

# Long term survivorship on TKI's in GIST

## Clinical aspects

**SPAEN conference 2021**

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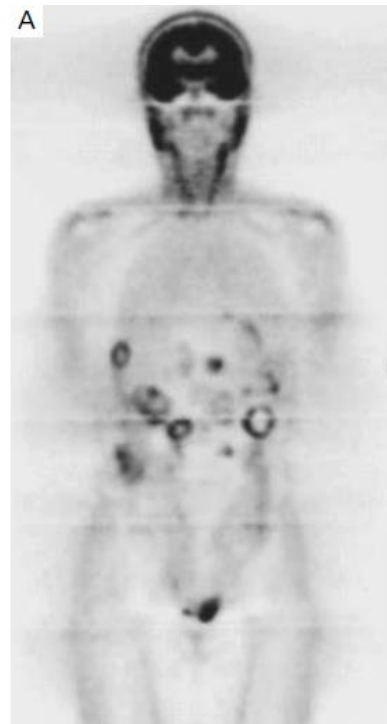


# TKI's and GIST 2 decades down the road NEJM April 5<sup>th</sup> 2001!

## Brief Report

### EFFECT OF THE TYROSINE KINASE INHIBITOR STI571 IN A PATIENT WITH A METASTATIC GASTROINTESTINAL STROMAL TUMOR

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RENAUD CAPDEVILLE, M.D., SASA DIMITRIJEVIC, PH.D.,  
BRIAN DRUKER, M.D., AND GEORGE D. DEMETRI, M.D.

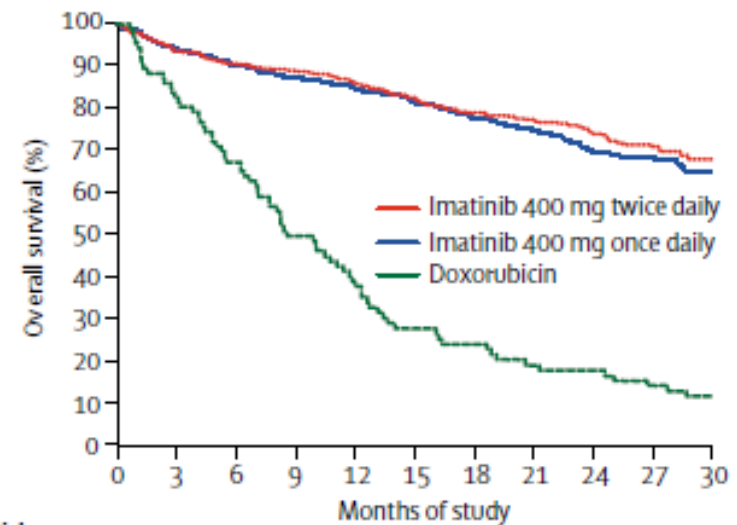
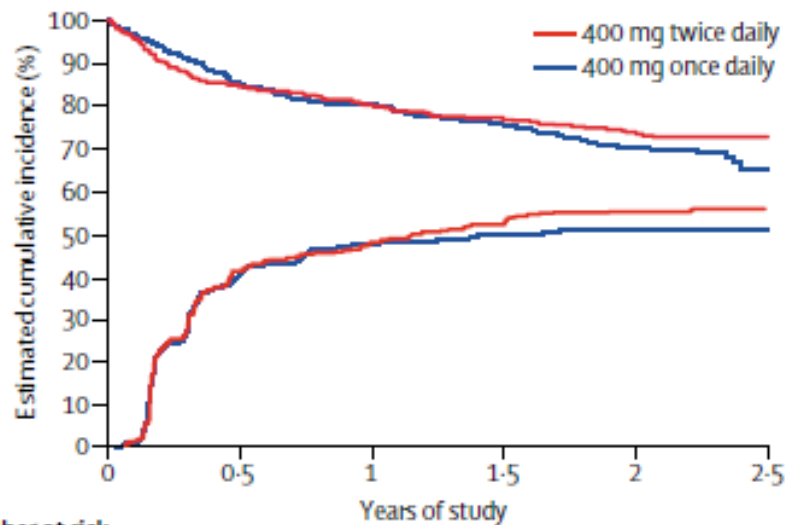


