NCCS Cancer Policy Roundtable Meeting

Reinvigorating the Cancer Clinical Research Enterprise

Peter C. Adamson, M.D.
The Children's Hospital of Philadelphia

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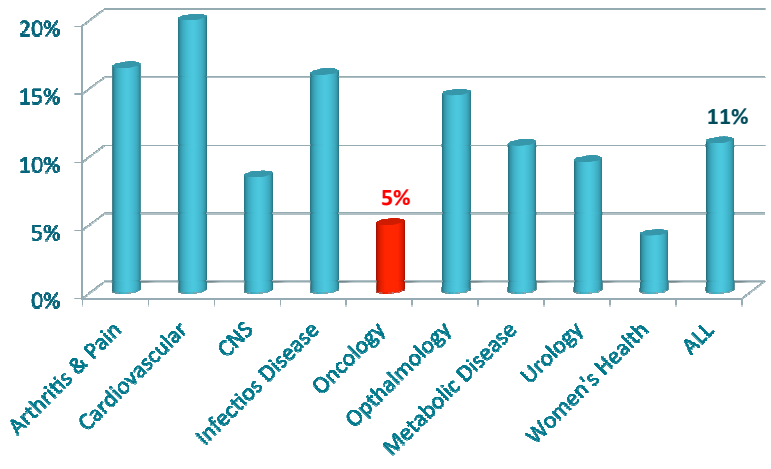
Success Rates for Drug Development



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Adapted from Nature Reviews: Drug Discovery, 3 (8): 711, 2004

NCI Cooperative Groups

A Brief History

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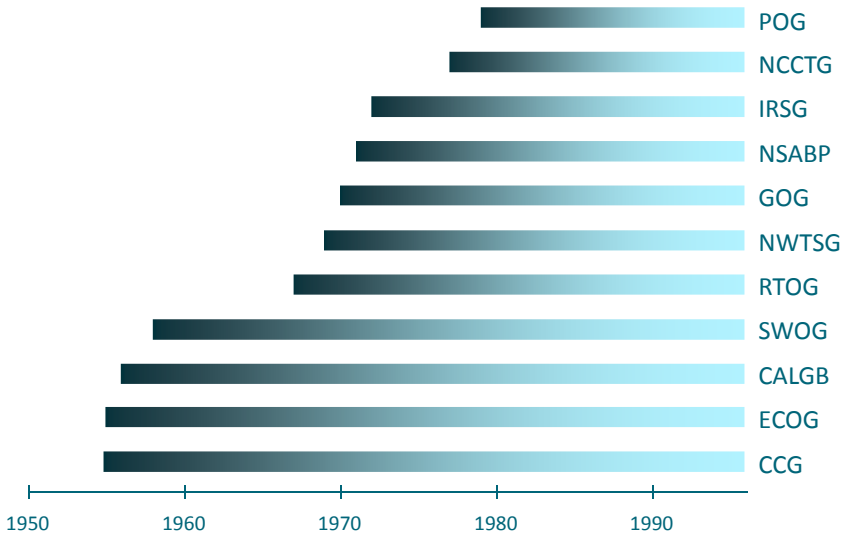
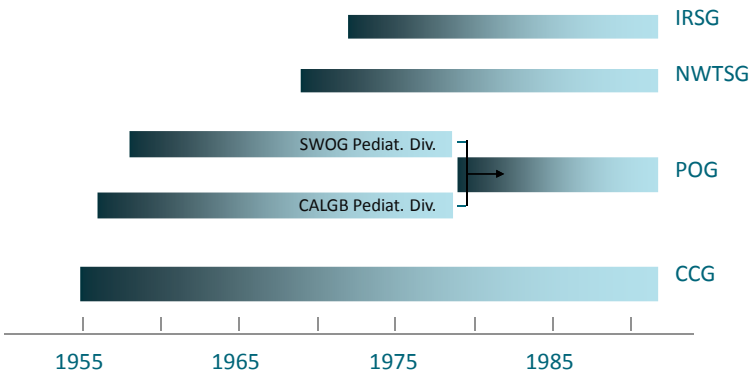
History of NCI Cooperative Groups



History of NCI Cooperative Groups



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History of NCI Cooperative Groups

POG
Pediatric Oncology Group

CCG

Children's Oncology Group

INTERGROUP
Rhabdomyosarcoma
STUDY GROUP

National Wilms' Tumor Study Group

2000

Group Mergers

- ECOG
- ACRIN

- RTOG
- NSABP
- GOG

- CALGB
- NCCTG
- ACOSOG

- SWOG

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New Drug Development Timelines

