Battling gastrointestinal stromal tumor

LIFE RAFT GROUP

February 2009 | In memory of Kathy Kinzig, Richard Inlander, Jeanette McIntosh, Francis Benninger, Beverly Wishon & Lee Emerson | Vol. 10, No. 2

2nd French national GIST conference a smashing success

By Estelle Lecointe
President, Ensemble contre le GIST

Sixty-five patients and caregivers came from all over France to attend the second National GIST conference organized by Ensemble contre le GIST, the Association Française des Patients du GIST (AFPG), at the Leon Berard Center in Lyon, on November 22, 2008.

Though the meeting held in Paris last year was already a great success (See article in December 2007 newsletter), this event appears to be one of the most important milestones in the story of Ensemble contre le GIST. Many of the participants were new members so this event was the very first opportunity to meet peers and chat with each other, thus breaking the "virtual limits" of a

French docs and A.F.P.G members

See FRENCH, Page 15

More front-line trials for GIST may help prevent resistance

By Jerry Call
LRG Science Coordinator

Gleevec for metastatic GIST has been one of the great success stories in cancer treatment. It is probably the biggest advance in solid tumors made over the last decade. Ten years ago, the response rate of GIST to the standard chemotherapies of the day was less than five percent. With Gleevec, 85 percent of patients experience benefit including shrinkage or significant periods of stable disease. As a result, Gleevec was approved for first-line treatment of metastatic or unresectable GIST in 2002.

With the excellent initial response rate

CALL

of Gleevec, why would patients want to forgo Gleevec and participate in a front-line trial? Despite the impressive initial response, half of patients will relapse within two years and 75 percent will relapse eventually. So far, Gleevec resistance is proving to be hard to overcome, with gains coming primarily with Sutent for wild-type GIST and for patients with KIT exon 9 mutations.

Nearly all of the current clinical trials for GIST involve either (1) trying to prevent a recurrence using Gleevec or (2) trying to treat the disease after it has become resistant. What has been miss-

See FIRST-LINE, Page 12

2008 Executive Director's Report

By Norman J. Scherzer
LRG Executive Director

The year 2008 witnessed the continued evolution of GIST patients transitioning from passive recipients of treatment to informed patients and caregivers, determined to assume

SCHERZER

greater responsibility for the management of their medical care and survival.

2008 Accomplishments

To help the patient community *become better informed*, the Life Raft Group launched a series of sophisticated initiatives:

- We hosted our fourth Life Fest Meeting in September in Chicago, bringing together the patient and medical professional community.
- We completely redesigned our Life Raft Group website in order to make information retrieval much more efficient.
- We continued to link patients around the world to treatment and support resources within their native countries and native lan-

See 2008, Page 8

Check out page 5 for the Top 3 LRG fundraisers!

New LRG clinical trials database explained

By Jerry Call, LRG Science Coordinator & **Jim Hughes**, LRG Clinical Trials Coordinator

You may not have noticed, but the clinical trials section of the Life Raft Group website has changed dramatically in the last month. This section of the website is now database-driven and has a lot more information. There are 56 trials recruiting, ongoing or completed that were specifically for GIST and GIST only. In addition, there are 23 trials that specifically allow or allowed GIST. **The LRG is currently tracking 115 trials that are or might be of interest to GIST patients.** With all of this information, moving to a database became a necessity.

A certain degree of complexity is inherent with large amounts of information. Here are some tips on using the new database. If you need more help, you can always contact LRG Science Coordinator Jerry Call (303-920-7290) or LRG Clinical Trials Coordinator Jim Hughes (847-866-8360).

All trial lists are sorted to try to put the most relevant trials at the top of the list. In order to do this we list all trials that are specifically for GIST and only GIST before trials that are for GIST but allow other cancers (such as GIST and sarcoma) and we list trials that allow all solid tumors last (typically phase I trials). In addition, we sort the list based on trial phase. Trials in later phases appear before trials in earlier phase, e.g., phase III trials appear before phase I trials. After that trials are sorted by drug name.

The database can be divided into five basic components.

The "Main Trial Page – This is the starting place for looking for a trial or just finding information about trials in general. There are a number of links with lots of information about how to navigate clinical trials. In addition, PDF versions of clinical trial information can be downloaded for those that prefer to print out trial information. The clinical trials strategy sheet is particularly interesting. It gives a visually oriented view of GIST clinical trials and the stages of drug development. In addition, the bottom portion of the page (make sure to scroll to the bottom) repeats the navigation links that appear at the top of all of the clinical trials pages and provides an explanation of what they do.

The "Search Trials" page – This is an advanced search page that lets you create searches that are more complex than the predefined searches. For example, if you wanted to find the trials for all of the HSP90 inhibitors that we are tracking, you could do that from this page. The resulting list would display the trials along with all of the sites.

From this list you can follow the links to more detailed information about the trial or trial sites as well as a link to the very detailed information in the clinicaltrials.gov database (follow the "NCT" link).

The Predefined Searches – The links in the second line at the top of the page are links to predefined searches. These include:

1. A link that returns all GIST trials that are testing a new drug or drug combination as first-line therapy. The hope with first-line trials is that they will be able to improve upon Gleevec as the first treatment GIST patients receive (after surgery). Currently there are 5 trials listed with another that is on temporary hold pending an internal review.
2. A link for trials for patients who are resistant to Gleevec and/or Sutent. This is probably the most popular trial search and currently returns 42 trials.
3. A link to "All Trials" – This returns every trial in the database including older trials that have been

See DATABASE, Page 8

The Life Raft Group

Who are we, what do we do?

The Life Raft Group is an international, Internet-based, non-profit organization offering support through education and research to patients with a rare cancer called GIST (gastrointestinal stromal tumor). The Association of Cancer Online Resources provides the group with several listservs that permit members to communicate via secure e-mail. Many members are being successfully treated with an oral cancer drug Gleevec (Glivec outside the U.S.A.).

How to join

GIST patients and their caregivers may apply for membership free of charge at the Life Raft Group's Web site, www.liferaftgroup.org or by contacting our office directly.

Privacy

Privacy is of paramount concern, and we try to err on the side of privacy. We do not send information that might be considered private to anyone outside the group, including medical professionals. However, this newsletter serves as an outreach and is widely distributed. Hence, all articles are edited to maintain the anonymity of members unless they have granted publication of more information.

How to help

Donations to The Life Raft Group, incorporated in New Jersey, U.S.A., as a 501(c)(3) nonprofit organization, are tax deductible in the United States.

To donate by credit card, go to www.liferaftgroup.org/donate.htm

Donations by check can be made to The Life Raft Group and should be mailed to:

The Life Raft Group
40 Galesi Dr., Suite 19
Wayne, NJ 07470

Disclaimer

We are patients and caregivers, not doctors. Information shared is not a substitute for discussion with your doctor. As for the newsletter, every effort to achieve accuracy is made but we are human and errors occur. Please advise the newsletter editor of any errors.

February 2009 US clinical trials update

By Jim Hughes
LRG Clinical Trials Coordinator

United States

Imatinib + Bevacizumab Phase III: Over 210 Coalition of Cancer Cooperative Groups (CCOP) sites are now recruiting. Please use www.clinicaltrials.gov or cancertrialshelp.org for more detailed site contact information.

Masitinib Phase III: This is a new US and international Phase III trial, more details can be found in Jerry Call's article on page 1.

IPI-504 Phase III: New trial sites have been added in Aurora Colo., Washington DC, Miami Beach, Flor., Chicago Ill., and New York, N.Y.

BIIB021 Phase II: Inclusion criteria have been expanded.

Dasatinib Phase II: A new site has been added at the University of Iowa in Iowa City, Iowa.

Trials listed as "Ongoing but not recruiting:

Imatinib + Pegylated Interferon-1 2B Phase II; Perifosine + Imatinib Phase II; XL820 Phase II; OSI-930 Phase I. Exelixis has informed us that the XL820 trial is closed. We will continue to follow these trials in the LRG database.

LBH589 Phase I: The trial may now be primarily for breast cancer patients so we have dropped the listing for the newsletter but will continue to cover it in the LRG database.

