

# Dallas hosts Life Fest '06 Sept. 15-17

Bringing together the top GIST researchers, patients who need them

**S**ave the date! The LRG board of directors and staff have announced plans for Life Fest 2006.

For those who attended Life Fest 2004 or the very first meeting held in May, 2002 in Cambridge, Mass., you know what a truly wonderful event is planned. It's a chance to put faces to names, and to meet close "cyberfriends" you've never seen before.

As board member John Poss puts it, "It's like a giant group hug."

The meeting will be held Sept. 15-17 in Dallas, Texas, at the Adams Mark hotel, located in the heart of downtown, a short walk from the Arts District and only a tram ride away from the many other attractions the city has to offer. It will be a perfect opportunity to take a little vacation.

Kerry Hammett and members of the Life Raft's Southwest chapter have graciously volunteered to be the official hosts for the event. Tricia McAleer, LRG executive assistant, met with the group to focus on the needs of the GIST community and how this meeting can be structured to best serve them.

The meeting will consist of three main elements:

— The initial progress report from the Life Raft's Resistance Research Team. Life Fest attendees will be the first to hear about and discuss the latest developments in the fight against resistance.

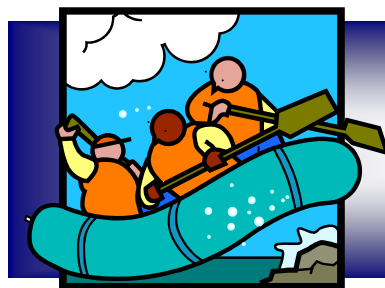
— Patient and caregiver support and education.

— Cutting-edge information on new drugs, clinical trials and access to treatment.

Here are comments from those who attended Life Fest 2004:

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Battling gastrointestinal stromal tumor



## LIFE RAFT GROUP

March-April 2006

In memory of Maj. Thomas More Quigley  
and David Rankin

Vol. 7, No. 3

# Life Raft funds 10 research projects

Eight experts to lead studies of imatinib resistance

**By Norman J. Scherzer**  
Life Raft Executive Director

**A**fter many months of work assembling a world-class research team, creating the first strategic research plan for GIST and building a grants infrastructure, the first round of Life Raft Group grants have been awarded.

The framework will allow for unprecedented collaboration between researchers. Team leaders will coordinate their projects across institutional and national boundaries.

Following sign-off by the Life Raft's outside reviewers, initial two-year re-

search grants have been awarded to Catholic University in Leuven, Belgium, Dana-Farber Cancer Institute/Brigham & Women's Hospital in Boston, Oregon Health & Science University/Portland VA Research Foundation, Memorial Sloan-Kettering Cancer Center in New York, Stanford University in Palo Alto, Calif., and the University of Washington.



**SCHERZER**  
The framework will allow for unprecedented collaboration between researchers. Team leaders will coordinate their projects across institutional and national boundaries.

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Institution	Principal investigator	Grant
Memorial Sloan-Kettering*	Besmer, Antonescu	\$373,750
Dana-Farber/Brigham & Women's	Fletcher	\$259,000
Oregon Health & Science University/Portland VA Research Foundation	Corless, Heinrich	\$251,000
University of Washington	Rubin	\$213,750
Catholic University, Leuven, Belgium	Debiec-Rychter	\$206,000
Stanford University	Van de Rijn	\$206,500

\*Memorial Sloan-Kettering grant includes \$175,000 dedicated to pediatric GIST research.

# Maybe There Is A Better Way

By Norman J. Scherzer  
LRG Executive Director

My views about research have changed in the past few years. I once thought it was sufficient to make a donation in the name of research. It seemed like the right thing to do. I gave little thought to how much of the donation was taken off the top for administrative overhead or how realistic the research was. There was a good feeling about the mystique of donating to research that was reinforced by knowing that lots of us were joining together.

What's wrong with this? It certainly makes people feel good. It makes me feel good. It particularly gives a sense of purpose to cancer patients who face an ongoing battle against feeling helpless. It makes a lot of researchers and medical institutions very happy.

But how effective is it in finding a cure for cancers?

Imagine buying a house the same way. We find a broker or a builder and we hand him a check in the name of house building. No clear direction. No plan of action. No coordination. And administrative overhead of 50 percent or more. We return some time later and find that our house has bathrooms without toilets, no front door, and windows that do not open. All because no one was in charge and each subcontractor chose

not to share information with the others.