NCI Expanding Infrastructure

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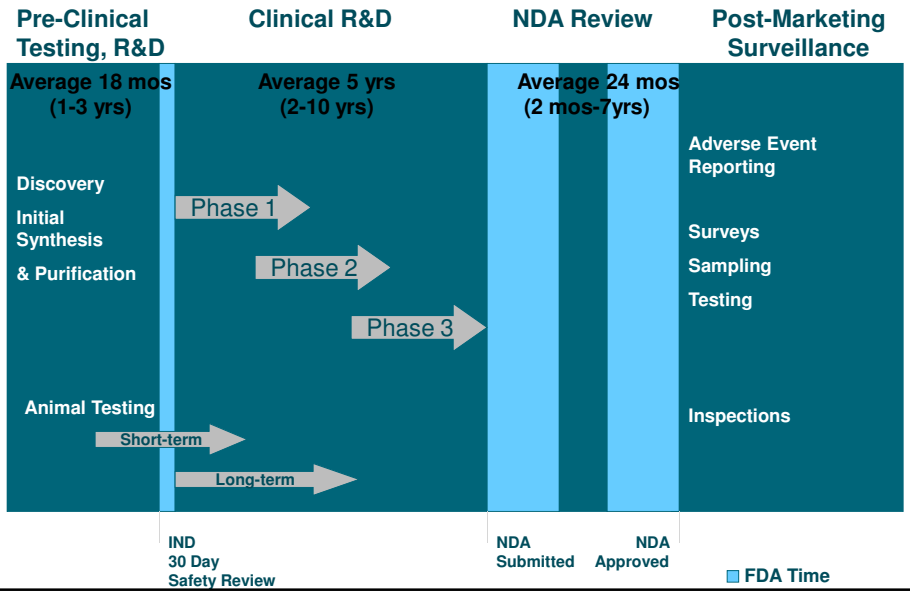
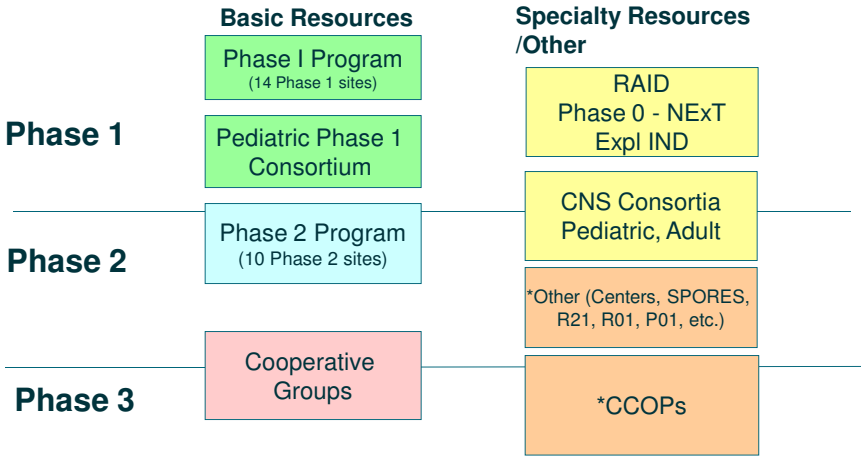
New Drug Development Timeline