CNF2024 Phase I: This trial has been is listed as "completed". This usually means that data collection has been completed. We will continue to follow this trial in the LRG database.

BAY73-4506 Phase 1: (New Trial) This is a multi-targeted kinase inhibitor that blocks tumor growth through multiple targets (i.e. Raf-1, BRAF, VEGFR 2/3, c-kit, PDGFR, and FGFR-1).

PX478 Phase 1: (NT) This drug is an oral HIF-1α Inhibitor. This type of inhibitor may have activity against certain pediatric type GISTs with defects in the SDH gene(s). These types include Carney Stratakis syndrome and possible Carney's Triad.

R1507 Phase 1: (NT) R1507 is a human monoclonal antibody and an inhibitor of IGF-1R.

Sorafenib + Vorinostat Phase 1: (NT) This trial combines a broad spectrum c-KIT plus inhibitor Sorafenib (Nexavar) with a Histone Deacytelase (HDAC) inhibitor Vorinostat (Zolinza). This combination has been shown effective against CML cell lines in the lab.

Sunitinib + CP-751,871 Phase 1: (NT) This phase I trial combines a potent KIT inhibitor (Sutent) with an IGF-1R inhibitor. This combination might be especially appropriate for wild-type GIST since Sutent is a potent inhibitor of wild-type KIT and since IGF-1R is over-expressed in wild-type GIST.

International

Imatinib or Sunitinib Phase III: New recruiting sites have been added in the United Kingdom and Germany.

Go to www.liferaftgroup.org/treat_trials.html for more detailed information on all trials.

Due to space issues, we do not list site information for trials with more than 10 sites, we encourage our readers to go to our new LRG clinical trials database at ***www.liferaftgroup.org/treat_trials.html*** *for full details. A detailed tutorial on how to use this database can be found on the opposite page.*

Imatinib + Bevacizumab

Imatinib with or without Bevacizumab in patients with metastatic/unresectable GIST

Phase: III
Conditions: GIST
Strategy: Block KIT Protein and inhibit GIST tumor blood vessel growth
NCT#: NCT00324987
Sites: Over 210 sites are now recruiting. Please see www.liferaftgroup.org/treat_trials.html for site info

IPI-504

Study of IPI-504 in GIST patients following failure of at least imatinib and sunitinib

Phase: III
Conditions: GIST
Strategy: Destroy mutant KIT/PDGFRA protein
NCT#: NCT00688766
Contact: GIST Phase 3 Team, 1-877-504-4634
RINGtrialinfo@INFI.com
Trial Website: www.ringtrial.com
Sites: See www.liferaftgroup.org/treat_trials.html

Imatinib or Sunitinib

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

Phase: III
Conditions: GIST
Strategy: Block KIT/PDGFRA protein
NCT#: NCT00372567
Contact: Pfizer
pfizercancertrials@emergingmed.com
Telephone: 1-877-369-9753
Sites: **North Shore Univ. Health System,** Evanston, Ill.
Glenview, Ill.
Highland Park, Ill.
Karmanos Cancer Institute (KCI), Detroit Mich., 1-800-KARMANOS
Siteman Cancer Center, Creve Coeur, Mo.
St. Peters, Mo.
Washington Univ., St. Louis, Mo.
New York Presbyterian Hospital, Columbia University Medical Center, New York, N.Y.
Fox Chase Cancer Center (FCCC), Philadelphia, Penn.
1-800-FOX-CHASE
Margaret von Mehren, MD

Nilotinib (AMN107, Tasigna)

Evaluation of Nilotinib in advanced GIST previously treated with imatinib & sunitinib

Phase: III
Conditions: GIST
Strategy: Block KIT/PDGFRA protein
NCT#: NCT00782834
Contact: **FCCC**
Telephone: 1-800-FOX-CHASE
Sites: **FCCC,** Philadelphia, Penn.
Margaret von Mehren, MD

BIIB021 (CNF2024)

Open-Label, 18FDG-PET pharmacodynamic assessment of effect of drug in GIST

Phase: II
Conditions: GIST
Strategy: Destroy mutant KIT/PDGFRA protein
NCT#: NCT00618319
Contact: **Biogen-Idec**
oncologyclinicaltrials@biogenidec.com
Sites: **Memorial Sloan-Kettering Cancer Center (MSKCC),** New York, NY
Rochester, Minn.

See TRIALS, Page 9

KIT signaling & new approaches for GIST therapy

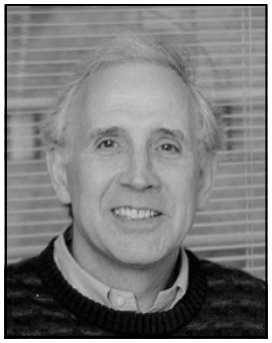
By Dr. Peter Besmer
LRG Research Team member
Memorial Sloan-Kettering Cancer Center

Salient features of GIST tumor cells are their expression of the Kit receptor tyrosine kinase and the fact that in a majority of GIST, the Kit receptor harbors an oncogenic mutation. Kit is a membrane molecule which resides on the surface of cells and consists of an extra-cellular domain (Outside the membrane), a transmembrane domain (Passes through the membrane), and an intracellular domain (Inside the membrane), carrying a protein kinase that phosphorylates tyrosine residues on substrate proteins.

In normal cells, Kit ligand/stem cell factor binds to the extracellular domain of Kit and activates the Kit protein kinase. Ligand mediated activation of Kit sets in motion distinct signaling cascades, including the phosphatidyl inositide 3-kinase cascade, the Ras MAP kinase cascade, Src family kinase signaling and signaling by Stat transcription factors.

Kit is expressed and functions in several distinct cell types in the body, yet in these different cell types the intracellular machinery available to transmit signals from the Kit receptor may vary. Therefore, in different cell types the consequences of Kit receptor signaling are distinct.

In the gut Kit is expressed in pacemaker cells, "Interstitial Cells of Cajal", which are responsible for normal gut movement. Lack of Kit in these cells results in the disappearance of these pacemaker cells and impaired gut movement. Thus Kit is a critical signaling entity in the pacemaker cells of the gut. It is believed that an oncogenic mutation in the Kit receptor in these pacemaker cells first produces hyperplasia and eventually after acquisition of more mutations, malignant GIST.
Therefore, oncogenic/constitutive Kit receptor signaling appears to be critical


BESMER

in GIST, in the development of the tumor as well as in the proliferation and survival of GIST tumor cells.
In agreement with the notion that Kit signaling has a critical role in tumor maintenance, the tyrosine kinase inhibitor, Gleevec, which blocks Kit receptor function as well as a few related tyrosine kinases, is being used with great success to treat a majority of patients with GIST. However, most of the time Gleevec treatment results in a partial response or stable disease. Clearly some tumor cells survive, but their proliferation is impaired. This could indicate on one hand that inhibition of oncogenic Kit is incomplete, or that other signaling mechanisms may compensate for the loss of Kit signaling.

Improving therapeutic outcome in treating GIST patients remains a great challenge. A prerequisite for this is a detailed understanding of how Kit transmits its signals intracellularly to mediate its function in tumor cells as well as the identification of compensatory signaling mechanisms in tumor cells originating either from other receptors or from the extracellular matrix.

One approach for improving clinical efficacy is to develop drugs which are better inhibitors of Kit and or which have broader activity; this means that they inhibit Kit as well as other receptor kinases. An example of this second category would be Sutent, which is in use in Gleevec-resistant patients.

A second approach is to identify intracellular molecules which are critical in mediating Kit function and to develop inhibitors against them. Cellular processes such as cell proliferation and cell survival are produced by complex signaling networks emanating from several input signals. Thus, critical signaling pathways may be used by Kit as well as the elusive parallel receptor signaling pathways and therefore inhibition of intracellular signaling molecules in combination with Kit receptor inhibitors could be effective in inhibiting multiple signaling cascades at once.