That is the state of most cancer research today. Fierce competition. No overall plan. No coordinator. Administrative overhead that can exceed 70 percent. There is intensive input by researcher, institution and pharmaceutical companies, but virtually no input by the consumer — the patient.

*Maybe there is a better way.*

Start with some of the best researchers. Ask them to expand to a larger planning group by adding other scientists that bring synergy and value-added expertise to the table. Then, ask that group to create a plan that focuses on the most likely ways to find a cure, and to create a coordinated approach that cuts across institutional and national boundaries.

Challenge the researchers to agree to replace competition with collaboration and to strive for excellence over consensus. Reduce the administrative overhead that comes off the top from over 70 percent to no more than 10 percent.

When you've done all that, then give those researchers the money to implement the strategic plan they created and hold them accountable for the results.

That is what the Life Raft Group is attempting. Not because we want to supplant the expert scientists. Not because we want to control others. Only because we must think smart to survive by leveraging limited resources in a race to find a cure for a rare disease — GIST.

## March clinical trial update for resistant GIST

By Jerry Call

**AMN107 + Gleevec**

Patient enrollment has been temporarily stopped while the protocol undergoes dose-related changes. The trial is expected to reopen for accrual soon at both Dana-Farber in Boston and Fox Chase in Philadelphia.

**PTK787/ZK222584**

Recently added to the Clinical Trials.gov database is a trial known as "PTK787/ZK222584 in the Treatment of Metastatic GISTs Resistant to Imatinib." This is a phase II study being done at the University of Helsinki in Finland. This trial listed a start date of September 2004.

PTK787/ZK222584 was synthesized and developed by Novartis Pharma AG and Schering AG. It is a tyrosine kinase inhibitor and inhibits VEGF receptors as well as KIT and PDGFRB.

**GLIVEC**

Also just added to the Clinical Trials.gov database is a trial called "Open-Label Trial of Glivec with Unresectable or Metastatic Malignant Gastrointestinal Stromal Tumors." This study is designed to improve GIST treatment in several Central and Eastern European Countries. The rationale is to assess the clinical and biological activity of imatinib and to compare the data with historic data. This trial includes sites within Austria, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Lithuania, Romania, Serbia and Montenegro, Slovakia and Slovenia. Details can be found at the Web site, [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov).

## PedsChat, the first pediatric GIST listserv

As part of its program for pediatric GIST patients, the Life Raft has set up a pediatric listserv called PedsChat. It has been well-used as of late.

Caregivers and pediatric GIST patients who would like to become members should e-mail Elizabeth at [ebraun@liferaftgroup.org](mailto:ebraun@liferaftgroup.org) or call our offices at (973)837-9092.

— By Elizabeth Braun



# Mansfields look to the future despite worries

*This article is part of the “Caregivers of the Life Raft Group” series. The series focuses on the spouses, children, siblings or friends who walk alongside the patients in sickness and in health.*

**By Erin Kristoff**

**G**ail & Tim Mansfield have enjoyed a lot in their retirement. Tim is always working on cars and doing jobs around the house. He takes walks with Gail almost every morning and rides his bike every afternoon. Gail keeps herself equally busy; she is an avid quilter and is currently learning watercolor painting. Since their retirements in 2000 and 2001, the Mansfields have made the most of their time at home and spend as much time as possible together.

Tim was diagnosed with GIST in July of 1994 on his 52nd birthday. Gail had to take him to the hospital due to flu-like symptoms. “He was in intensive care in

the hospital and they couldn’t figure out why he was bleeding internally. They gave him several pints of blood. Finally, there was this really great surgeon who just wouldn’t give up. He said, ‘I want to open you up.’ He found a 9 cm. GIST tumor in his stomach.”

The tumor was removed and doctors sent the couple on their way. No one mentioned a follow-up. And Gail and Tim went on about their lives. Both enjoying their jobs. Tim used to build and maintain the large computers used to develop the new Intel processors. Gail worked in the reliability department of a large company that made test equipment, testing the durability of integrated circuits.



