



Navigating GIST Clinical Trials

The Life Raft Group

June 12, 2008



Some observations:

“Annually, only 3% of adult patients participate in cancer clinical trials.”

Lara et. al; Evaluation of factors affecting awareness of and willingness to participate in cancer clinical trials; *Journal of Clinical Oncology*, 2005 Dec 20;23(36):9282-9.
<http://jco.ascopubs.org/cgi/reprint/23/36/9282>

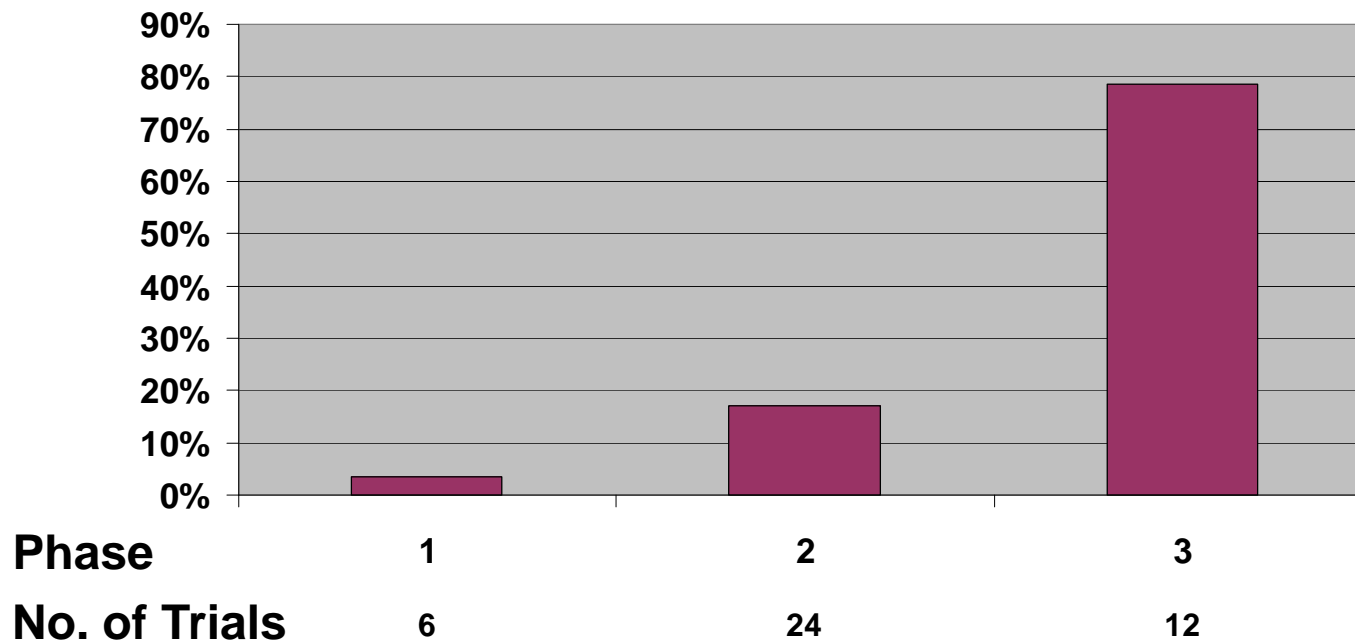
“Of all patients approached with a trial, 75% consented but no more than 20% of patients who were eligible were offered a trial...”

Siminoff, Thomas; Why Learning to Communicate With Our Patients Is So Important: Using Communication to Enhance Accrual to Cancer Clinical Trials *Journal of Clinical Oncology*, Vol 26, No 16 (June 1), 2008: pp. 2614-2615
<http://jco.ascopubs.org/cgi/content/full/26/16/2614>

GIST Treatment Trials Starting 2000-2008

(From clinicaltrials.gov)