## After 2001

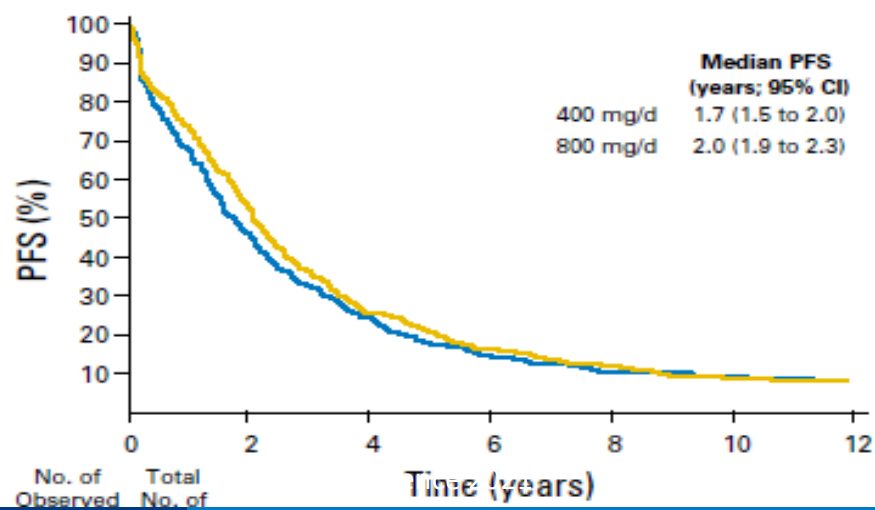
- Unprecedented efficacy
  - Moderate toxicity
  - Rapid development and registration
  - First patients had extensive disease
  - Side effects profile was partly different from CML
- 
- But: Questions on long term antitumor- and side-effects



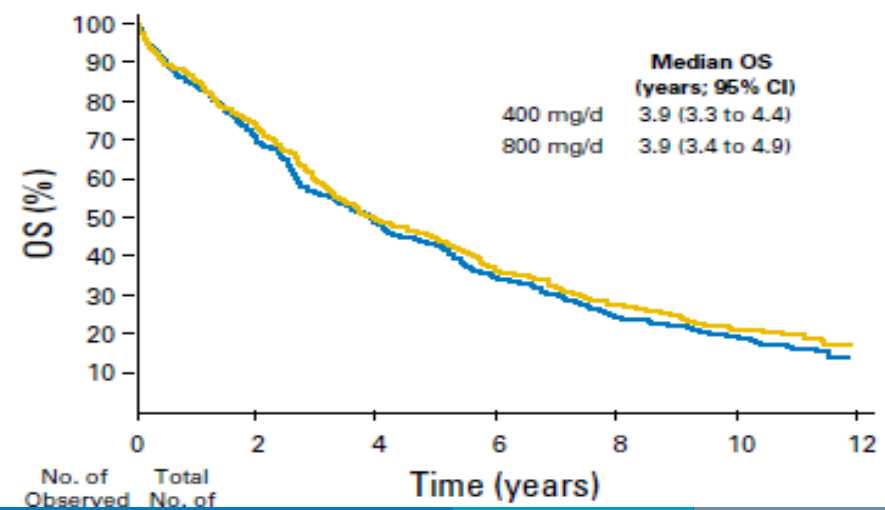
# Efficacy: Long term outcome of imatinib in EORTC phase 3 trial (Lancet 2004 and JCO 2017)