Gail and Tim Mansfield

“I would build special boards and power [the circuits] up and put them in these special ovens,” Gail says. “We were simulating warm, moist conditions

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## Optimizing therapy for GIST: A discussion

M.D. Anderson’s Trent responds to common questions from patients

**By Jerry Call**

**N**ovartis Oncology recently hosted a Web cast titled, “Optimizing Therapy in CML and GIST: Bringing Hope to Patients.” Dr. Jonathan C. Trent, assistant professor, Department of Sarcoma Medical Oncology, M.D. Anderson Cancer Center, gave the GIST presentation.

Trent noted that the sarcoma community enrolled large numbers of patients into clinical trials rapidly, since no effective therapy existed prior to Gleevec. Prior to Gleevec, objective response rates (OR) were around 5 percent. The Gleevec studies found OR rates that ranged from 48 percent to 71 percent.

The largest study was the European

Table 1 — Reasons for initial dose reduction*			
Arm A (400 mg/day)		Arm B (800 mg/day)	
Primary Toxicity	No. of Pts	Primary Toxicity	No. of Pts
Rash	5	Edema	42
Edema	4	Nausea	26
GI bleeding	4	Fatigue	20
Nausea	3	Rash	20
Pain	3	Diarrhea	15
Dyspnea	3	Vomiting	12
Creatinine elevation	2	Pain	10
Diarrhea	2	GI bleeding	8

NOTE: Some patients had multiple primary toxicities

\*U.S./Canada phase III data. Incidence and reasons for dose modification of standard-dose vs. high-dose imatinib in the Phase III Intergroup Study S0033 of patients with unresectable or metastatic gastrointestinal stromal tumor. P. Dileo, et al, 2005 ASCO

Organization for Research and Treatment of Cancer study which randomized patients into groups of 400 mg. or 800 mg. He noted that patients receiving 800

mg. had a four- month advantage in progression-free survival. In the U.S. study the difference in progression-free sur-

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# Imatinib resistance focus of intense study

By **Dr. Jonathan Fletcher**

**T**he research program implemented by the Life Raft Group will support highly integrated research that characterizes mechanisms by which gastrointestinal stromal tumors (GISTs) develop resistance to therapeutic KIT inhibition. The studies will evaluate therapeutic modalities that can be combined with imatinib treatment to improve response duration and approach a cure for patients with GIST.



**FLETCHER**

The studies will be conducted by investigators with a leadership role in GIST research and whose laboratories are primarily focused on GIST science. Each investigator is committed to working together, integrating research results, and identifying promising approaches that will enhance the cornerstone role of imatinib therapy for GIST patients.

The scientific themes have been organized into 10 priority research programs including two highly annotated GIST tissue banks to support the projects.

## **Priority Project A:**

Dr. Peter Besmer, Memorial Sloan-Kettering Cancer Center

### **Oncogenic KIT Signaling Mechanisms**

Besmer is one of the co-discoverers of the KIT protein. He has studied KIT oncogenic mechanisms for more than 15 years. He is superbly positioned to orchestrate Project A with objectives of understanding how activated KIT molecules translate their abnormal activity into GIST cell proliferation and survival. These will be performed in human GISTs, in cells transformed by

mutant KIT oncogenes, and in transgenic mouse GIST models. These studies will inform us of critical pathway attack points that can be paired with imatinib to develop therapeutic synergies.

## **Priority Project B:**

Dr. Matt van de Rijn,  
Stanford University

### **KIT/PDGFRα wild type GISTs**

Van de Rijn is an expert in gene and protein profiling in GIST and is well qualified to coordinate Project B. This project seeks to identify alternative oncogenic mechanisms in GISTs lacking KIT or PDGFRα mutations. The alternate oncogenic mechanisms will be identified by profiling the genes and proteins expressed in these GISTs. These studies will identify “escape” mechanisms by which GISTs can activate proteins that are not susceptible to imatinib inhibition. Investigators will evaluate the hypothesis that such mechanisms can then be targeted to develop therapeutic synergies with imatinib.

## **Priority Project C:**

Drs. Christopher Corless and  
Michael Heinrich, Oregon Health  
& Science University

### **Primary Imatinib Resistance**

Corless and Heinrich are leaders in genomic evaluation of KIT mutations and imatinib response mechanisms in GISTs. This project will evaluate the mechanisms accounting for lack of clinical response to imatinib in a subset of GIST patients. These studies will then determine whether novel kinase inhibitor drugs are better suited for inhibiting the particular KIT (or PDGFRα) mutations that show primary resistance to imatinib. In addition, proteomic methods will be used to determine why the subset of GISTs with exon 9 KIT mutations have an

unsatisfactory response to imatinib.