Improved treatment strategies for GIST may require the use of multiple drugs simultaneously, but working out and fine tuning such cocktail approaches will take time. Important tools in such preclinical investigations will be the GIST mouse models that have been developed in the recent past by the LRG Research Team and other doctors (See Dr. Besmer's article on "The use of mouse models to investigate GIST" in the March 2007 LRG newsletter).

Glossary

KIT- a protein, expressed on Interstitial cells of Cajal, which regulates their replication; GIST cells usually express a mutated form of KIT.
Tyrosine kinase- enzymes which catalyze phosphorylation of tyrosine residues in proteins, often leading to activation of the protein/enzyme

Phosphorylation- addition of a phosphate group; this is a common chemical modification of proteins and often alters the activity of an enzyme
Substrate- a molecule that is acted upon by an enzyme
Kit ligand/stem cell factor: a cytokine which binds c-Kit
Cytokine- a type of signaling molecule that is used in cellular communication
Signaling cascades- a process in signal tranduction in which the products of one reaction are consumed in the next reaction
Interstitial cells of Cajal- specialized cells, found throughout the gastrointestinal tract that are essential for normal gastrointestinal motility; these are the cells from which GISTs arise.
Hyperplasia- A general term referring to the proliferation of cells within an organ or tissue beyond that which is ordinarily seen.
Inhibitor- a compound (e.g. drug) which blocks the activity of an enzyme; Gleevec works by inhibiting c-kit
Proliferation- to cause to grow or increase rapidly

LRG holiday campaign update: Top fundraisers shine

By Tricia McAleer
Director of Operations

For years the LRG has counted on its members for support. And for years they have pulled through. Since the start of the Cure Campaign, Life Rafter's have raised over 42,000 dollars for GIST Research! We would like to thank our top three fundraisers – Pat Lemeshka, Rachel Tate and Butch Eller (Pictured below from left to right) for all their hard work. With their help and your continued support, we hope to make this our most successful campaign yet. Look out for our next campaign update in next month's newsletter!

You can also view these photos and submit your own at: www.acureisinourreach.org.

What Does a Cure Mean For You?

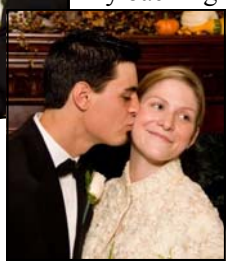
An answer to my prayers

I would be able to love him longer

Many more cruises with our dear and crazy

Congratulations Ashley Young!

Recently, we reported that Pediatric GISTer, Ashley Young married her boyfriend of over three years, Mark Vincent, on November 8, 2008. We asked Ashley for wedding pictures and how she felt about her new husband.



"I remember waking up from surgery, getting my full gastrectomy and wanting to see him. I thought he was at work but instead he was worriedly waiting with my family, for an endless amount of hours without knowing if he would be able to see me at all, if I would be in the ICU or not. He came in and of course, I was hooked up to all types of tubes and he rubbed my forehead, pushed my hair aside and I opened my eyes and he said, "You're so beautiful. I love you so much." And the he kissed me on my forehead. "Out of everyone close to me, he is the only one who can pat my back right when I can't swallow so I don't throw up. He rubs my back and comforts me, helps me change bandages and gives me shots of B-12 and Zofran. I know that he could be out somewhere with his friends having fun, but he sacrifices over and over just to be able to hold my hand.

"He always helps me through whether by laughter or wiping my tears. I can't look at his smiling face when he cracks a cheesy joke and not laugh, no matter how ridiculous the situation may be."

The newlyweds pose with Ashley's parents.

Ashley also celebrated her 7-year Cancerversary on January 18! She celebrated with a dinner party, surrounded by her siblings and friends. To take her mind off her diagnosis, Ashley cooked the whole meal herself! Prime rib and tortellini? **Bravo!**

Pat George: the man, the myth, the legend

Man pays Corner students to learn

Pat George, LRG member and volunteer is well-known in the LRG email community. He can often be found cheering someone up, spurring someone on, or imparting some of his Alabama wisdom on us all. It is hard to think of Pat outside of the GIST community, but when we received a copy of this article from the North Jefferson News, we thought it would show a image of Pat outside of GIST.

By Melanie Paterson

A Huffman man has taken it upon himself to further the educations of students in rural north Jefferson County — even though he knows none of them.

On Wednesday, Pat George will give a vocabulary test at Corner Middle School. He made the test, will administer it and provide the cash rewards for top scorers.

"I tried to figure out some way to award academic excellence," said George. "Athletes are not the ones to pay the bills when the time comes. ... This encourages academic excellence."

George does not have a background in education, but rather is a retired employee of the City of Birmingham.

George and his wife Anne do all of the work from scratch, along with a team of people to "make sure I don't make mistakes," he said.

Pat (right) with another email community celebrity, Tom Overley, at Life Fest 2008.

He creates the test from a Merriam-Webster dictionary, which he said is what the students use in class.

"It takes hundreds of man hours to do one of these," he said. George said it takes about 200 hours to create each test. He makes three exams, one each for the letters A, E and I to have different tests for sixth, seventh and eighth-graders.

Each test will have 120 questions with four multiple-choice answers.

"You get 120 answers out of the dictionary, but then you have to come up with 360 deceptive lies out of an active imagination," said George.

He then lays out the test and makes test booklets and answer sheets.

This is the second year George will give the test and cash prizes at Corner Middle School.

It's his fourth year to give the test at Townley Junior High School in Walker County, where he got started with the project.

George got his start at both schools because of an old friend — his former first sergeant, Bill Hatcher, in his old Alabama National Guard unit.

"You always do what your first sergeant tells you to do," said George. "He's the one who got me in the door at Townley and he's the one who got me in the door at Corner."

Hatcher is an assistant teacher and bus driver at Corner, according to George.

George coordinates his work at Corner through middle-school counselor Nancy Osborn.

There are usually up to 15 children taking the test.

Cash prizes go to the top 10 scorers, totaling $303 for each school.

In addition, George and his wife provide hot cheeseburgers and French fries to the students after they've completed the test. He said he's also known to generously distribute chocolate among teachers.

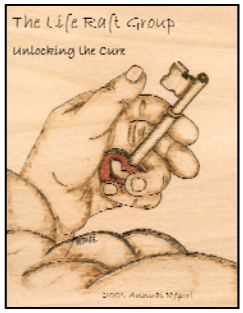
It's not cheap to create and give the tests. George said it costs up to $600 out of his pocket to administer the test at each school.

"It gets downright expensive," he said. "But maybe I'll inspire a few. If you don't do something with what you've got while you can, you'll regret it when you can't .

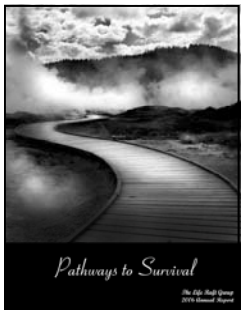
Reprinted with permission from the North Jefferson News.

We Want You!

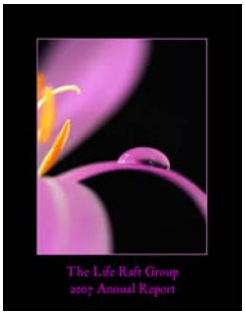
For the past three years, we have used artwork from LRG members as covers of the LRG Annual Report. This year we are asking anyone who would like to submit their own artwork to us at liferaft @liferaftgroup.org. If you have any questions, contact us at (973) 837-9092. Read on for some of the inspiration behind past covers.



This is actually a wood carving made by Rachel Tate, that has hung in the LRG office since its beginnings.



Mark Thomas donated this piece to the LRG, just before he passed. We chose to honor his photography skill on our cover.



Pediatric GISTer, Rachel Gilbert used photography to lift her spirits. She has become a wonderful artist!

Don't miss out on your opportunity to shine!

2nd NIH Pediatric GIST clinic proves successful

On January 22-23, 2009, the National Institutes of Health (NIH) held its second Pediatric and Wild-type GIST Clinic.

