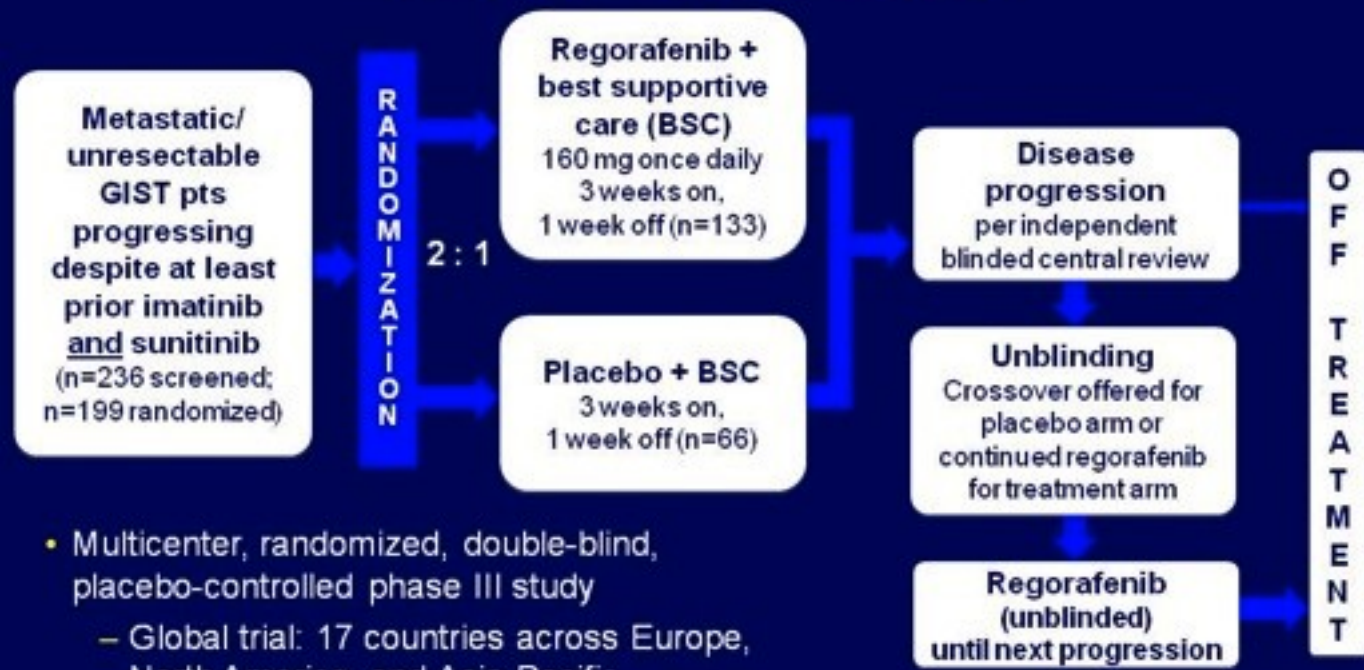


Time to Tumor Progression





GIST – Regorafenib In Progressive Disease (GRID): Study Design



- Multicenter, randomized, double-blind, placebo-controlled phase III study
 - Global trial: 17 countries across Europe, North America, and Asia-Pacific
 - Stratification: treatment line (2 vs >2 prior lines), geographical location (Asia vs "Rest of World")