## **Priority Project D:**

Dr. Maria Debiec-Rychter,  
Catholic University of  
Leuven, Belgium

### **Stable Disease**

Debiec-Rychter is a leader in GIST research in the European community, and her group has extensive experience researching mechanisms of imatinib response and resistance. Project D evaluates stable disease in patients who initially have a therapeutic response to imatinib, but in whom the clinical response then plateaus, leaving the patients with substantial amounts of radiographically evident tumor. The project will determine why subsets of GIST cells continue to survive in the face of imatinib therapy, even though the overall GIST lesion was responsive to imatinib. In addition, these studies will evaluate serum markers for imatinib response which will be used to monitor patients during imatinib therapy. Finally, the studies will identify cell signaling pathways which remain activated in stable GIST lesions during imatinib therapy. Together, these studies will provide a better understanding as to why GIST cells persist during imatinib therapy and the insights needed to develop complementary therapies that synergize with imatinib in treating stable GIST lesions.

## **Priority Project E:**

Drs. Christopher Corless and  
Michael Heinrich, Oregon Health  
& Science University

### **Secondary Imatinib Resistance**

This project addresses the major problem of secondary resistance mechanisms in patients who have had

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## PROJECTS

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an exemplary response to imatinib but in whom one or more GIST lesions then progress. The goals in these studies are to use various cell culture assays to understand why certain mutations are resistant to imatinib, and to identify alternate kinase inhibitors that can effectively attack these mutations. Transgenic mouse models will also be employed in these studies, to provide more comprehensive evaluations of drugs which might synergize with imatinib and assist patients who have developed imatinib resistance.

**Priority Project F:**  
Dr. Jonathan Fletcher,  
Harvard Medical School

### **Secondary Imatinib Resistance**

Fletcher has studied GIST oncogenic mechanisms for 15 years and his group is working on novel therapeutic approaches that regulate KIT synthesis and degradation. This project will evaluate therapeutic approaches that destroy KIT oncoproteins, and will be focused initially on HSP90 inhibitors. HSP90 is required to stabilize KIT oncoproteins in GIST cells irrespective of whether the KIT oncoproteins are resistant or sensitive to imatinib. These studies will be performed in GIST cells, mouse GIST models, and in non-GIST cells transformed by genetic transfer of the types of imatinib-resistant KIT oncoproteins found in progressing GISTs.

**Priority Project G:**  
Dr. Brian Rubin,  
University of Washington  
**Murine Models**



Some of the research team members met at a conference in 2005. From left are Dr. Brian Rubin, Dr. Peter Besmer, Dr. Michael Heinrich, Life Raft Science Coordinator Jerry Call, Dr. Maria Debiec-Rychter, Dr. Matthew van de Rijn, Dr. Jonathan Fletcher, Dr. Cristina Antonescu and Life Raft Research Coordinator Elizabeth Braun.

Rubin is an internationally acclaimed expert in GIST pathology and a leader in creating laboratory mice that develop GIST tumors. The goal of this project is to evaluate novel therapies for GIST in transgenic mice that develop GISTs because of germline KIT mutations. This project complements the studies of primary and secondary imatinib resistance in human cells (Projects D and E) but with the focus here being exclusively on *in vivo* data obtained from mouse models.

**Priority Project H:**  
Dr. Jonathan Fletcher,  
Harvard Medical School  
**Resource Development**

Fletcher will coordinate the development of GIST cell lines as well as non-GIST cells (Ba/F3 cells) transformed by introduction of imatinib-sensitive and imatinib-resistant KIT genes. Collectively these resources will enable the various project investigators to investigate mechanisms of GIST imatinib resistance, and to validate new therapies that synergize with imatinib in killing GIST cells.