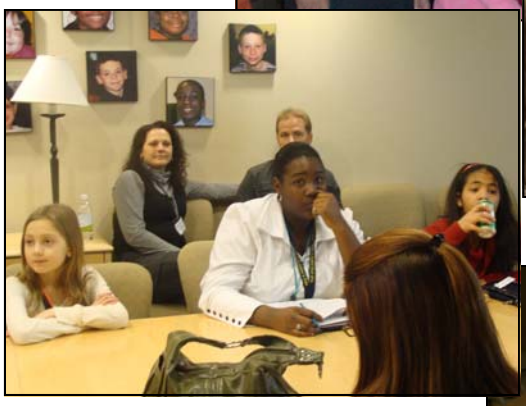
Some comments were:

"I really enjoyed the clinic. I thought that everyone we encountered that works for the NIH was extremely kind, supportive and knowledgeable. I especially enjoyed being able to connect with other young adults with GIST. To be able to talk face to face with someone who knows firsthand about living with the uncertainty of a future, who understands about planning your life in three month increments in between scans and yet is still is hopeful. And I feel that all of us there were hopeful. The research being done gives us hope that there may be a cure in our lifetime. And that is just amazing! As a GIST patient, my biggest fear is leaving my little girls motherless at such young ages. This opportunity really impressed upon me that so much has been learned about GIST since my diagnosis (in 2002) that I can't wait to see what the next six years will bring!!"

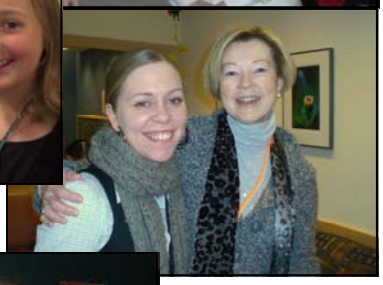
"The NIH Clinic was a fantastic way to share information, help with the research and gather information. We are extremely grateful for the opportunity to meet the experts in the field of GIST research. However, we wish that we never had to have the experience. The easiest way to say it is, 'It's an incredible place that you never want to be.'"

Here are just a few pictures from the weekend. You can view a slide show at the new LRG Pediatric GIST site, www.pediatricgist.org/CenterofExcellenceNIHClinic/tabid/63/ Default.aspx

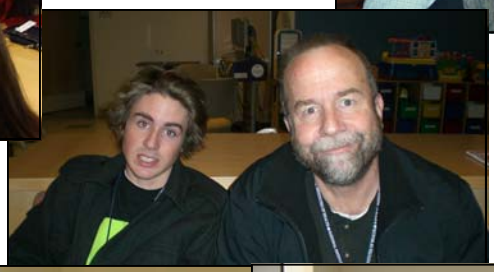
Above: Doctors and advocates take a moment for a photo op at the NIH clinic on January 22-23. Below: Survivors, caregivers and advocates break for dinner.



Brittany & Josalin



Above: Pediatric GISTers listening to presentations by specialists. Right: Spencer & Dan Coulson



Above: LRG staffer, Tricia McAleer & member, Alice Sulkowski share a laugh.

Participants prepare for Dr. Janeway's presentation.

Drs. Janeway, Demetri & Pappo discuss Pediatric GIST news.

DATABASE

From Page 2

completed. We include older trials so that users can see the key trials in GIST.

4 A link to all "Recruiting" trials. This list combines First-line, Gleevec/Sutent resistant and Preventative trials.

5 A link to "Preventative (Adjuvant) Treatment" trials. Note that most of these trials are no longer recruiting. Neoadjuvant trials are also included in this search.

A link to the "Clinical Trial Site List" – This list tracks over 180 sites.

Full site list

University of Chicago	Chicago	IL	USA
Karmanos Cancer Institute	Detroit	MI	USA
MD Anderson Cancer Center	Houston	TX	USA
New York University	New York	NY	USA
H. Lee Moffit Cancer Center	Tampa	FL	USA
Wake Forrest	Winston-Salem	NC	USA
Washington Cancer Institute	Washington	DC	USA
Helsinki University Central Hospital	Helsinki		Finland
Istituto Nazionale Dei Tumori	Milan		Italy
Warren Grant Magnuson Clinical Center	Bethesda	MD	USA
Site name unknown, Pomona 91767	Pomona	CA	USA

A link to the "Drug Watch List" – This page is the place to go if you just want more information about a particular drug. The list itself shows the various names for the drug, the manufacturer and the drugs known targets. From this list you can follow links to detailed information about each drug. In addition to the basic information about the drug, this page has links to further information, each trial with this drug that we are tracking, and a link to trial results if available. If the drug is approved, the links area will lead you to the manufacturer's drug page, financial assistance plans, prescribing information and more. In addition, there are links at the bottom of the page to predefined searches for the drug in clinicaltrials.gov (good for trials), ASCO (good for trial results) and Pubmed (good for general information). You can also get to the same drug information by clicking on the drug link near the top of each detailed trial record.

Drug Watch List

BEZ235	Novartis	PI3K Class I mTOR Raptor mTOR Rictor
IPI-493	Infinity	HSP90
AUY922	Novartis	HSP90
BGT226	Novartis	PI3K mTOR
MP470	SuperGen	KIT AXL PDGFRA c-Met Rad51

Why do we have a standalone database for GIST clinical trials?

There are now 115 trials related to GIST in our database. While we use ClinicalTrials.gov as a key source of our data, there are a few reasons why an LRG database is a good tool for GIST patients.

In a broad database like clinicaltrials.gov you may encounter issues like:

- A trial is too broadly classified as GIST
- Relative articles for sarcoma or solid tumors would not be listed in a search for GIST
- Some trials are simply not listed
- Site information is missing

The LRG database has already factored in these issues and does the background research for you. Each search you do is focused on GIST.

Don't forget! You can watch Jim Hughes' webcast explain how to navigate clinical trials at www.liferaftgroup.org/library_videos.html.

2008

From Page 1

guages through our growing Global GIST Network.

● We expanded our increasingly creative outreach in various ways. We amplified our presence in the world of Web 2.0, started a campaign to find out exactly what a cure for cancer would mean to LRG members and the general community, and initiated an online Spanish Speaking social network for GIST patients and their families.

● We created a new and comprehensive clinical trials database to provide both patients and physicians with the most up-to-date listing in the world for finding GIST related clinical trials.

● We created and hosted a series of webcasts on such topics as Familial GIST, Pediatric GIST, navigating clinical trials, the LRG Dosage Study and being a caregiver. Equally as important, we gained the ability to archive these webcasts so that they can be viewed at any time by anyone.

● We composed an array of new educational pamphlets for the GIST community on such topics as: "Living Well with Side Effects," "Financial and Logistical Assistance for GIST Patients," "Managing your GIST Care," "Email Community: Frequently Asked Questions" and "Mutational Testing." In addition, our GIST informational pamphlet became available in two additional languages, Hebrew and Urdu.

To help the GIST patient community to *survive*:

● We entered our third year of grant support for our world class research

See 2008, Page 14

TRIALS

From Page 9

Dasatinib

Trial of dasatinib in advanced sarcomas

Phase: II
Conditions: GIST
Strategy: Block KIT/PDGFRA protein and related GIST tumor signal paths
NCT#: NCT00464620
Contact: Kathy Granlund
kegrandlund@sarctrials.org
Telephone: 734-930-7607
Sites: Please see www.liferaftgroup.org/treat_trials.html for site info

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: Block KIT/PDGFRA protein and stimulate immune system to destroy GIST cells
NCT#: NCT00585221
Contact: **Ongoing but no longer recruiting**

BAY 73-4506

Phase I study of BAY 73-4506

Phase: I
Conditions: Solid Tumors
Strategy: Block KIT
Contact: **S. Texas Accelerated Res. Therapeutics (START),** San Antonio, Texas
Tracy Dufresne, RN
Telephone: 210-593-5265
Sites: **MDA,** Houston, Texas
713-792-3245
Jon Trent, MD

BEZ235

A Phase I/II study in patients with advanced solid malignancies

Phase: I
Conditions: Solid Tumors
Strategy: Block KIT signal path
NCT#: NCT00620594
Contact: Novartis
Telephone: 862-778-8300
Sites: **NCI,** Las Vegas, Nev.
702-822-5282
Sarah Cannon Res. Institute, Nashville, Tenn.
Howard Burris, MD, 615-329-7274