CTEP Therapeutics Development



*Non-CTEP Funded Resources

Courtesy of Jeffrey Abrams, MD NCI-CTEP

New Drug Development Timelines

Clinical Trials

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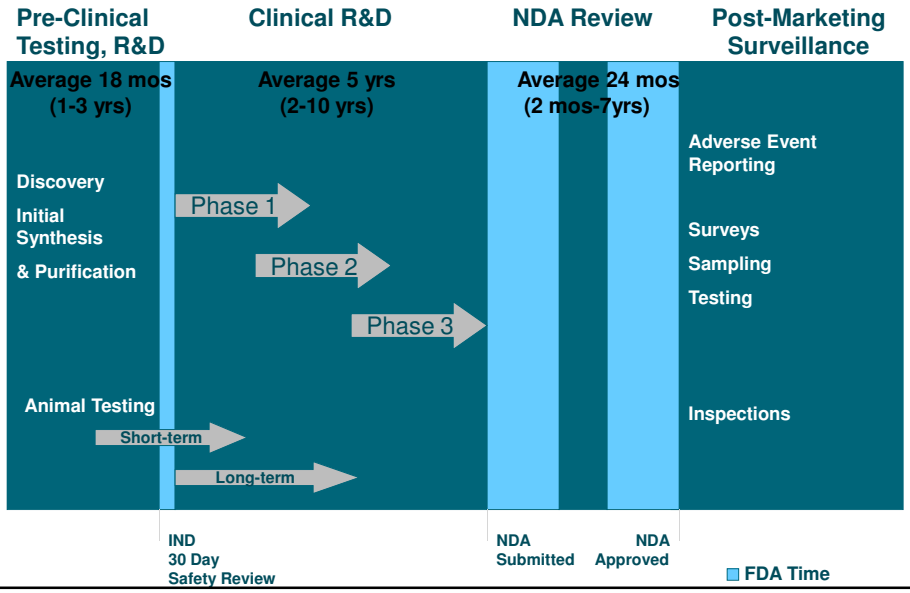
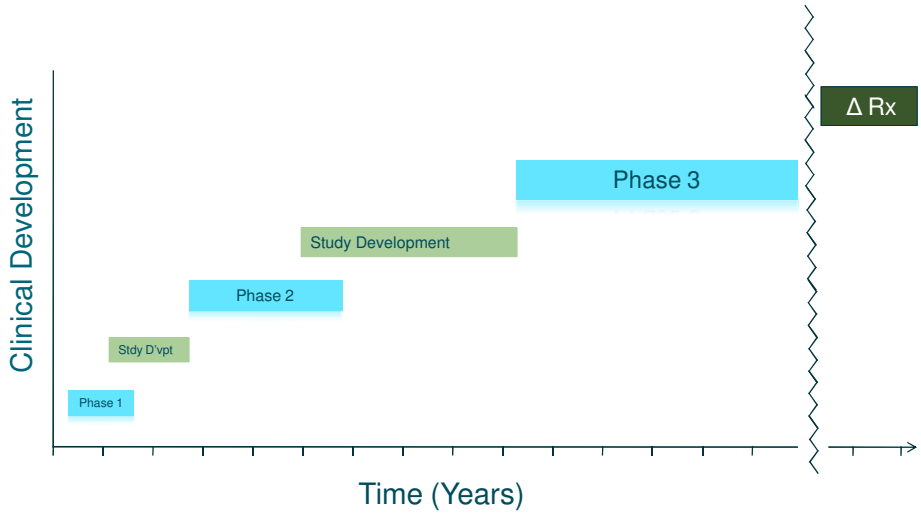
New Drug Development Timeline



Clinical Development Timeline



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Concept to Trial Timeline

Clinical Trial Idea Creation

Concept Development

Concept Approved

Process Takes up to 7 Years

Courtesy of David Dilts

New Drug Development Timelines

Investigator Perspective

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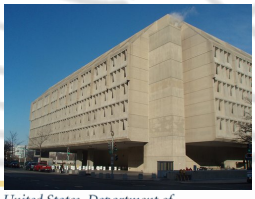
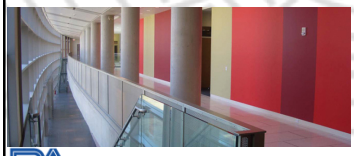


United States Department of Health & Human Services

Academia

NATIONAL INSTITUTES OF HEALTH



FDA U.S. Food and Drug Administration

Industry

Scientific Review

Concept Incubation

Idea → Disease Committee Review → Cooperative Group Review → Concept

- Target
- Drug
- Patient Population

- Competing Ideas
- Research Landscape

- Scientific Mission
- Prioritization
- Resources

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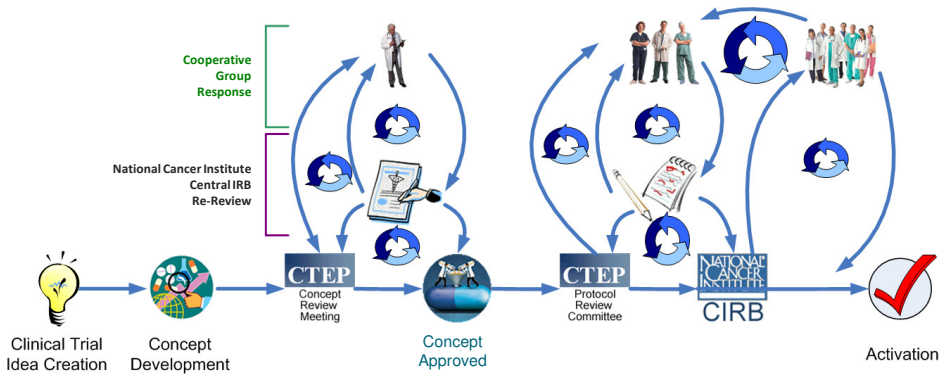
Concept to Trial Timeline