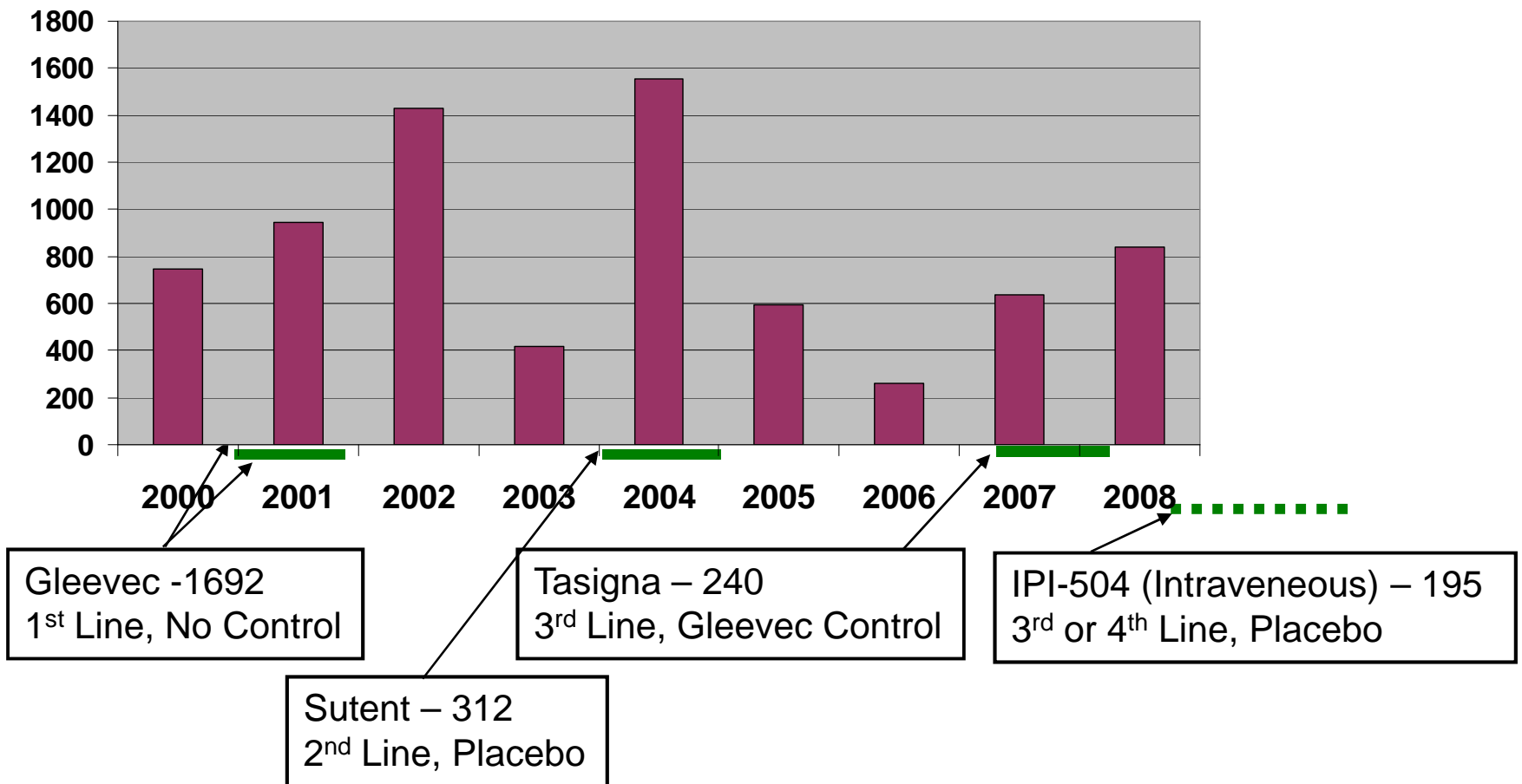
Planned Accrual (% of Total) by Trial Phase



Worldwide Planned Accrual 2000-2008
7,365 patients in Phases 1-3
Includes Adjuvant Trials

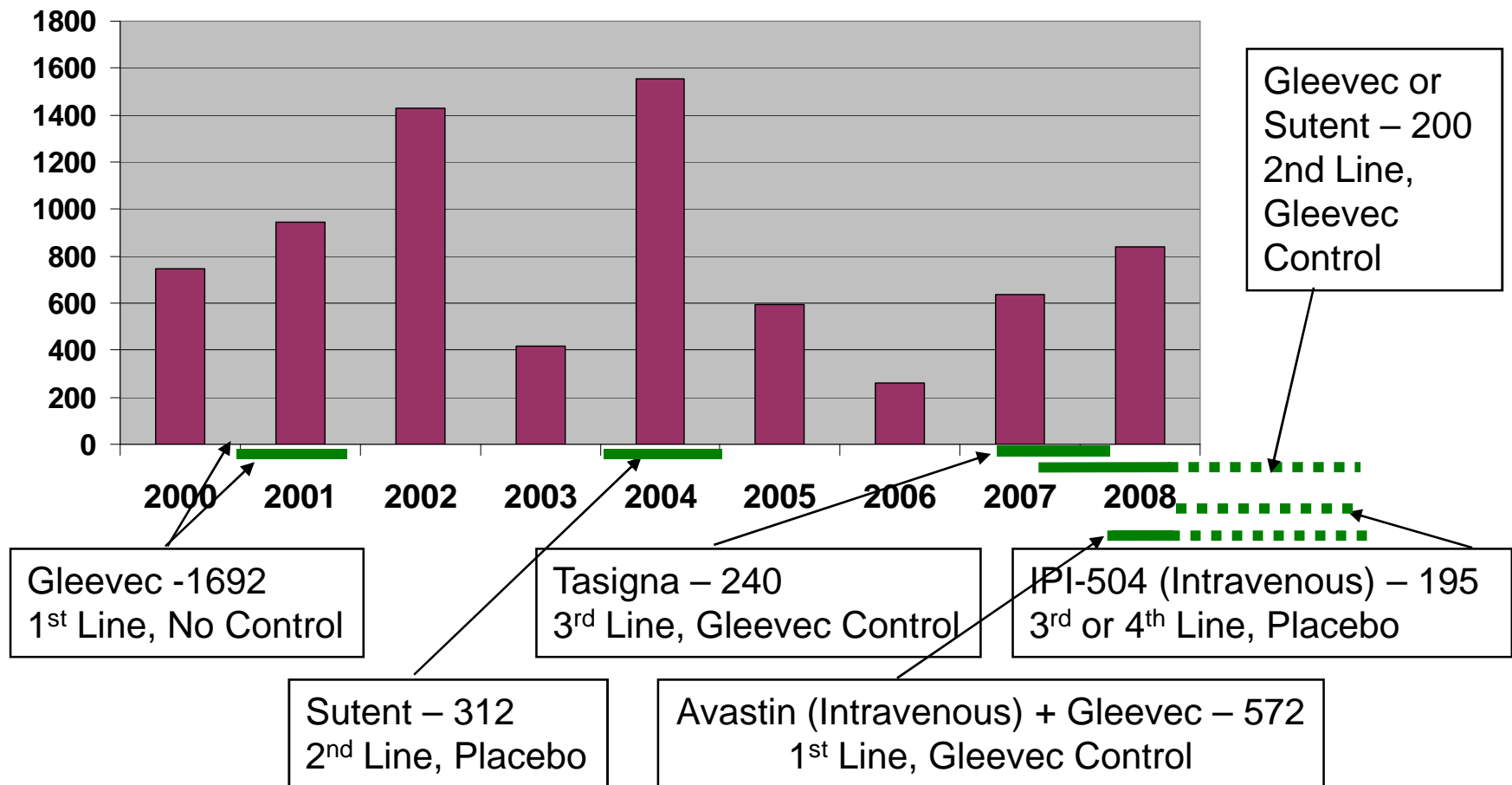


Planned Accruals by Trial Start Year, Phase 1-3 GIST Treatment Trials Worldwide in ClinicalTrials.gov