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: Block KIT+Block KIT signal path
NCT#: NCT00265798
Contact: **Univ. Of Chicago Cancer Res. Center,** Chicago, Ill.
Telephone: 773-834-7424
Sites: **City of Hope**, Duarte, Calif.
Warren Chow, MD, 866-434-4673 x64215
USC-Norris Cancer Center, Los Angeles, Calif.
Hein-Josef Lenz, MD, 323-865-3955
UC-Davis, Sacramento, Calif.
David Gandara, MD, 916-734-3771
Cancer Care Specialists, Decatur, Ill.
James Wade, MD, 217-876-6617
Illinois Cancer Care, Peoria, Ill.
John Kugler, MD, 309-243-3605
Central Illinois Hem/Onc, Springfield, Ill.
Edem Agamah, MD, 217-525-2500
Univ. of Michigan, Ann Arbor, Mich.
Scott Schuetze, MD, 734-647-8925
MSKCC, New York, N.Y.
David D'Adamo, MD, 212-639-7573
Medical College of Wisconsin Milwaukee, Wis.
Stuart Wong, MD, 414-805-4603

AUY922

Phase I-II study to determine the MTD of AUY922 in advanced solid malignancies and efficacy in HER2+ or ER+ locally advanced or metastatic breast cancer.

Phase: I
Conditions: Solid Tumors
Strategy: Destroy mutant KIT/PDGFRA
NCT#: NCT00526045
Contact: **Novartis**
Telephone: 800-340-6843
Sites: **UCLA**, Los Angeles, Calif.
Carolyn Britten, MD, 310-825-5268
Dana Farber Cancer Institute (DFCI), Boston, Mass.
Stephen Hodi, MD, 617-632-5053
Washington Univ., St. Louis, Mo.
Paula Fracasso, MD, 314-362-6565
Nevada Cancer Inst. (NCI), Las Vegas, Nev.
Sunil Sharma, MD, 702-822-5360
Medical College of Georgia, Augusta, Ga.
Thomas Samuel, MD, 706-721-2505
Cancer Therapy and Research Center (CTRC), San Antonio, Texas
Monica Mita, MD, 210-562-1797
MD Anderson Cancer Center (MDA), Houston, T.X.
Vassiliki Papadimitrakopoulou, MD, 703-792-6363

Perifosine + Imatinib

Phase II study in GIST patients

Phase: II
Conditions: GIST
Strategy: Block KIT/PDGFRA protein and downstream signal path
NCT#: NCT00455559
Contact: **Ongoing but no longer recruiting**

BGT226

A phase I/II study of BGT226 in patients with advanced solid malignancies including those with advanced breast cancer

Phase: I
Conditions: Solid Tumors
Strategy: Block KIT signal path
NCT#: NCT00600275
Contact: Novartis
Telephone: 800-340-6843
Sites: **NCI,** Las Vegas, Nev.
Sunil Sharma, MD
DFCI, Boston, Mass.
Melissa Hohos, 617-632-2201
Massachusetts General Hospital, Boston, Mass.
Natasha Isaac, 617-726-6225
CTRC, San Antonio, T.X.
Jerry Medina, 210-450-1789
Francis J. Giles, MD

BIIB021 (CNF2024)

Once or twice daily administration of BIIB021 to solid tumor subjects

Phase: I
Conditions: Solid Tumors
Strategy: Destroy KIT
NCT#: NCT00618735
Contact: **Biogen-Idec**
oncologyclinicaltrials@biogenidec.com
Sites: **Premiere Oncology,** Santa Monica, Calif.
Lee Rosen, MD, 310-633-8400
START, San Antonio, TX
210-593-5265

Doxorubicin + Flavopiridol

Doxorubicin and Flavopiridol in treating patients with metastatic or recurrent unresectable sarcomas

Phase: I
Conditions: GIST/Sarcoma
Strategy: Freeze the GIST cell division cycle
NCT#: NCT00098579
Contact: David D'Adamo, MD,
Telephone: 212-639-7573
Sites: **MSKCC,** NY, N.Y.

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TRIALS

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GDC-0941

An open-label phase I, dose-escalation study in patients with locally advanced or metastatic solid tumors

Phase: I
Conditions: Solid Tumors
Strategy: Block KIT signal path
Sites: **DFCI**, Boston, Mass.
Melissa Hohos
617-632-2201
TGen, Scottsdale, Ariz.
480-323-1339

Imatinib + Sunitinib

Imatinib & sunitinib in treating GIST patients

Phase: I
Conditions: GIST
Strategy: Block KIT
NCT#: NCT00573404
Contact: Cancer Information Program
Telephone: 800-811-8480
Sites: **Vanderbilt-Ingram CC**,
Nashville, TN
800-811-8489
Franklin, Tenn.
615-343-4128

IPI-493

Phase I dose escalation study of IPI-493

Phase: I
Conditions: Solid Tumors
Strategy: Destroy mutant KIT/PDGFRA
NCT#: NCT00724425
Sites: **Premiere Onc.,** Scottsdale, Ariz.
Patricia Shannon, RN
480-860-5000 ext 223
Santa Monica, Calif.
Marilyn Mulay, NP, 310-633-8400
San Diego Pacific Onc. and Hem. Assoc., Encinitas, Calif.
Karen Brady, RN, 760-752-3340
Univ. of Colorado, Aurora, Colo.
Stacy Grolnic, RN, 720-848-0655

MP470

MP470 in treating patients with unresectable or metastatic solid tumors

Phase: I
Conditions: Adv. Solid Tumors
Strategy: Block KIT
NCT#: NCT00504205
Contact: **TGen,** 480-323-1255
Sites: **START,** San Antonio, Texas
Anthony Tolcher, MD, 210-593-5255
Virginia Piper CC, Scottsdale, Ariz.
Raoul Tibes, MD, 480-323-1350

PX-478

Phase I trial of PX-478

Phase: I
Conditions: Solid Tumors
Strategy: Block related tumor signal paths
NCT#: NCT00522652
Sites: **TGen,** Scottsdale, Ariz.
Lynn Hull, 480-323-1071
MDA, Houston , Texas
Hala Abdulkadir, 713-792-9944

PX866

Phase I trial of oral PX866

Phase: I
Conditions: Solid Tumors
Strategy: Block KIT signal path
NCT#: NCT00726583
Sites: **Univ. of Colorado,** Aurora, Colo.
Sharon Hecker, 720-848-0667
MDA, Houston, T.X.
Rhonda Clement, 713-563-3559

R1507

A multiple ascending dose study in children & adolescents with advanced solid tumors

Phase: I
Conditions: Solid Tumors
Strategy: Block related tumor signal paths
NCT#: NCT00560144
Contact: 973-235-5000
Reference study ID#:
PDO_NO21200
Sites: **MSKCC,** New York , N.Y.
212-639-8267
MDA, Houston, T.X.
Rhonda Clement, 713-563-3559
Denver, Colo.
Bethesda, Md.

SF1126

Phase I open label, safety, pharmacokinetic & pharmacodynamic dose escalation study of SF1126 given twice weekly by IV to patients with advanced or metastatic tumors

Phase: I
Conditions: Solid Tumors
Strategy: Block KIT signal path
Contact: **TGen,** Scottsdale, Ariz.
Telephone: 480-323-1339
Sites: **Arizona Cancer Center,** Tucson, Ariz.
Daruka Mahadevan, MD, 520-694-2873
Indiana University, Indianapolis, Ind.
Elena Chiorean, MD, 317-278-6942

SNX5422

Safety study of SNX-5422 to treat solid tumor cancers and lymphomas

Phase: I
Conditions: Solid Tumor
Strategy: Destroy KIT
NCT#: NCT00647764
Contact: Pfizer Onc. Clinical Trial Information
Telephone: 1-877-369-9753
Sites: Bethesda, Md.