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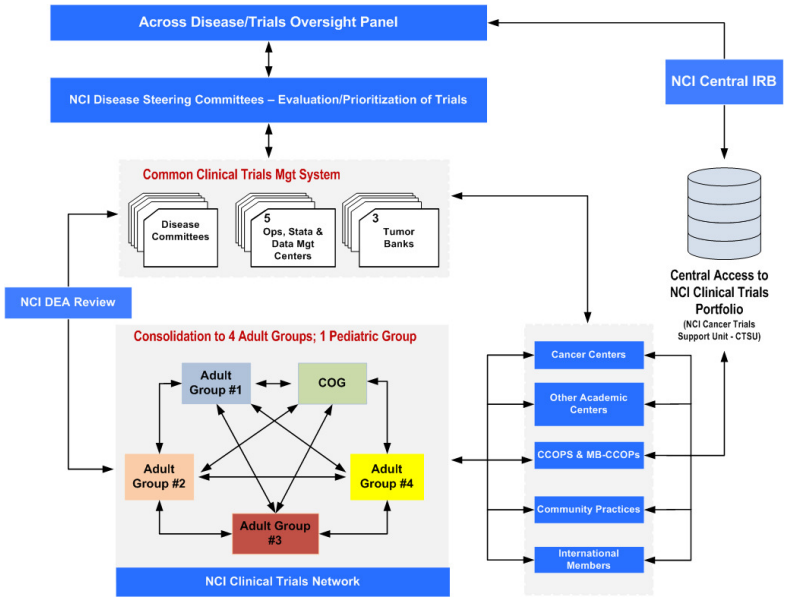
Courtesy of David Dilts

National Cancer Institute

Proposed New Organizational Structure of the Program



Fail Early

Sept-Oct 1998 — Google

Nov 1998 – July 1999 — Google!

Aug 1999 - Present — Google

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"I have not failed, I have just found 10,000 ways that won't work"

Thomas Edison

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Clinical cancer research needs a system that can strategically fail early

Cooperative Group Clinical Trials

- Efficient
- Effective

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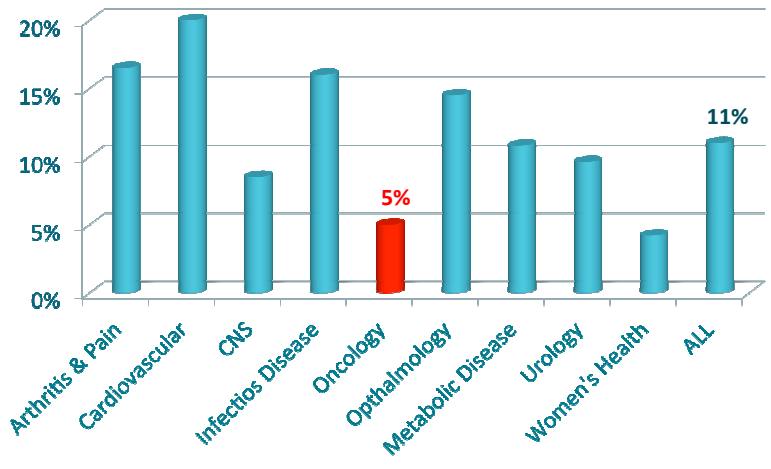
Success Rates for Drug Development