Planned Accruals by Trial Start Year, Phase 1-3 GIST Treatment Trials Worldwide in ClinicalTrials.gov





Today's Objectives

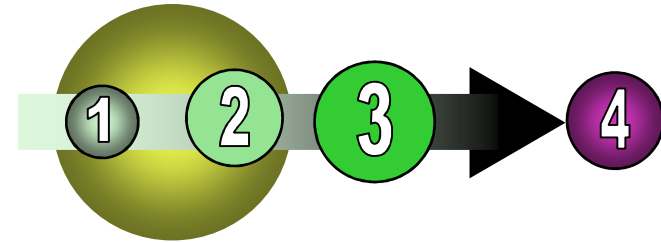
- What are clinical trials?
- How do I find GIST trials?
- What do you look for in a trial?
- What are the LRG Tools for finding Trials.
- How do You Decide on a Trial?
- What is new in GIST Trials?



What are clinical trials?

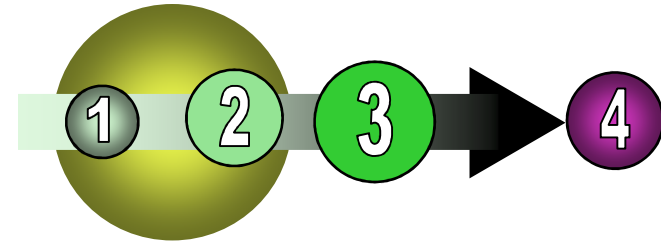
- Phases: I-4
- Types: Interventional, Observational
- Designs:
 - Inclusion Criteria: Newly Diagnosed vs. Pre-Treated
 - Controls: Active, Placebo
 - Neo-Adjuvant/Adjuvant

Phase 1



- Is the drug safe?
 - ❑ Usually 20-60 patients at one or a few sites
 - ❑ First use of drug in humans
 - ❑ Determines whether patient can tolerate the dosage given *MTD* – Max Tolerable Dose
 - ❑ Early patients may not get a therapeutic response because they are on the lowest dosage.
 - ❑ Later patients may have increased risk of side effects due to a very high dosage level.

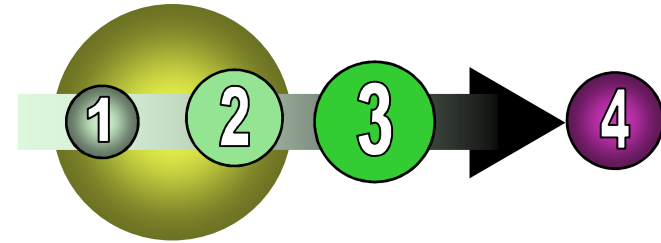
Phase 2



- Is the drug effective in treating GIST?
 - Usually 100-300 patients at 3-10 sites
 - Can be combined with Phase 1

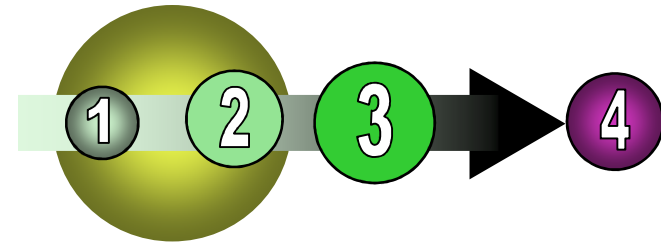
Gleevec was approved for GIST based on Phase II trial results

Phase 3



- Is the treatment better than current standard?
 - Compare trial treatment to current standard of treatment for GIST
 - Usually 300-1,000 patients at 10-100 sites
 - Often Randomized
 - Active Control
 - Placebo Control

Phase 3

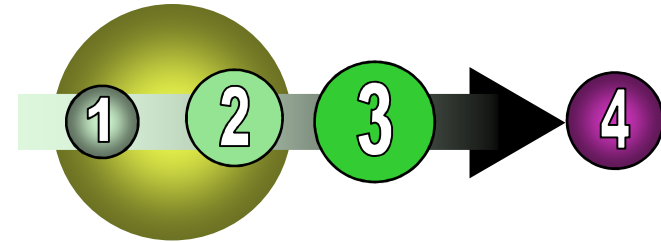


- Is the treatment better than current standard?
 - Compare trial treatment to current standard of treatment for GIST
 - Usually 300-1,000 patients at 10-100 sites
 - Often Randomized
 - Active Control
 - Placebo Control

Current Phase III Trials in GIST

- *Gleevec with/without Avastin, Gleevec Control – US, Canada*
- *Sutent or Gleevec, Gleevec Control – US and International*
- *IPI-504, Placebo Control – US and International (pending)*