SNX5422

Safety and pharmacology in patients with refractory solid tumor malignancies

Phase: I
Conditions: Solid Tumor Malignancy
Strategy: Destroy KIT
NCT#: NCT00506805
Contact: Pfizer Onc. Clinical Trial Information
Telephone: 1-877-369-9753
Sites: **TGen,** Scottsdale, Ariz.
Joyce Ingold, RN, 480-323-1339
Ramesh Ramanathan, MD
Sarah Cannon Res. Institute,
Nashville, Tenn.
Jessica Gilbert, 615-329-7238

SNX5422

SNX-5422 in treating patients with solid tumor that has not responded to treatment

Phase: I
Conditions: Solid Tumors
Strategy: Destroy KIT
NCT#: NCT00644072
Sites: **Warren Grant Magnusen Clinical Center,** Bethesda, Md.
1-888-NCI-1937

Sorafenib + Vorinostat

Phase I Vorinostat+Sorafenib in patients with advanced solid tumors

Phase: I
Conditions: Solid Tumors
Strategy: Block KIT+Unblock cell death genes+ Destroy KIT
NCT#: NCT00635791
Sites: **Univ. Of Colo.,** Aurora, Colo.
Stacy Grolnic, 720-848-0655

STA-9090

Once-weekly study in solid tumor patients

Phase: I
Conditions: Solid Tumors
Strategy: Destroy KIT
NCT: NCT00687934
Sites: **Premiere Onc.,** Santa Monica, Calif.
Lee Rosen, 310-633-8400
US Oncology-Dayton Onc. & Hem.,
Kettering, Ohio
Robert Raju, 937-293-1622

STA-9090

Twice-weekly study in solid tumor patients

Phase: I
Conditions: Solid Tumors
Strategy: Destroy KIT
NCT: NCT00688116
Sites: **DFCI,** Boston, Mass.
Melissa Hohos, RN, 617-632-2201
KCI, Detroit, Mich.
Pat LoRusso, MD, 315-576-8716

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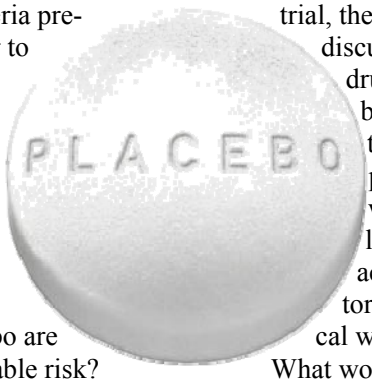
LRG stance on placebo highlighted in Cancer World

The Life Raft Group's stand on placebo-use in clinical trials for cancer patients was recently highlighted in the November/December issue of European magazine, Cancer World. Here are a few excerpts (the full article can be found at www.cancerworld.org/magazine:

"With regard to the criteria presented in the ASCO paper to justify placebo-controlled trials, [Scherzer] poses this question: who decides? Who decides that such a trial design is necessary on this or that methodological criterion? And who decides that the patients exposed to placebo are not placed at an unacceptable risk?

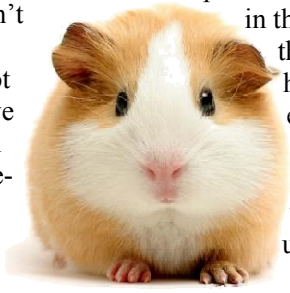


"If you propose giving a placebo to terminally ill patients to demonstrate that their disease progression or death rate will be greater if they are not given the drug, you must assume the burden of demonstrating that there are no alternatives, and that patients on the placebo arm really won't suffer serious irreversible harm," says Scherzer."

A Conflict of Interests

"Scherzer puts it this way: "We find ourselves comparing the needs of those who are exposed to a placebo against those who might benefit in the future. We agree with ethicists who state that you've got to look at it in the present tense. Good outcomes, no matter how noble, cannot justify research that fails to protect the health and safety of those who participate, particularly terminally ill patients who may have no access to other treatments..."

"[Dr. Peter] Reichardt puts it this way: "If patients argue 'we don't want a placebo trial,' this could result in the trial not happening… Patients have to understand that no trial means no further improvements, no new treatments and no future achievement." Given the element of conflict of interests in this situation, it might be argued that the only ethical way to proceed would be to allow the patients some say in the way that phase III trials are designed. This is something Reichardt strongly advocates. "Once a new treatment has shown activity in an early trial, then we can sit down and discuss how can we bring this drug further. Then we start by asking: What kind of trial would be needed to prove efficacy? What would be the target population? What would be acceptable to the regulators? What would be practical with respect to numbers? What would be acceptable to sponsors in terms of money? What would be acceptable to patients as potential candidates for the trial? At that moment the voice of the patient groups could be necessary.



"They can bring their arguments, and learn what it means if they say 'we cannot accept this', and we will say, 'OK then we cannot do the trial', and then they would say 'we want the trial'. And then we can start discussing how to go about this." The suggestion provokes a certain nervousness among many sponsors, who fear that patient groups could end up holding a gun to their heads. Yet far more damage is already being done by some patient communities who effectively sabotage trials they don't like, by refusing to enroll. There has to be a better way. "Nobody has a greater interest in fast-tracking testing and approval of new drugs than a cancer patient has," says Scherzer. "The whole process would ultimately be a better process if patients like us were seriously engaged in the decision-making process from the very beginning. We might help come up with a protocol that everybody could live with. When you leave out the guinea-pig – in this case the patient – I do think that is by its nature somewhat unfair."

TRIALS

From Page

Sunitinib + CP-751

Phase I combination study in advanced solid tumor patients

Phase: I
Conditions: Solid Tumor
Strategy: Block KIT+Block related tumor signal paths
NCT#: NCT00729833
Contact: Pfizer CT Call Center
Telephone: 1-800-718-1021
Sites: **FCCC,** Philadelphia, Penn.
1-888-FOX-CHASE
Premiere, Onc., Santa Monica, Calif.
Lee Rosen, 310-638-8400
START, San Antonio, Texas

XL147

Study of safety and pharmacokinetics of XL147 in adults with solid tumors

Phase: I
Conditions: Solid Tumors
Strategy: Block KIT signal path
NCT#: NCT00486135
Contact: Exelixis Contact Line
Telephone: 866-939-4041
Sites: **DFCI**, Boston, Mass.
Pilar de la Rocha Mur, 617-632-5841
Mary Crowley Med. Res. Ctr.,
Dallas, Texas
J. R. Dolan, 214-658-1943

XL765

Study of safety and pharmacokinetics of XL765 in adults with solid tumors

Phase: I
Conditions: Solid Tumors
Strategy: Block related tumor signal paths
NCT#: NCT00485719
Contact: Exelixis Contact Line
Telephone: 866-939-4041
Sites: **KCI,** Detroit, Mich.
Theresa Laeder, 313-576-9386
START, San Antonio, Texas
Gina Mangold, 210-413-3594

Mark your calendars!

- Julie Cramer's GIST Benefit Ball will be held at The Mansion on Main Street in Voorhees, NJ on **February 14**. Visit www.gistbenefitball.org for more information.
- The Italian GIST group will be meeting on **February 21**, please email Anna Costato at anna.costato@virgilio.it for details.
- Also meeting on **February 21** will be Pennsylvania GISTers, please email musikwithkim@yahoo.com for information.
- CancerCare is hosting a "Treatment Update on GIST" workshop on **March 3**. Go to www.cancercare.org to register.

FIRST-LINE

From Page 1

ing is an attempt to improve upon and lengthen the excellent initial response to Gleevec. This appears to be changing. Within the last 18 months, five new approaches designed to improve initial results have entered into clinical trials.

Masitinib (AB1010)

This drug is commonly spelled as either masitinib or masatinib

Masitinib (Manufactured by AB Science in France) is a c-Kit/ PDGFRa inhibitor similar to imatinib and nilotinib. After promising phase I/II results, masitinib is moving into a phase III trial for first-line therapy in GIST.