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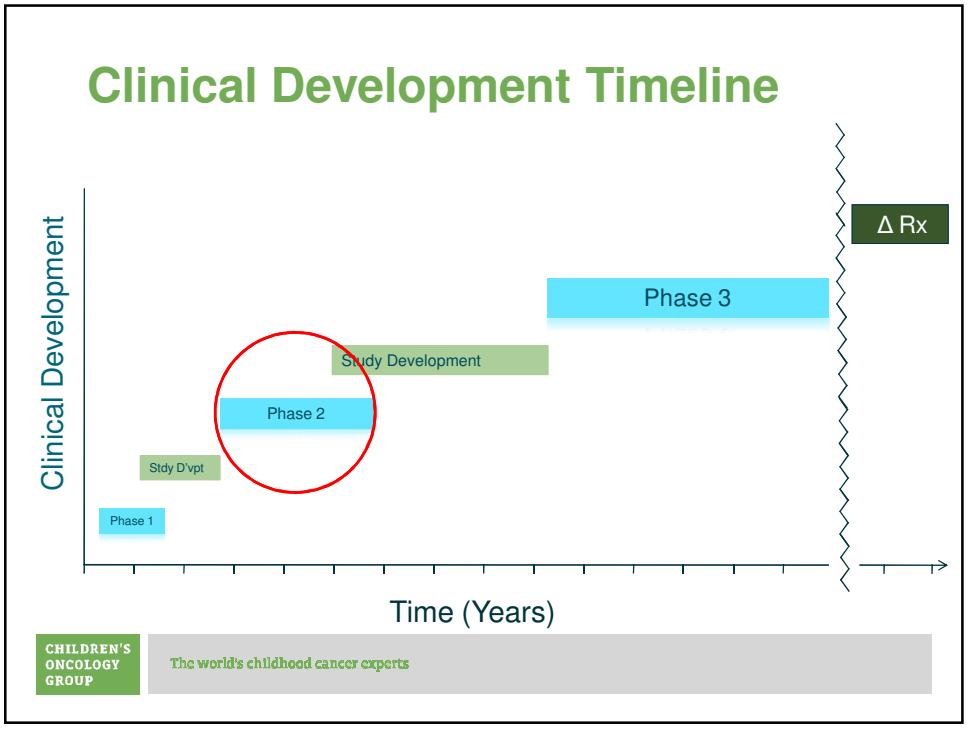

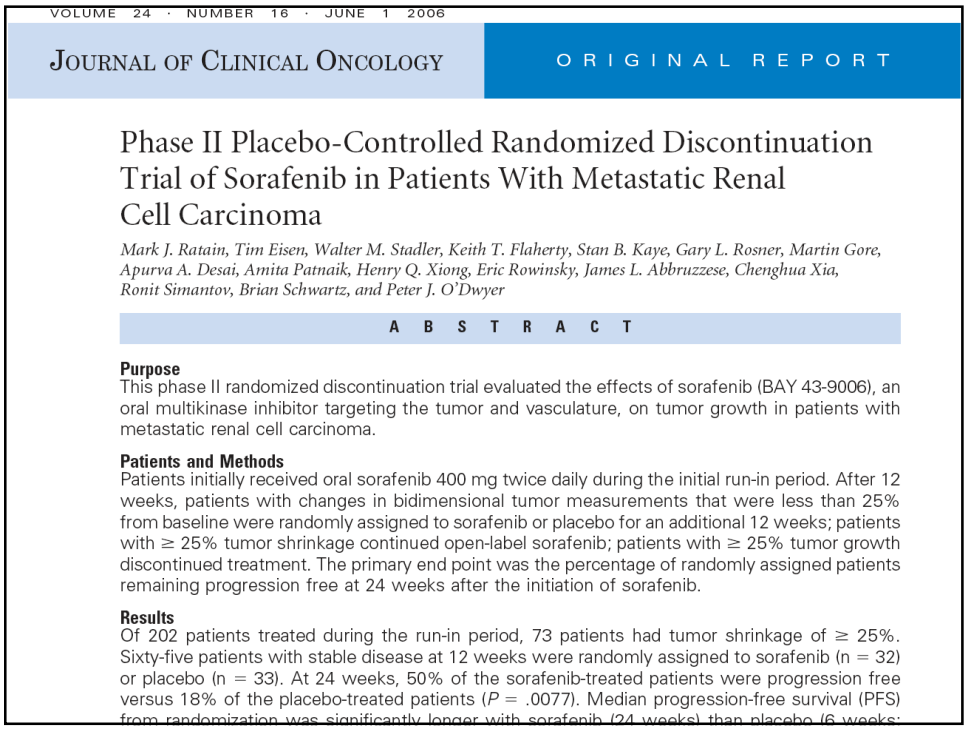

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ORIGINAL REPORT

Phase II Placebo-Controlled Randomized Discontinuation Trial of Sorafenib in Patients With Metastatic Renal Cell Carcinoma

Mark J. Ratain, Tim Eisen, Walter M. Stadler, Keith T. Flaherty, Stan B. Kaye, Gary L. Rosner, Martin Gore, Apurva A. Desai, Amita Patnaik, Henry Q. Xiong, Eric Rowinsky, James L. Abbruzzese, Chenghua Xia, Ronit Simantov, Brian Schwartz, and Peter J. O'Dwyer