**Priority Project I:**  
Dr. Cristina Antonescu, Memorial  
Sloan-Kettering Cancer Center

### **Pediatric GIST**

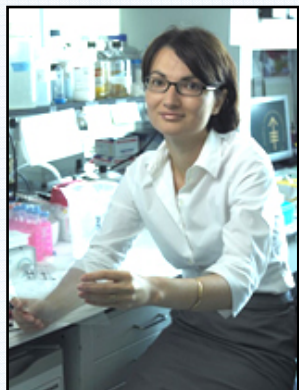
Antonescu is one of the world's leading authorities in GIST pathology, and her group has played a leadership role in characterizing the various genetic aberrations responsible for GIST. Her work is particularly focused on pediatric GISTs, which are notoriously resistant to imatinib therapy. The important goals of this study — performed by gene expression array profiling — are to identify mechanisms by which KIT is activated in pediatric GISTs, and to understand why these activation mechanisms are imatinib resistant.

**Priority Project J:**  
**Tissue Banks**

The above mentioned research projects will be supported by a highly annotated GIST tissue bank which will be co-led by Matt van de Rijn at Stanford (adult GIST tumors), and Cristina Antonescu at MSKCC (pediatric GIST tumors).



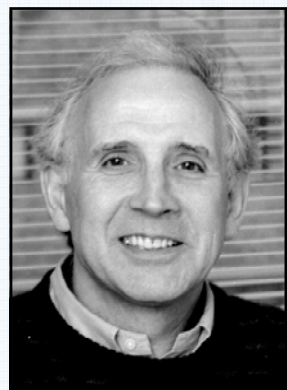
## The LRG Research Team



**Dr. Cristina Antonescu**  
Memorial Sloan-Kettering Cancer Center  
*Researcher, grant recipient*



**Dr. Maria Debiec-Rychter**  
Catholic University of Leuven, Belgium  
*Researcher, grant recipient*



**Dr. Peter Besmer**  
Memorial Sloan-Kettering Cancer Center  
*Researcher, grant recipient*



**Dr. Jonathan Fletcher**  
Brigham and Women's Hospital  
*Researcher, grant recipient*



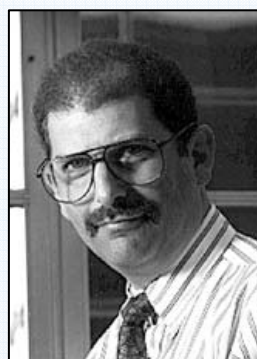
**Dr. Peter Blume-Jensen**  
Merck Research Laboratories  
*Grant review panel*



**Dr. Michael Heinrich**  
Oregon Health & Science University  
*Researcher, grant recipient*



**Dr. Christopher Corless**  
Oregon Health & Science University  
*Researcher, grant recipient*



**Dr. Lee Helman**  
National Cancer Institute  
*Grant review panel*

## The LRG Research Team



**Dr. Laurie Letvak**  
Novartis Oncology  
*Grant review panel*



**Mr. Norman Scherzer**  
The Life Raft Group,  
Executive Director



**Dr. Paul Meltzer**  
National Human  
Genome Research  
Institute  
*Grant review panel*



**Mr. Gerald Knapp**  
The Life Raft Group,  
Board of Directors



**Dr. Matthew van de Rijn**  
Stanford University  
Medical Center  
*Researcher, grant recipient*



**Dr. Brian Rubin**  
University of  
Washington  
*Researcher, grant recipient*

**In addition to Scherzer and Knapp, the Life Raft Group is represented by:**

**Elizabeth Braun**, Research  
& Administrative Coordinator

**Jerry Call**,  
Science Coordinator

**David Josephy, Ph.D.**,  
Science Team

**Mr. Michael Josephy**,  
Science Team

**Richard Singleton, Ph.D.**,  
Science Team



## LIFE FEST

From Page 1

“Anyone out there who was not able to attend — you were missed — but please try to make earnest plans, God willing, to get to the next Life Fest,” said Alice Sulkowski of Tennessee. “We really do have to keep meeting like this!” Said Sarah Buch of Colorado, “Just got back from the Orlando meeting and am still overwhelmed! What a wonderful group of members we have, and what a wonderful event we had take place. The doctors and expert lectures, as well as seminars held by our own members, were phenomenal!”

Life Fest '06 will include general sessions, the chance to speak with GIST specialists, and breakout sessions where patients discuss their GIST battles and share side effects management, communicating with doctors, accessing treatment and receiving overall support.

All GIST patients, caregivers and their families are welcome. All involved are working hard to make sure it is a fantastic, memorable, wonderful meeting.