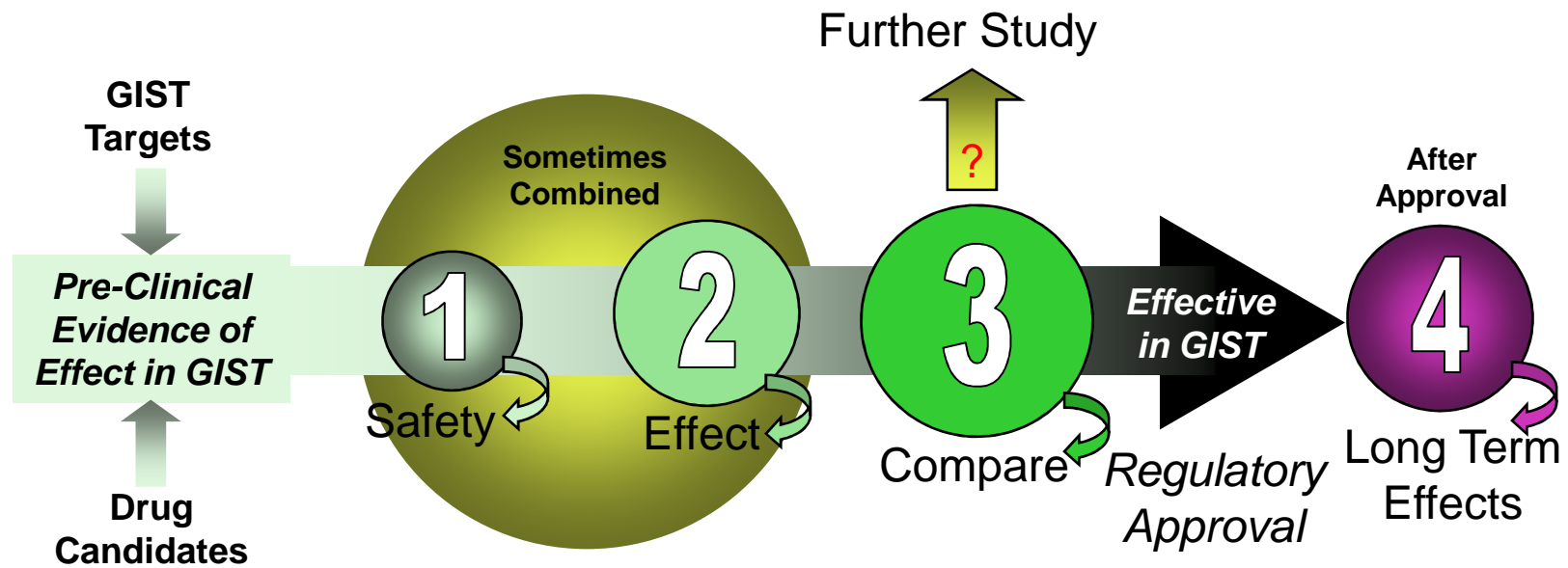
Phase 4



- Post Approval

- Studies long-term side effects and efficacy

Clinical Trial Phases



• *Approx 10% of drugs that start get approved*



Types of Trials

- Intervention

- Drug – 98% of GIST Trials
- Radiation
- Procedure
- Observation

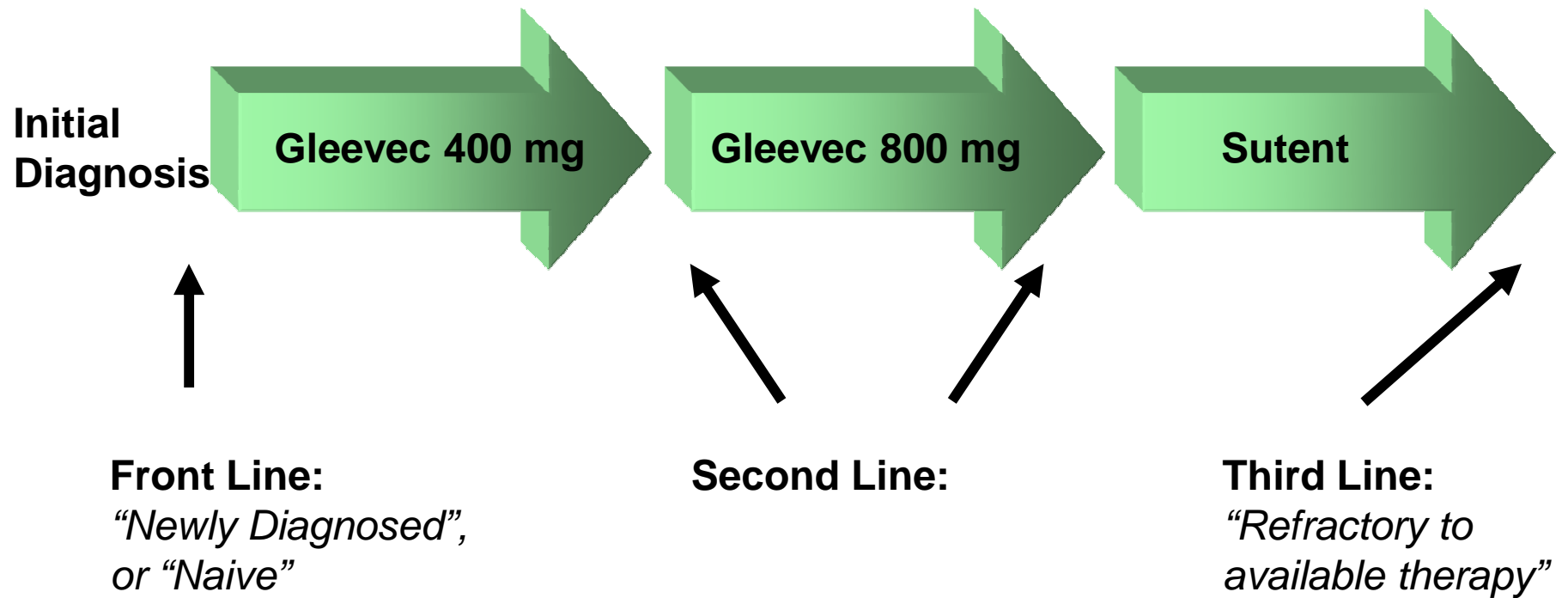


FDA Procedures that look like trials

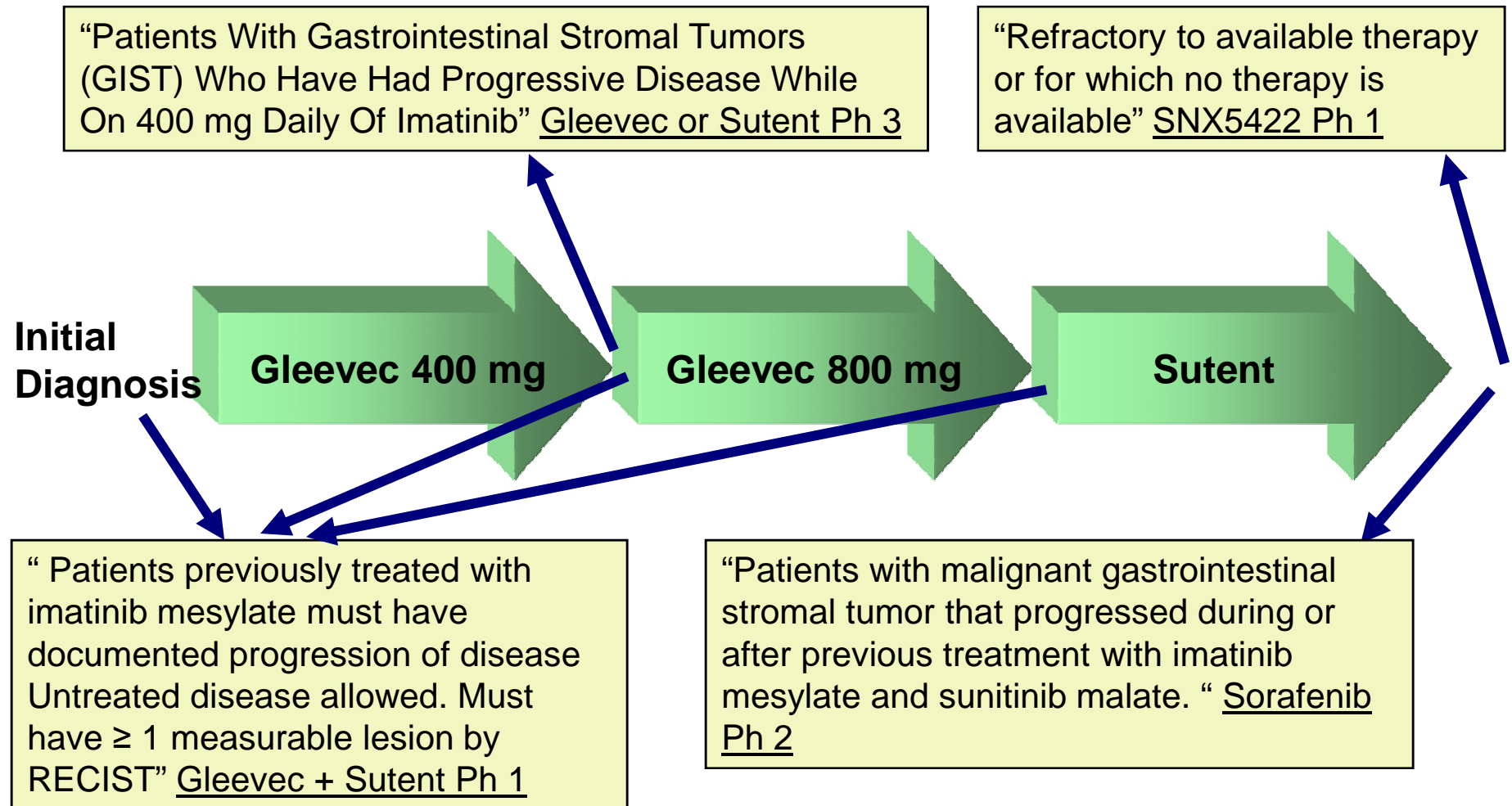
- Expanded access
- Treatment IND
- Compassionate access

Trial Designs

Newly Diagnosed vs. Pre-Treated



Newly Diagnosed vs. Pre-Treated



Always ask the clinical trial site....



Newly Diagnosed vs. Pre-Treated

- Prior treatment dose requirements
 - Failed at Minimum 400 mg Gleevec
(AMN107 Phase 3)
 - Failed at Minimum 50 mg Sutent
(Sorafenib Phase 2)
- Restrictions on prior therapies
 - No TKI's other than Gleevec and Sutent
(AMN107 Phase 3)
 - No prior HSP-90 therapy
(IPI-504 Phase 3)

Trial Design

- Randomized

- Two + arms – experimental and controls
- Patients assigned randomly to an arm
- Double Blinded – Patients and Site team unaware which arm patients are assigned.

- Controlled

- Active – Usually current standard treatment
- Active/Historical - Patients continue prior therapy
- Inactive – Placebo: No treatment



Trial Design



- Neo-Adjuvant

- Before surgery to reduce the size of the tumors and to reduce the need to remove healthy tissue

- Adjuvant

- After surgery where all detectable disease has been removed, but where there remains a statistical risk of relapse due to microscopic disease

Remember: Before & After

How do I find GIST trials?