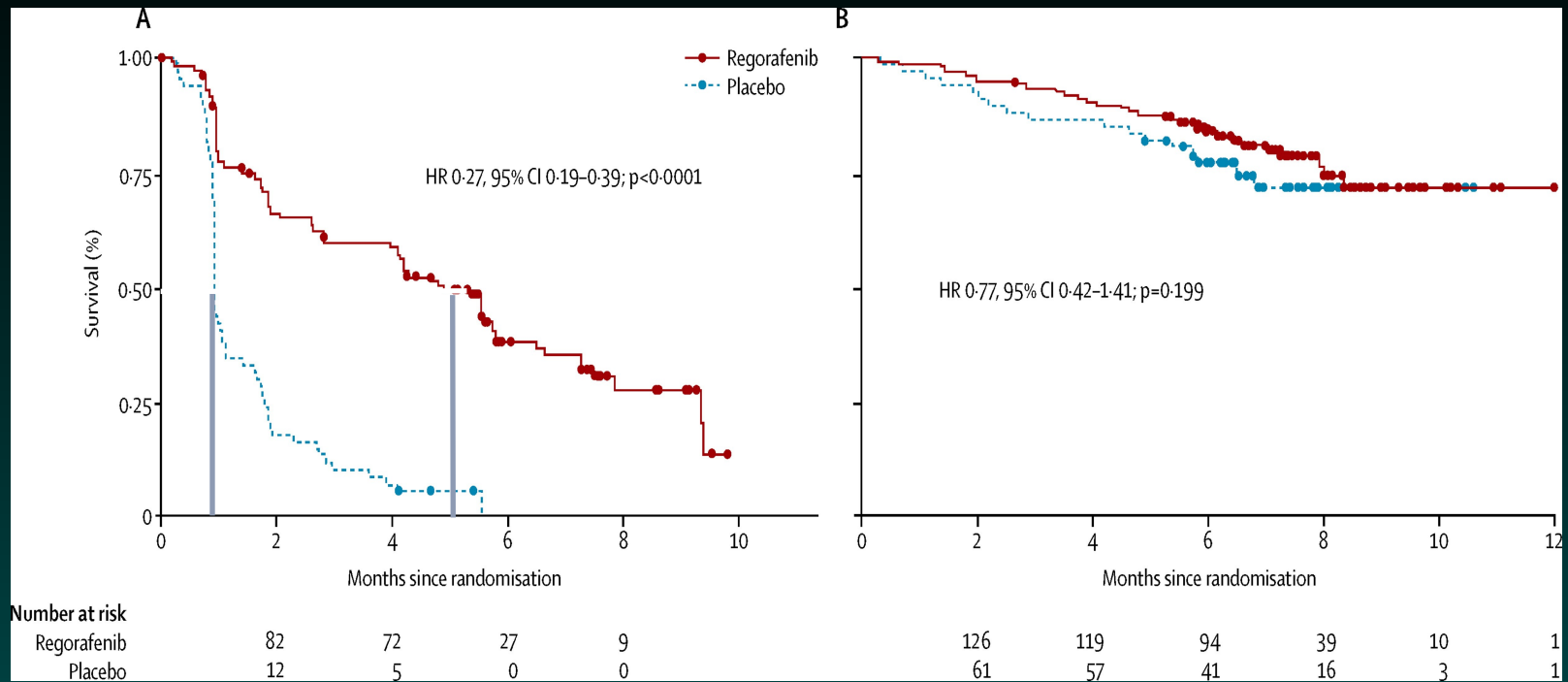


Figure 2 Kaplan-Meier survival analysis after treatment with regorafenib or placebo (A) Progression-free survival, per central review (primary endpoint, final analysis). (B) Overall survival (interim analysis). HR=hazard ratio.