Please check the Life Raft Web site, [www.liferaftgroup.org](http://www.liferaftgroup.org), and upcoming newsletters for meeting arrangements as they are finalized. Full details will soon be available.

## Maj. Quigley fought GIST 9 years

**M**ajor Thomas More Quigley, USMC (ret.), died March 9 in Tucson, Ariz., surrounded by his family. He was 40 and had battled GIST for nine years.

Quigley was born Nov. 11, 1965 in Chicago Heights, Ill. and moved to Tucson with his family in 1969. He attended Salpointe Catholic High School and received his undergraduate degree from the University of Arizona in 1987. A member of the Naval ROTC program, he was commissioned a second lieutenant in the United States Marine Corps in August 1987.

Promoted to first lieutenant two years later, Quigley served during Desert Shield and in the combat zones of Desert Storm. He finished his Marine Corps career as a major in the Marine Aviation Weapons and Tactics Squadron.

Following his medical retirement from the Marine Corps, Quigley successfully pursued a civilian career in technology information, going back to school, receiving an MBA degree from the University of Phoenix and serving the people of Pima County as information system and help desk manager through the end of 2005. He found time for fishing



**QUIGLEY**

trips to the White Mountains with his several brothers, also bringing along his son, Christopher when school allowed.

Quigley is survived by his wife, Sylvia Reid; his son, Christopher

Jack; parents, retired judge John M. Quigley and Esther Quigley; a sister, Mary Colette Skowron (Steve), brothers John Michael Jr. (Trudy), Dan (Ane Marie), Christopher, Patrick (Sherie) and Kevin (Julie); 32 first cousins and a very large extended family, including several aunts and uncles.

A Mass was celebrated March 16 at St. Thomas the Apostle Catholic Church. In lieu of flowers, the family asks that contributions be made to the Maj. Thomas More Quigley, USMC (Ret) Scholarship Fund. This fund will be used to assist students attending Salpointe Catholic High School. Contributions may be mailed to: Kevin D. Quigley, Quarles & Brady, 2 N. Central Ave., Phoenix, AZ 85004-2391.

## Pediatric GIST Newsletter plans launch this spring

**By Elizabeth Braun**

**R**achel Gilbert and Ashley Young have agreed to be editors for the new Pediatric GIST Newsletter. It will be published on a quarterly basis, starting at the end of April.

Rachel was diagnosed with GIST when she was only 15. As a strong and healthy gymnast, it was difficult for her to deal with the changes GIST brought to her life. She has survived the last three-and-a-half years by focusing on the positive. She has chosen to fully embrace life and smiles everyday.

Ashley, now 20 years old, was diagnosed at only 16. She has worked hard

to balance work, school and social activities with the pain and fatigue that GIST has caused.

Ashley is very excited about being able to help other young people with GIST. She is looking forward to providing insight and fun for the newsletter.

For the first edition, Sue Cohen of Tomorrow's Children, a program for children with cancer, is writing an article. Cohen joined the Life Raft Group at the first pediatric meeting last May.

Jerry Call, unsurprisingly, will be contributing a science article. There will be several exciting announcements about upcoming programs and events.

The goal of the Pediatric GIST News-



**GILBERT**



**YOUNG**

letter will be to have fun while providing people with pediatric GIST news that they need.

Keep your eyes open for the first edition of the Pediatric Newsletter.



# Patient status after four years on Gleevec

By Jerry Call

The 2006 American Society of Clinical Oncology gastrointestinal conference was held in January. Dr. Charles Blanke, Oregon Health & Science University, updated the results of the original phase II trial of Gleevec for GIST. This was the earliest trial and the results represent the most mature response data available.

This trial was for patients with unresectable or metastatic GIST. Many of the patients had very advanced disease.

Even in this advanced stage of GIST, the median overall survival in this trial was 4.8 years. Blanke said that patients with “stable disease” and those that had minor shrinkage that didn’t qualify as a response did just as well as those with a partial response (see Figure 1).

Overall, two-thirds of the patients had a partial response to Gleevec; only 12 percent had initial progression. The median (50 percent of patients) time to response was 12 weeks, however, the time to response varied from three weeks to 171 weeks. Two of the 147 patients had a complete response.

A patient’s mutation status (genotype) was the best predictor of both response and overall survival. Patients with a KIT exon 11 mutation had the best partial response rates (87 percent, see Figure 2) and the longest overall survival (see Figure 3). The median overall survival has not been reached for patients with KIT exon 11 mutations.