ClinicalTrials.gov



A public service of the US National Institutes of Health

- 23,926 Active trials of all types worldwide
- 7,634 Active cancer trials worldwide
- 4,976 Active cancer trials in US

Cancer.gov



A public service of the National Cancer Institute

- 7,563 Active cancer trials worldwide
- 4,743 Active cancer trials in US

As of 2:30 pm CDST 6/5/08

ClinicalTrials.gov



- **Guidance for Industry Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions:** March 2002, Center for Drug Evaluation and Research (CDER), FDA, USDHHS.

“Section 113 of the Modernization Act requires you (Industry) to submit information to the data bank about a clinical trial conducted under an investigational new drug (IND) application if it is for a drug to treat a serious or life-threatening disease or condition and it is a trial to test effectiveness (42 U.S.C. 282(j)(3)(A)).”

“The data bank was established as required under section 113 of the Food and Drug Administration Modernization Act of 1997 (Modernization Act). “

Standard Searches

- Starting points

www.clinicaltrials.gov

www.cancer.gov

- For category searches select:

“Gastrointestinal Stromal Tumor”

- For keyword searches try the line below with the quotes:

“gastrointestinal stromal” OR “gastro-intestinal stromal” OR GIST

Remember : “You say tumor...I say tumour”

So skip the word ‘tumor’. You don’t need it!.... 😊



Registry Comparison

- NIH/NLM: clinicaltrials.gov

- Required by FDA
- Probably more complete
- All sites all trials
- Easy to bookmark a search
- Map
- Downloadable data
- RSS Feed “Changes within last 14 days”



- NCI: cancer.gov

- Cancer only
- Mirrors NIH/NLM
- Recruiting sites in active trials only
- Suggested search terms and lists
- “Within miles of Zip code” search
- Patient version
- Occasionally has more site contact info
- Good other resources for patients



When in doubt – use both

Standard Searches

- Searching with the pre-defined condition category “Gastrointestinal Stromal Tumor” for Active Trials
 - clinicaltrials.gov - 40 Trials
 - cancer.gov - 53 Trials
 - emergingmed.com - 92 Trials

We are currently reporting on 32 trials of these trials in the US and Internationally





Standard Search Issues

- Sometimes trials for “Gastrointestinal Neoplasms” are included as GIST
- Some Phase I trials for “Solid Tumors” “Soft Tissue Sarcoma” or Sarcoma will accept GIST patients but are not included. (EmergingMed seems to include them all!)
- Trials mentioning GIST but not for GIST get included.

Another observation...

“The Center for Information and Study on Clinical Research Participation (CISCRP)—online survey in 2005 among nearly 5000 (public) registry users



“Registry users most want easy-to-process, summary trial information; details on whether the trials are being conducted in conveniently accessible locations; and investigative site contact information.”

” Getz; Forgotten Voices in the Transparency Debate; Applied Clinical Trials, April 1, 2006;
<http://appliedclinicaltrialsonline.findpharma.com/appliedclinicaltrials/article/articleDetail.jsp?id=316473&pageID=1&sk=&date=>

LRG Resources

- The LRG Newsletter

Battling gastrointestinal stromal tumor



**LIFE RAFT
GROUP**

June 2008

In memory of Tony Paonessa, Ronna Lindeken, Jim Barth, Nancy Romero, Brian Denkers, Alice Greenwood & Tony Petruzzello

Vol. 9, No. 6

June 2008 US clinical trials update

By Jim Hughes
LRG Science Team member

AMN107 Phase III: This trial has met accrual goals and enrollment is now closed.

Sunitinib or Imatinib: Five new sites have been added in the United States. Four new international sites have also been added:

1. Lai Chi Kok, Kowloon, Hong Kong
2. Tuen Mun, New Territories, Hong Kong
3. Milano, Italy, 20133,
4. Seoul, Republic of Korea, 135-710

Imatinib + Pegylated Interferon-a 2B: This trial now has an NCT number and the contact information has changed. Contact Jessica Moehle, 801-587-4438 at the Huntsman Cancer Institute.

Sorafenib Phase II: Contact information has been updated.

Perifosine + Sunitinib: Trial is ongoing but not recruiting.

Imatinib or Sunitinib

Safety and effectiveness of daily dosing with sunitinib or imatinib in patients with GIST

Phase: III
Conditions: GIST
Strategy: Inhibit KIT and/or impede tumor vascularization

Imatinib + Pegylated Interferon-a 2B

Phase II study combines targeted therapy with immunotherapy. Imatinib + Pegylated Interferon-a 2B in imatinib-naïve GIST patients

Phase: II
Conditions: GIST
Strategy: Kill GIST cells
NCT#: NCT00585221
Contact: **Huntsman Cancer Institute**
University of Utah, Salt Lake City, Utah
Jessica Moehle
Telephone: 801-587-4438

Perifosine + Imatinib

Phase II study of Perifosine + Gleevec in GIST patients

Phase: II
Conditions: GIST
Strategy: Multiple Targets
NCT#: NCT00455559
Contact: **Online Collaborative Onc. Group**
ocogtrials@ocog.net
Telephone: 415-946-2410
Sites: Los Angeles, Calif.
Sant Chawla, Md.
Coeur D'Alene, Idaho
Park Ridge, Ill.
Oncology Specialists
Kathy Tolzein, RN
847-268-8200
Grand Rapids, Mich.
Savva, Penn

Sorafenib (Nexavar)

Sorafenib in treating patients with malignant GIST that progressed during or after previous treatment with imatinib and sunitinib.