**A**



**B**

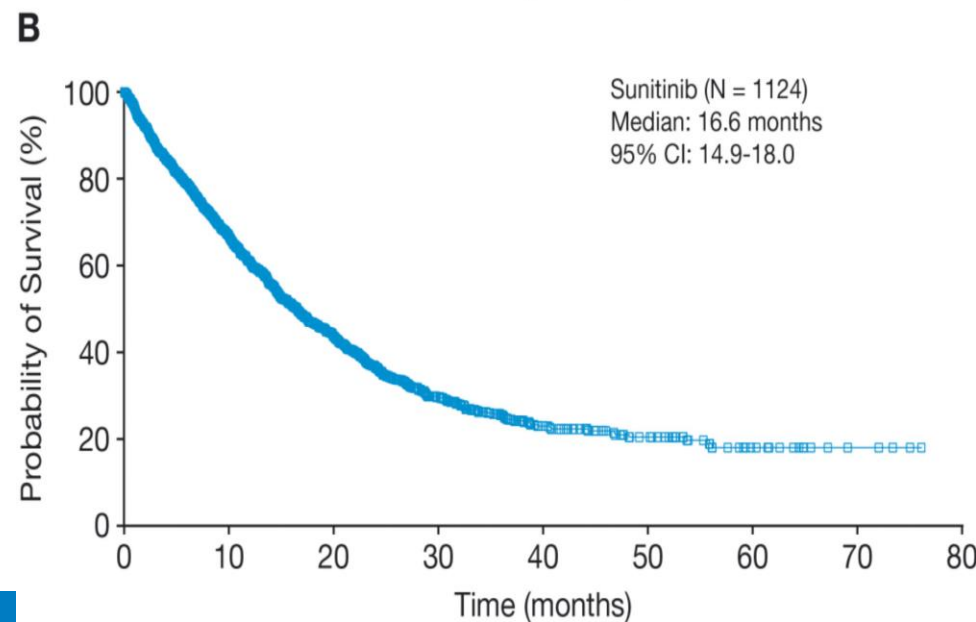
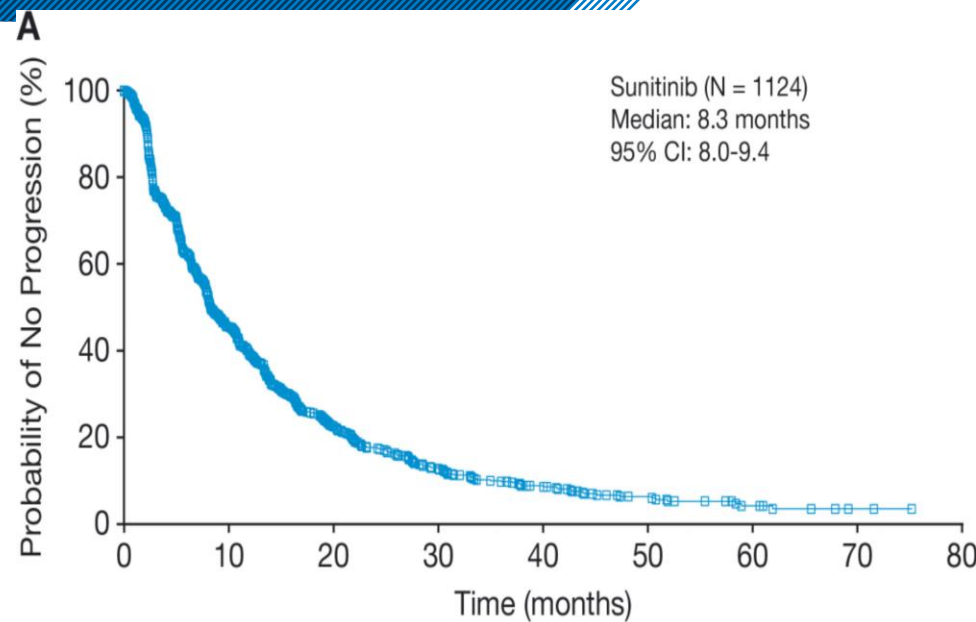
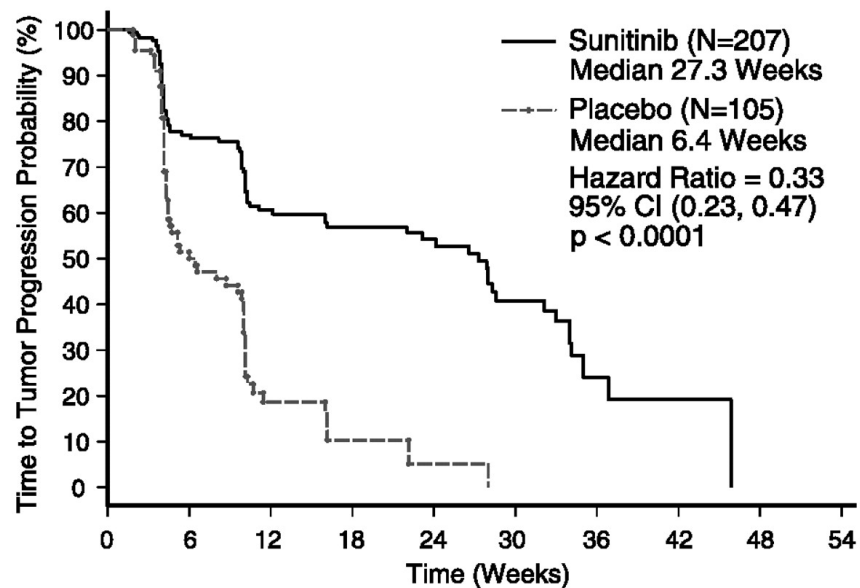