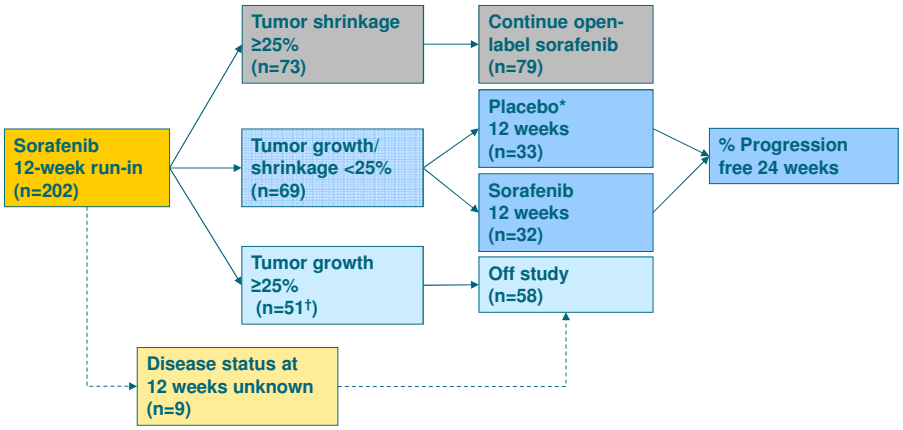
A B S T R A C T

Purpose
This phase II randomized discontinuation trial evaluated the effects of sorafenib (BAY 43-9006), an oral multikinase inhibitor targeting the tumor and vasculature, on tumor growth in patients with metastatic renal cell carcinoma.

Patients and Methods
Patients initially received oral sorafenib 400 mg twice daily during the initial run-in period. After 12 weeks, patients with changes in bidimensional tumor measurements that were less than 25% from baseline were randomly assigned to sorafenib or placebo for an additional 12 weeks; patients with ≥ 25% tumor shrinkage continued open-label sorafenib; patients with ≥ 25% tumor growth discontinued treatment. The primary end point was the percentage of randomly assigned patients remaining progression free at 24 weeks after the initiation of sorafenib.

Results
Of 202 patients treated during the run-in period, 73 patients had tumor shrinkage of ≥ 25%. Sixty-five patients with stable disease at 12 weeks were randomly assigned to sorafenib (n = 32) or placebo (n = 33). At 24 weeks, 50% of the sorafenib-treated patients were progression free versus 18% of the placebo-treated patients (P = .0077). Median progression-free survival (PFS) from randomization was significantly longer with sorafenib (24 weeks) than placebo (6 weeks;

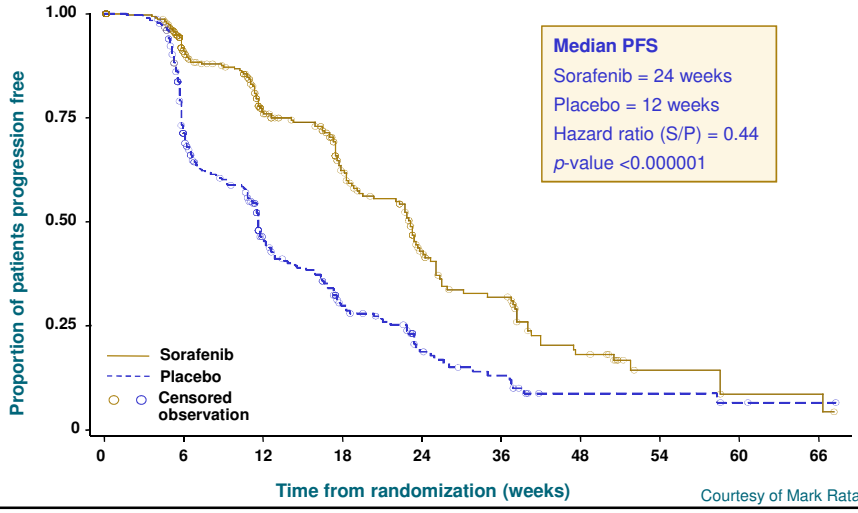
Study Design: Patient Flow



*Placebo patients who progressed could cross over to sorafenib
†Including 36 patients without bidimensional tumor measurements, but with radiological evidence of progression

Courtesy of Mark Ratain, MD

Progression Free Survival: Randomized Patients



Courtesy of Mark Ratain, MD

Smart Drugs

Smart Trials