Phase: II
Conditions: GIST
Strategy: Multiple Targets
NCT#: NCT00265798
Contact: **Univ. Of Chicago Cancer Res. Center,**
Chicago, Ill.
Ravi Salgia, MD
rsalgia@medicine.bsd.uchicago.edu
Blase Polite, MD
bpolite@medicine.bsd.uchicago.edu
Telephone: 773-834-7424
Sites: **City of Hope,** Duarte, Calif.
Warren Chow, MD, 626-256-4673
USC-Norris Cancer Center,
Los Angeles, Calif.
Hein-Josef Lenz, MD,
323-865-3955
UC-Davis, Sacramento, Calif.
David Gandara, MD,
916-734-3771
Decatur Memorial Hospital,
Decatur, Ill.
James Wade, MD, 217-876-6617
Oncology/Hematology Assoc.,
Peoria, Ill.
John Kugler, MD, 309-671-5180
James Knost, MD,
jknost@ohaci.com
Central Illinois Hem/Onc,
Springfield, Ill.
Edem Agamah, MD, 217-525-2500
Univ. of Michigan, Ann Arbor, Mich.
248-763-2121

LRG Resources

■ The Web Page:

http://www.liferaftgroup.org/treat_trials.html

The screenshot shows the Life Raft Group website. At the top, there is a navigation bar with the logo "LIFE RAFT GROUP" and the tagline "ensuring that no one has to face GIST alone". To the right of the logo is a search bar labeled "Enter Search Term" and a "Make a Difference DONATE TODAY" button. Below the navigation bar is a main content area with six columns of links: "About the LRG", "Patient Support", "LRG Research", "LRG Library", and "Medical Professionals". On the left side of the main content area, there is a sidebar with a photo of a woman and child, and a text box that reads: "My name is Barbara. I am the mother of three children and the Nonna to six grandchildren." Below the main content area, there is a "Clinical Trials" section with a large "C" icon. This section is divided into two columns: "Navigating Clinical Trials" and "GIST Clinical Trial Maps".

LIFE RAFT GROUP
ensuring that no one has to face GIST alone

Enter Search Term

Make a Difference
DONATE TODAY

HOME

About the LRG
Who We Are
Join
Contact Us
News
LRG Members

Patient Support
Our Newsletter
Request Pamphlets
Join Support Group
Talk to Us
International Support

LRG Research
Our Research
Patient Registry
Tissue Banks
Familial GIST
How You Can Help

LRG Library
Newsletters
Webcasts & Videos
Publications
Books
Links

Medical Professionals
Register as Specialist
Subscribe to Newsletter
Your Patient Support
Clinical Trials
Our Research

About GIST
Understanding GIST
Initial Treatment
Preventative Treatment
Managing Recurrence
Survival Strategies
Pediatric GIST
Familial GIST

Frequent Topics
Gleevec
Sutent
Surgery
Mutational Testing
Side Effects
FAQs

Accessing Treatment
Advocacy
Clinical Trials
Financial & Logistical

Clinical Trials

Navigating Clinical Trials
Links to other pages on this website

[Main Clinical Trial Page](#)
[Clinical Trial Results](#)
[Preventative Treatment Trials](#)
[Definitions](#)
[GIST Cancer Center Trial List](#)
[Predefined Trial Searches](#)

Latest clinical trial information (Updated May 2008-PDF-64KB)!!

[Navigating Clinical Trials Pamphlet](#)

GIST Clinical Trial Maps
Links to ClinicalTrials.gov web site. Click on region, country and state to drill down to detail listings.

[US trials](#)
[European Trials](#)
[World Trials](#)
[Adjuvant Trials](#)
[US - HSP-90 Trials](#)
[US - PI3K Trials](#)

LRG Resources

■ LRG Brochure – “Navigating GIST Clinical Trials”

http://www.liferaftgroup.org/docs/Pamphlets/Clinical_Trials.pdf

Clinical Trial Phases:

Before it is tested in humans, a new drug must exhibit some effectiveness against GIST in the lab. Candidate drugs from the lab enter clinical trials that are designed to answer fundamental questions about the drug in humans.

Phase 1: Is the drug safe?
 • Usually 20-60 patients at one or a few sites
 • First use of drug in humans
 • Determines whether patient can tolerate the dosage given
 • Early patients may not get a therapeutic response because they are on the lowest dosage. Later patients may have increased risk of side effects due to a very high dosage level.

Phase 2: Is the drug effective in treating GIST?
 • Usually 100-300 patients at 3-10 sites
 • Can be combined with Phase 1

Phase 3: Is the drug better than current standard?
 • Compares drug to current standard of treatment for GIST
 • Usually 300-1,000 patients at 10-100 sites

Phase 4: Post Approval
 • Studies long-term side effects and efficacy

Five-Year GIST Survivors at Life Fest 2006

You do not face GIST alone

The Life Raft Group was formed in 2000 by GIST patients, many of whom were participants in the Phase II trial of STI-571 (Gleevec/Glivec). Many of those patients are still here today because they made the choice to participate. Gleevec is available today because of those first GIST patients who stepped forward. To have GIST is to be a member of a community actively pursuing a cure.

International Patients

Patients outside the United States who try to enter a clinical trial in another country may have a different process to go through than U.S. citizens. To learn more about international access to clinical trials, visit the Global GIST Network at www.globalgist.org.

The Life Raft Group

The LRG is an international patient support organization for people with GIST and their family members. The mission of the Life Raft Group is to ensure the survival of GIST patients while maintaining the quality of their lives. To accomplish this mission the Life Raft Group devotes its efforts to: Information & Support, Treatment Surveillance, Research, Patient Consultation & Assistance, and Advocacy.