Blanke’s conclusions:

— Gleevec is well tolerated and remains the most effective therapy for patients with advanced GIST.

— Survival strongly correlates with response or achievement of stable disease.

— The median onset of response is relatively fast (12 weeks); however, 25 percent of patients respond after 23 weeks.

— Drug efficacy is related to kinase genotype.

— Despite the potential emergence of Gleevec resistance, a significant fraction of patients remain on drug long term.

Figure 1. Overall Survival by Best Response (Kaplan-Meier Estimate)

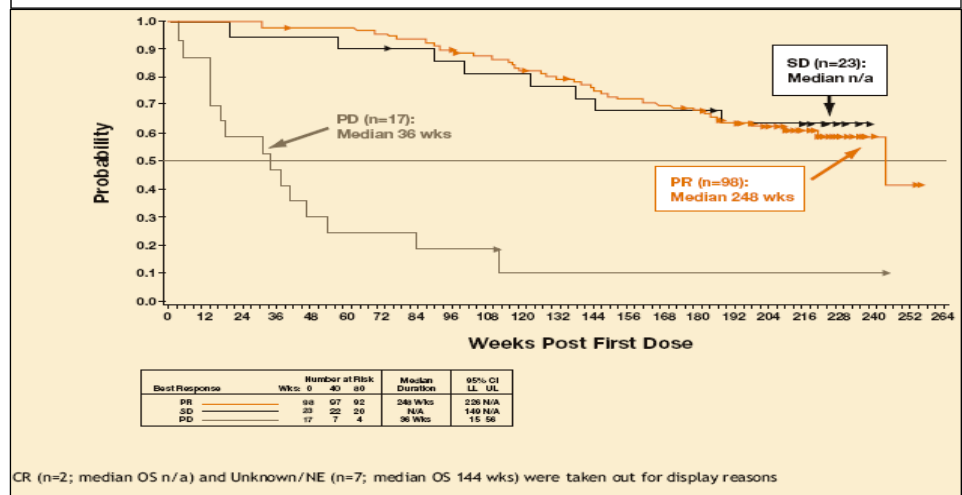


Figure 2. Genotype vs. Clinical Response

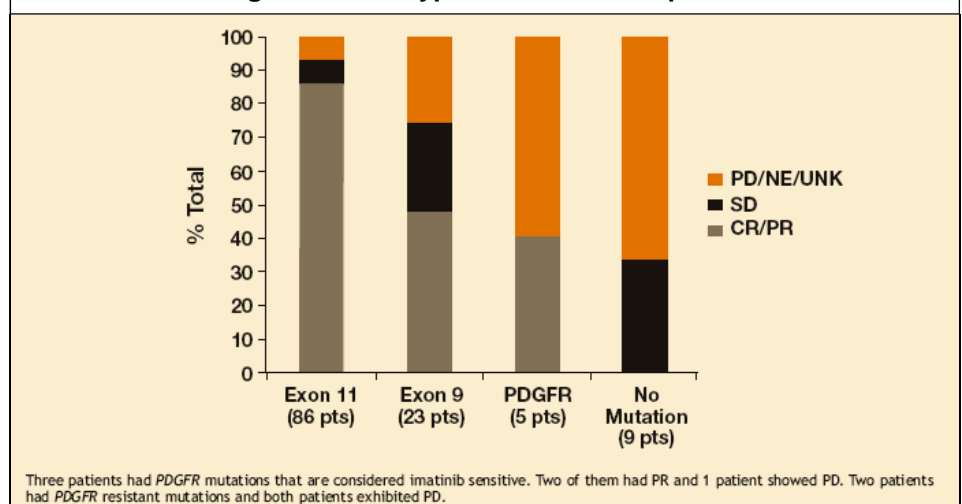
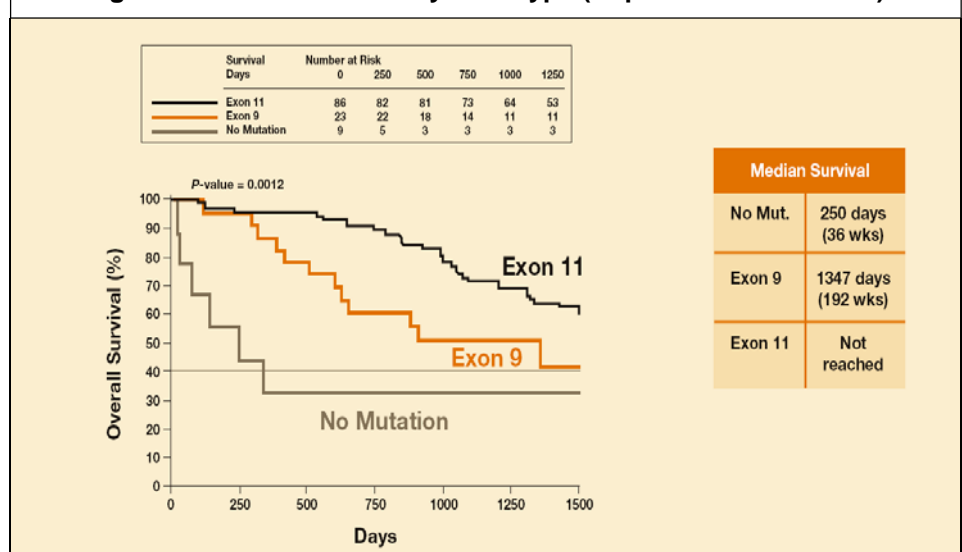