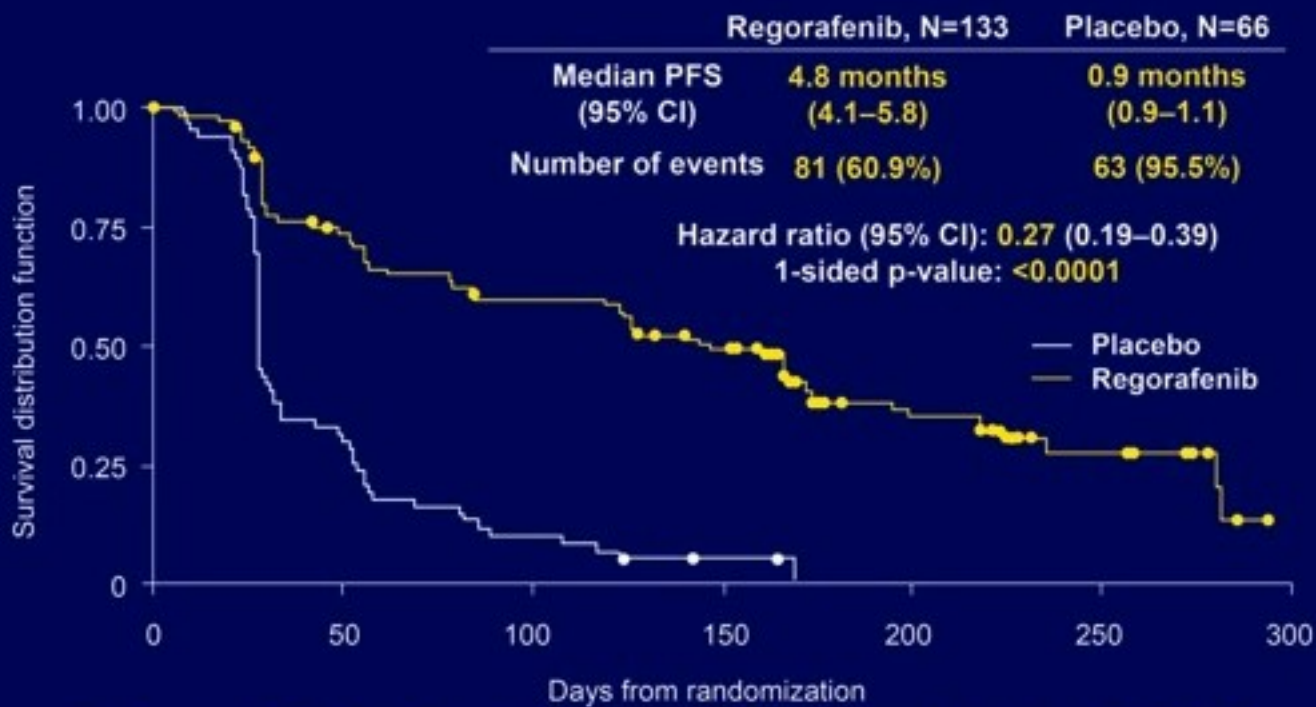
George D Demetri , Peter Reichardt , Yoon-Koo Kang , Jean-Yves Blay , Piotr Rutkowski , Hans Gelderblom , Peter H...

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



GRID Study: Progression-Free Survival (primary endpoint per blinded central review)