Contact Us

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 Fax: 973-837-9095
www.liferaftgroup.org
 E-mail: liferaft@liferaftgroup.org

Special Thanks

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Navigating GIST Clinical Trials

An easy-to-use guide about GIST clinical trials and tips to help you decide which trial to choose

Ensuring that no one has to face GIST alone

GIST stands for gastrointestinal stromal tumor. This pamphlet is intended to answer some of your questions about GIST clinical trials. It is intended to guide those considering options after treatment failure. It is not a substitute for your physician's guidance and care.



More Details about Clinical Trials

- ClinicalTrials.gov – “Understanding Clinical Trials”
<http://clinicaltrials.gov/ct2/info/understand?flds=Xabj>
- Cancer.gov – “Educational Materials”
<http://www.cancer.gov/clinicaltrials/learning>



Deciding - What are the benefits?

- Option to access treatment after standard treatment fails
- Receive treatment at major GIST trial center
- Expanded treatment options
- Help future GIST patients



Deciding - What are the risks?

- The new drug may not work for you
- Side effects may occur
- Additional testing, time and travel
- Some costs may not be covered by insurance



How to choose a clinical trial

Decide on a set of criteria that are important to you. This will keep you focused. Examples:

- Proximity to home, job and family
- Sarcoma expertise of physician
- Potential drug risks and benefits
- Follow-up schedule and options
- Newer untried strategy



Ask Questions

- How does the new treatment work differently for you?
- Which trial offers the best chance of survival?
- What are the chances it will benefit you?
- What are the options if the trial does not work for you?
- Will this trial limit future options?
- How much time do you have to decide?
- If phase 1, will the dose be therapeutic?

High Stakes Decision Making*



1. Allow yourself the time to decide.
2. Get emotional support.
3. Make sense of controversies.
4. Manage your decision like you manage other complex projects.
5. Give yourself permission to experiment.
6. Recognize your preferences.
7. Remain vigilant about ignorance. Seek those who will teach and learn with you.
8. Delegate.
9. Keep records.
10. Keep your sense of humor.

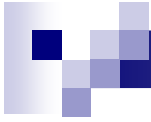
***Top Ten Decision Lessons from the Community Breast Health Project (CBHP) in Palo Alto, CA**
By Jeff Belkora, September 1997 <http://www.guidesmith.org/top-ten-lessons/>



What's New - ASCO 2008

- HSP-90 inhibitors move to center stage
 - IPI-504 Phase III Placebo Controlled
 - 50 sites
 - 195 Patients
- IGF-1R Identified as a potential target in GIST
 - Wild Type & Pediatric
 - Multiple Phase 1, 2 & 3 trials with IGF-1R inhibitors
 - R-1504 – Roche: Pediatric GIST MSKCC
 - NVP-AEW541 – Novartis: tested against GIST in Vitro
 - CP-751,871 – Pfizer: Phase III Combination trials in carcinoma







Coalition of
CANCER COOPERATIVE GROUPS

THE VOICE FOR
CANCER
CLINICAL TRIALS



Cancer Clinical Trials (CCT) Awareness and Attitudes in Cancer Survivors (Ca. surv.)

Comis, R.L., Colaizzi, D., Miller J.D.
Coalition of Cancer Cooperative Groups, Philadelphia PA;
Northwestern University, Chicago, IL

Poster presented at the American Society of Clinical
Oncology Annual Meeting, Atlanta, GA, June 5, 2006
Abstract No. 6061 – Poster No. H1



Perception of Advantages to Enrollment in a CCT Among Survivors Who Were Aware of the Possibility of a Trial at the Time of Diagnosis, and Enrolled

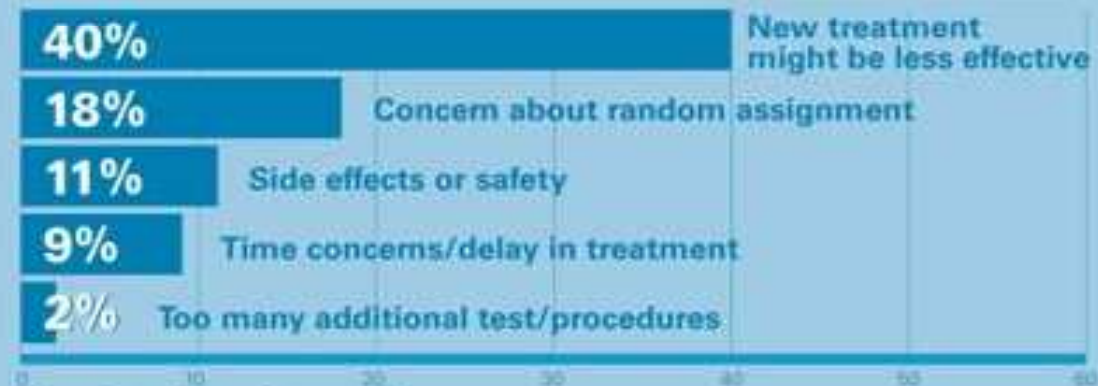


Number of survivors = 60

These results are the product of a set of direct questions to each cancer survivor asking about awareness and enrollment. Up to two advantages were coded for each set of open-ended responses.



Perception of Disadvantages to Enrollment in a CCT Among Survivors Who Were Aware of the Possibility of a Trial at the Time of Diagnosis, but Declined



Number of survivors = 57

These results are the product of a set of direct questions to each cancer survivor asking about awareness and enrollment. Up to two disadvantages were coded for each set of open-ended responses.



Satisfaction with Participation in a CCT