This trial is open to patients with metastatic or non-resectable GIST and patients treated with adjuvant/neoadjuvant imatinib who relapsed after discontinuing imatinib (not imatinib-resistant). The trial is open in 14 sites in France, three sites in the United States and four sites in Lebanon, and is expected to enroll 222 patients. Unlike other tyrosine kinase inhibitors used in GIST, masitinib will be dosed based on each patients weight, 7.5 mg/kg/day. The trial is randomized and patients with receive either masitinib or imatinib (400 mg or 600 mg).

Benninger was 58

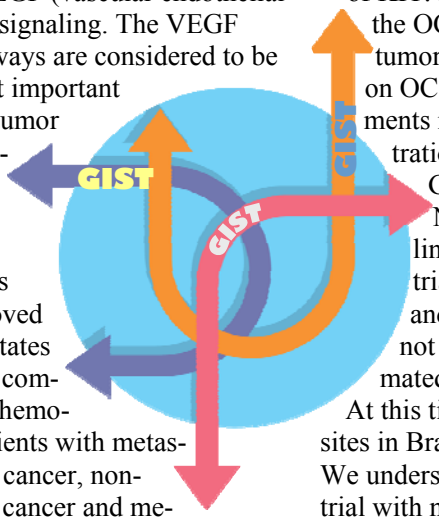
Francis James Benninger of Durham died December 26, 2008, in his 58th year. Francis was the husband of Bertha (Koeslag) and father of Cara, Kait and Aaron. Francis was the son of the late Cornelius (Corky) Benninger and is survived by his mother, Rosetta. Brother of James (Betty Lou) of Mississauga, Anne Marie (Moe) Webster of Waterloo, Helen of Durham, Rosemary (Wilf) Ringler of Durham, Neil (Bonnie) of Hanover, George of Mitchell and Alan (Holly) of Cape Breton. He was predeceased by three brothers, Jerome, John and Norbert. Memorial donations to the Grey Bruce Regional Health Centre Foundation - Oncology Department or to The Life Raft Group.

Imatinib + bevacizumab

This large phase III trial adds a second drug, bevacizumab (the approved name is Avastin) to the current front-line treatment, imatinib (Gleevec). Charles Blanke, MD, FACP, of the British Columbia Cancer Agency, is the study chair of this trial, which is currently recruiting in over 200 sites in the United States.

BLANKE

Bevacizumab (Avastin™) (Manufactured by Genentech, South San Francisco, Calif) was the first U.S. Food and Drug Administration (FDA)- approved biological therapy designed to inhibit the formation of new blood vessels to tumors. It works by blocking VEGF (vascular endothelial growth factor) signaling. The VEGF signaling pathways are considered to be one of the most important pathways that tumor cells use to promote the growth of new blood vessels. Bevacizumab is currently approved in the United States and is given in combination with chemotherapy for patients with metastatic colorectal cancer, non-small cell lung cancer and metastatic breast cancer.



According to Blanke, "Bevacizumab is one of the most exciting anticancer agents developed recently, and there are strong scientific reasons to think it will work effectively against GISTs. It is our hope that patients on this trial have a higher chance of remission and/or living longer and better with their GISTs."

This trial is randomized with half of the patients receiving imatinib, and the other half receiving imatinib plus bevacizumab. Bevacizumab is given intravenously every 21 days. Patients will have mutational screening with a priority given to quickly identify patients with a KIT exon 9 mutation. Patients with exon 9 mutations will be placed on a higher dose of Gleevec (800 mg if tolerated) (Please see the LRG Dosage Study in the March 2007 newsletter).

Nilotinib

Most Life Raft Group members have heard of nilotinib or AMN107 (Manufactured by Novartis and approved as Tasigna). It is currently in a large phase III trial for third-line therapy after failure of Gleevec and Sutent. Nilotinib is a more powerful inhibitor of KIT and PDGFRA than Gleevec. In particular, Dr. Cristina Antonescu and her colleagues at Memorial Sloan-Kettering Cancer Center have shown that nilotinib is a very potent inhibitor of wild-type KIT. It is also a strong inhibitor of the most common secondary mutation in GIST, the V654A mutation in exon 13 of KIT. Nilotinib does not depend on the OCT1 protein for uptake into tumor cells (Gleevec *is* dependent on OCT1) and in test tube experiments reaches much higher concentrations inside tumor cells than Gleevec.

Nilotinib has moved into first-line trials with a small phase II trial in Bad Saarow, Germany and a larger phase III trial that is not yet recruiting, but has an estimated enrollment of 736 patients. At this time there are only two trial sites in Brazil listed on clinicaltrials.gov. We understand that another front-line trial with nilotinib is planned that will include sites in the United States, but it is not yet listed and details are lacking.

In the phase II trial in Brazil, all patients will receive nilotinib. The phase III trial will be randomized with patients receiving either imatinib or nilotinib.

Imatinib + pegylated interferon-a 2B

This front-line trial is being conducted at the Huntsman Cancer Institute at the University of Utah by Dr. Lei Chen. "The two major obstacles of durable remission in cancer patients are acquired drug-resistant clones and tumor stem cells" according to Chen. "Although GIST has initial excellent response, more than half of patients develop Gleevec resistance in less than two years. The responders are committed to Gleevec life-long because of the 'tumor stem cell', which will regenerate as soon as Gleevec is discontinued. GIST is a

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FIRST-LINE

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great model to prove the concept of combination targeted therapy and immunotherapy."

In order to stimulate/optimize an immune response against GIST, this phase II trial adds pegylated interferon α 2b (PEG-intron, Schering Plough) to Gleevec. "If given at the right dose, [with the] right timing, combined with the right drug, interferon α holds the greatest potential in breaking immune tolerance and shifting to immune stimulation against patients' tumors," said Chen, "with pegylated interferon α 2b we expect much improved toxicity."

NOTE: The imatinib + pegylated interferon-a 2B trial is currently ongoing, but not accepting new patients pending an internal review.

Dasatinib (BMS-354825)

This small phase II trial is investigating how well dasatinib works when given as front-line therapy in GIST. Also known as SPRYCEL, Dasatinib (manufactured by Bristol-Myers Squibb) is a potent but less selective inhibitor of KIT, PDGFRA and the SRC kinases. This trial is being sponsored by the Swiss Group of Clinical Cancer Research and is only open at Center Hospitaleir Universitaire Vaudois in Lausanne, Switzerland.

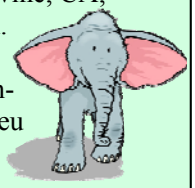
These five different approaches for front-line therapy are a welcome addition to the GIST clinical trial world. Improving therapy while GIST tumor cells are still sensitive to treatment is a significant step towards a "cure".

Given the limited patient pool, one wonders if this important strategy will be tested in a trial.

Patient accrual may be a concern with front-line trials. The recent FDA approval of Gleevec for adjuvant therapy is likely to reduce the number of GIST patients available for front-line therapy, especially if these patients continue Gleevec indefinitely. Patients that have a recurrence while taking still taking adjuvant Gleevec would typically not be eligible for a front-line trial. Patients taking adjuvant Gleevec for a period of time (for example, a year) but who stop Gleevec before a recurrence and then have a recurrence later, may still be eligible for some front-line trials. In addition, it seems likely that most patients will just forgo a front-line trial and take Gleevec instead. Early indications are that one way pharmaceutical companies are dealing with the problem of a limited patient pool is to spread out the trials.

Inlander was 64

Richard Paul Inlander died in San Francisco on May 9th at the age of 64. He was born in Chicago, IL, on October 4, 1943 to Newton and Gladys (Lewin) Inlander. Richard relocated to the San Francisco Bay Area in 1961, to attend the University of California at Berkeley and Hastings College of the Law. He was active in the Jewish community, Congregation Sha'ar Zahav, Congregation Emanu El and Sinai Memorial Chapel, all in San Francisco. Richard is survived by his beloved and devoted friend of 22 years, Benjamin Schalit, San Francisco; his sisters, Martha Ross (Stanley) of Oakland, CA; Amy Jo Inlander, Flossmoor, IL; sons, Adam Louis Inlander (Ginny), New Albany, OH; Ethan Michael Inlander (Kim), Fayetteville, AR; and Nandi Deva Sundaram (Taylor Birdie Chi), Irvine, CA; and five grandchildren.