# How to become a long responder?

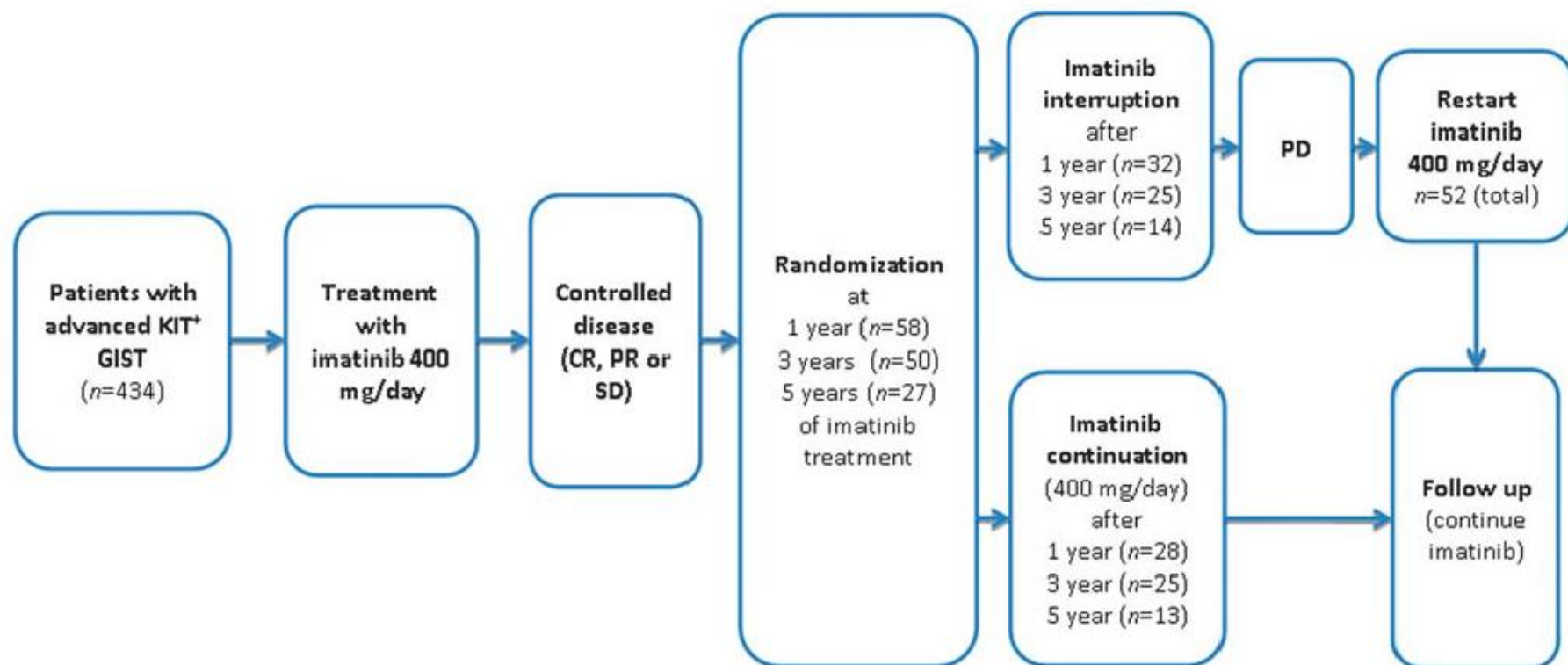
- Start at low tumor bulk
- So early diagnosis and treatment in progressing disease
- Adherence
  - Don't switch treatment too soon
- Consider local therapies for isolated progression
- Treatment in reference centers