**Regorafenib significantly improved PFS vs placebo (p<0.0001);
 primary endpoint met**

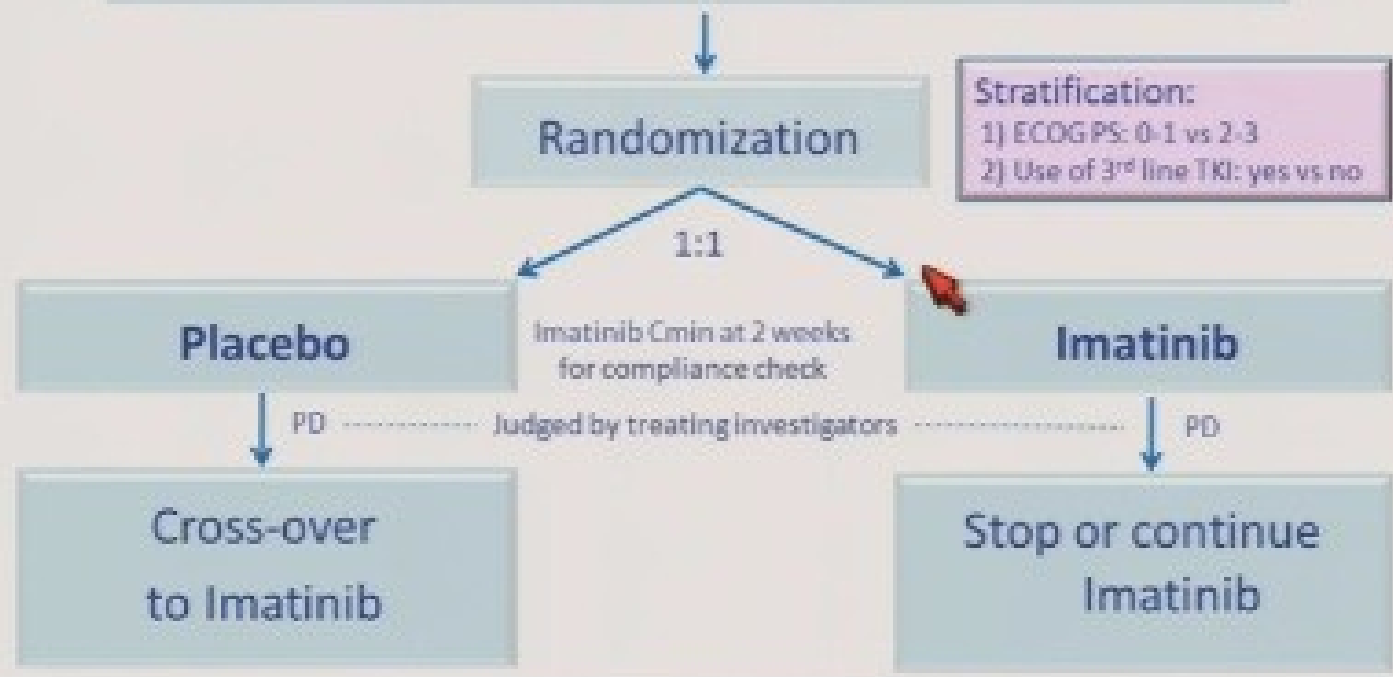
RIGHT Trial



Study Design: RIGHT

(Rechallenge of Imatinib in GIST Having no effective Treatment)

Patients with 1) Prior clinical benefit from 1st-line imatinib, and 2) Progression with both 1st-line imatinib and 2nd-line sunitinib, (Prior use of 3rd-line TKI is permitted)

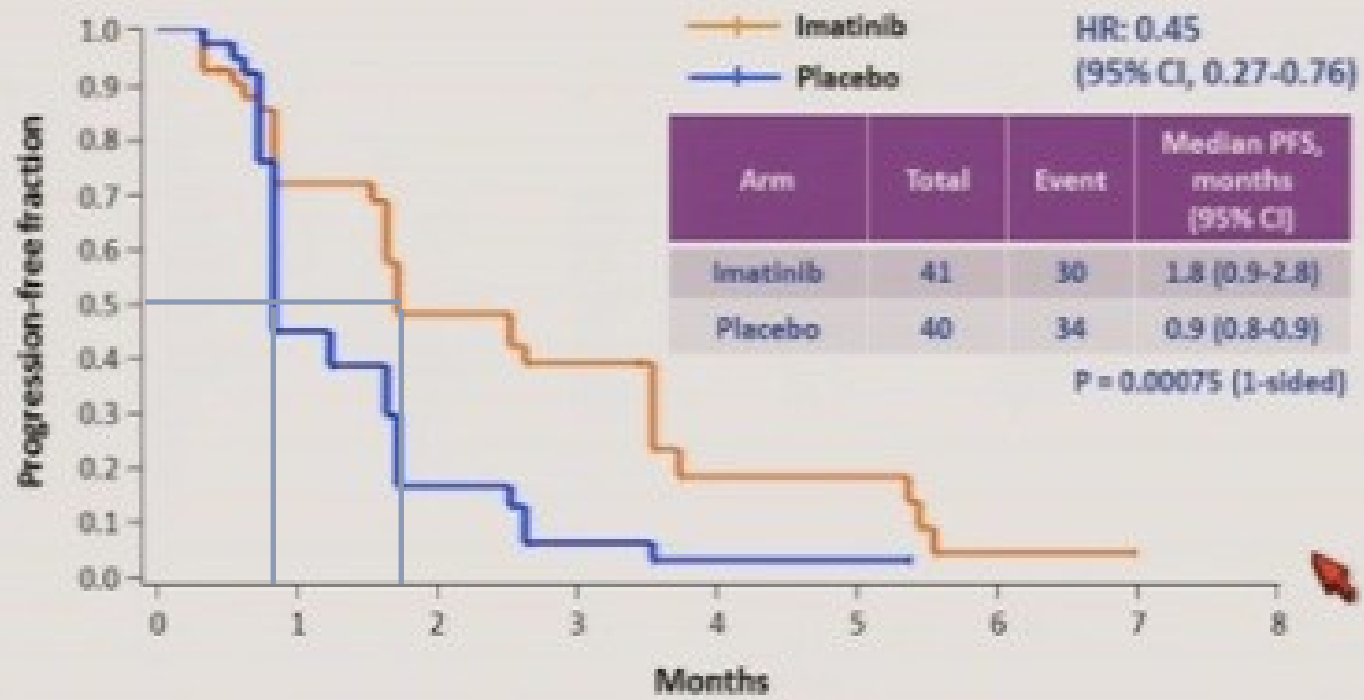


RIGHT Trial



Progression-Free Survival

(Primary endpoint per blinded external review)



RIGHT Trial



Overall Survival