Reflecting his lifelong love of elephants, Richard requested that in lieu of flowers, donations be made to the Elephant Sanctuary in Tennessee, www.elephants.com, or to a charity of your choice.

It's a girl!

Congratulations to LRG Board Member, Stan Bunn! Bunns' third child, Reese Taylor Bunn arrived on January 14. She weighed in at 6 lbs. 3oz. Both baby and momma are doing fine.

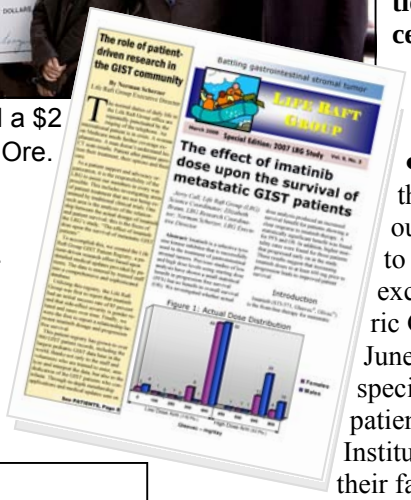
2008

From Page 8

team, which in 2008 expanded to ten scientists from the United States and Europe. In October, we brought together our entire team for a meeting in Portland, Oregon to discuss their progress in implementing our strategic plan to find and overcome GIST treatment resistance, as well as to discover new drugs to prevent any resistance at all.

The LRG Research Team is presented a $2 million check at a meeting in Portland, Ore.

- We began networking with biotech and other organizations to plan more effective clinical trials, especially for drugs that could be life-saving in the GIST community.
- We shared data that was drawn from our Life Raft Group Patient Registry concerning the relationship between the actual dosages of Gleevec that patients were prescribed (as opposed to their starting dosage) and both progression-free and overall survival rates. **In March, we once again alerted the patient and medical communities about our concern that many GIST patients are being underdosed.**



- We finally saw the culmination of our extensive efforts to create a center of excellence for Pediatric GIST patients in June. The opening of a specialty clinic for these patients by the National Institutes of Health at their facility in Bethesda, Maryland was momentous for both the LRG and the Pediatric GIST community.

2009 Objectives

Despite our ever-growing collection of accomplishments combined with the valiant battles of GIST patients, we are still strong believers that even one loss is one too many. Our major goal this year is to continue to address our two-prong strategy to improve patient survival.

- First, we intend to dramatically intensify our efforts to ensure that physicians understand and apply the very latest information for treating GIST. This includes routine mutational testing, a commitment to treat those patients with exon 9 mutations with higher doses of Gleevec and routine plasma level testing to help determine patient compliance levels and possible treatment for underdosing.
- On the research front, we intend to continue to fine-tune and expand the efforts of our research team, including their next planned meeting in Boston in March, and to develop new ways to improve the speed and efficacy of clinical trials.

You can read more about plasma and mutational testing in back issues of the LRG newsletter. Search the archives at www.liferaftgroup.org/newsletters.html.

Did you Hear...

If you have a diagnosis of GIST and are 18 years or older, Project FLAG needs you! - whether or not you have any cancer in your family. Project FLAG is led by the Dana-Farber Cancer Institute (Drs. Judy Garber, George Demetri, and Suzanne George); partners include Memorial Sloan-Kettering Cancer Center, Life Raft Group and others.

Project FLAG
Families Learning About GIST

By participating in Project FLAG, you will help researchers learn more about GIST in families. This information may help develop screening to detect and treat GIST early. Learn more and enroll at www.ProjectFLAG.org or call 1-800-828-6622 option #1.

Wife and mother passes at 61

Jeannette K. McIntosh, 67, of Scott, Ohio, died Sunday, Jan. 18, 2009, 9:53 a.m., at Van-crest Health-care Center in Van Wert, Ohio. She is survived by her husband, Russell McIntosh of Scott; whom she married Dec. 12, 1961; and children, Vicki L. Sexton of Fort Wayne, Jeff (Kim) McIntosh of Montpelier, Ohio and John L. McIntosh of Monroe, Wis. She was preceded in death by son, Curtis McIntosh. Preferred memorials to Arthur G. James Cancer Hospital in Columbus, Ohio or Liberty Baptist Church Building Fund. Condolences may be sent to agfhc@embarqmail.com

FRENCH

From Page 1

Attendees at the 2nd French GIST conference, held in Lyon, on November 22, 2008.

discussion forum. It was the very first time people could sit together and discuss their experience with the disease and its treatments, their life-projects and sometimes their difficulties. Many people actually recognized that they appreciated this "human dimension", which is sometimes missing on the internet. Some also admitted that the stories they heard and the people they met helped them to get to a new vision of their own situation.

We strongly believe this conference has, in many ways, helped to alleviate feelings of isolation some patients had before, as well as helped to strengthen the links between the members and lead to a better understanding of what living with GIST is really like.

Obviously, the major interest of such an event remains scientific and it was important to us to offer people the possibility to meet and exchange with renowned national GIST and sarcoma experts. Ensemble contre le GIST put together a terrific panel of GIST experts who proposed a very rich and educational program:

● Prof. JF Emile (Pathologist) and Dr. Bruno Landi (Hepato-gastro-enterologist):
"GIST diagnosis and mutational analysis"/"MolecGIST & EndoGIST studies"

● Dr. Eberhard Stoeckle (Surgeon): "Surgery of localized and metastatic GIST"

● Dr. Axel Le Cesne (Medical Oncologist): "GIST and Imatinib"

● Dr. Binh Bui (Medical Oncologist): "Imatinib and Pharmacokinetics"

● Prof. Florence Duffaud (Medical Oncologist):
"Compliance and management of treatment side-effects"

● Prof. Jean-Yves Blay (Medical Oncologist): "Treating resistance to imatinib: Second- and third-line therapies" & "Collaboration between A.F.P.G & Conticanet "

● Dr. Sophie Piperno-Neumann (Medical Oncologist): "Expert patient/ Physicians relationship"

Each session was followed by a discussion. It was very educational for both physicians and members as physicians discovered that many patients were extremely well informed and patients realized that sometimes (at least more often than they had imagined) doctors don't know the answers to all of their questions.

Patients also discovered what "compliance" was and were very surprised to learn about the rates of poor compliance. Surprisingly, when we asked the participants about their attitude towards treatment, the results were clear: everybody was 100 percent compliant. This was until the coffee break when some admitted they may have skipped their treatment "once or twice"!

This conference will remain a great memory. It took place in a very warm and friendly atmosphere where patients, caregivers and doctors could freely speak together in a different context than the one they're accustomed to. We ended the day with a piece of cake and a glass of champagne, promising to be compliant and to meet again next year. As a gift, people went back home with a pillbox in the color of Ensemble contre le GIST.

A CD providing the presentations of the conference as well as brief summaries of the sessions will soon be sent to members and put on our website (www.ensemblecontrelegist.org) for visitors.

A.F.P.G. gets new VP

"Change has come for Ensemble contre le GIST," that's what French members can say since unanimously electing Christian Mercier as the new Vice President during the second national GIST conference, held in Lyon.

Christian Mercier, 62, was diagnosed with GIST in 2001 and has been taking Glivec since April 2003. Retired from the banking sector, Christian Mercier now lives with his wife Brigitte near Arcachon, in southwest France. Christian is the father of a 30 year-old son and is the happy grandfather of a grandson named Etienne, who was born in Washington DC, the day before the US presidential election.

MERCIER

Since he became a member of Ensemble contre le GIST in March 2007, Christian has been highly involved in the group and its different events, and is particularly willing to focus on fundraising. His sense of humanity and his communication qualities make him an excellent liaison for the whole group to whom he regularly brings support on the forum of our website.

Since June 2008, Christian also acts as the official representative at the National Cancer Institute when the president cannot attend meetings.

Mercier succeeds Madeleine Joubrel who wished to resigned from her duties.

I and the members of the board are very happy about Christian's election and would like to wish him a very warm welcome in his new responsibilities.

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