# Sutent registration study vrs comp use



# What happens if we stop imatinib? BFR14 trial



Ann Oncol 2013



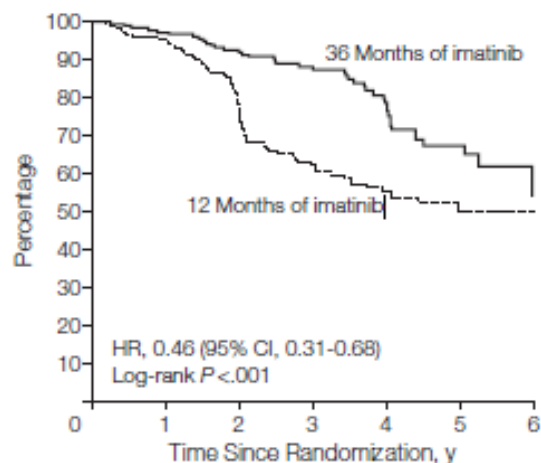
## Can we stop early or interrupt systemic treatment?

- Almost all patients progressed within 1 year after interruption
- High rate of tumour control achieved with re-initiation of treatment could allow periods of imatinib-free interval in cases of prolonged and uncomfortable side-effects.
- Rapid progression, a poorer quality of volumetric response at imatinib rechallenge and the growth of remaining persistent/resistant cells could impact the prolonged outcome of patients.
- For all these reasons, treatment interruption should not be recommended outside clinical trials unless patients experience substantial toxic effects.
- Although imatinib interruption may not affect the emergence of therapeutic resistance, the duration of response after imatinib reintroduction seems to be also influenced by the prior imatinib-free interval, since patients progressing rapidly after interruption had a dismal prognosis compared with those exhibiting a progression after  $\geq 6$  months.



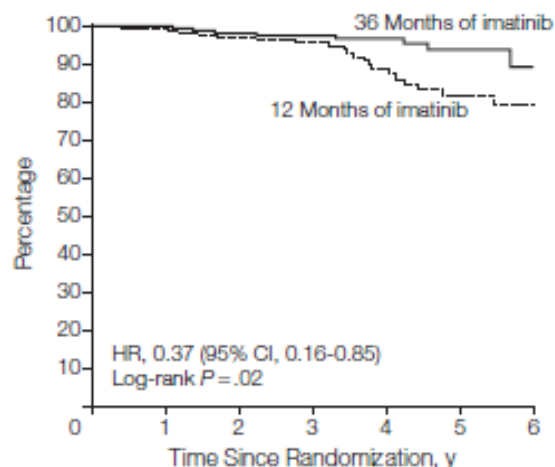
# GIST-adjutant imatinib: just a delay of progression?

**B** Recurrence-free survival: efficacy population



No. of patients	177	167	157	121	71	35	7
36 Months of imatinib	181	163	126	81	46	25	10
12 Months of imatinib							

**D** Overall survival: efficacy population



Imatinib for 3 years  
and regular follow up  
(standard treatment)

Imatinib for 5 years  
and regular follow up  
(extended treatment)

## Long term treatment

Influenced by plasma levels? (contradictory evidence)

Adherence seems to be high

Psychological factors

Reduce number of scans

GIST as chronic illness?



## Imatinib early toxicity versus late toxicity

Tumor burden related

Gastrointestinal symptoms

Periorbital edema

Skin rash

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Anemia

Muscle cramps

Fatigue

Eye symptoms

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Is it possible to stop after 10 years?  
Always consider comorbidity changes!

# Conclusions

GIST survival is increasing

QoL becomes just as important

Side effects may change and you can help us

Get treatment/guidance in reference centers and in studies!