Figure 3. Overall Survival by Genotype (Kaplan-Meier Estimate)



## TRENT

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vival was also present.

The following are a few questions that patients frequently ask Trent:

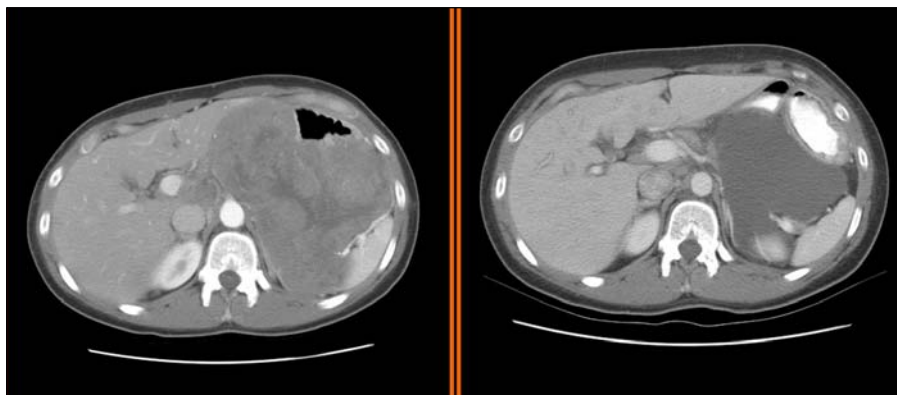
### How do I manage or prevent side effects?

The longer progression-free survival time noted in the EORTC study has a cost: increased side effects from the higher dose. The U.S./Canada phase III study found that the reasons for dose reductions were different for patients starting at 400 mg. versus those starting at 800 mg., as shown in Table 1.

Trent noted that not only did patients starting at 800 mg. of Gleevec have more frequent and worse side effects, but they also required dose reductions and dose interruptions much more frequently. In the EORTC study, patients starting at 800 mg. interrupted treatment 64 percent of the time and reduced their dose 60 percent of the time, compared to 40 percent and 16 percent, respectively, for patients starting at 400 mg. The side effects were mostly fatigue and edema, with few effects on blood counts.

Data from the U.S. phase III trial showed that patients starting at 800 mg. required a dose reduction 44 percent of the time. Only 10 percent of patients on 400 mg. needed to reduce their dose. For patients starting at 400 mg. and then crossing over to 800 mg. due to disease progression, only 16 percent required a dose reduction).

**Figure 1:** Decrease in GIST intravenous contrast uptake after patient is treated for 8 weeks with imatinib mesylate



Images courtesy of New England Journal of Medicine

According to Trent, “toxicity doesn’t markedly increase after a patient has been on 400 mg. for a while and then increases the dose to 800 mg. In patients whom require a higher dose of Gleevec, I slowly titrate to the target dose over several weeks or even months.”

### How do I know if Gleevec is helping me?

The mindset of many oncologists is based on studies from the 1970s that resulted in the “WHO” (World Health Organization) criteria, that later evolved into RECIST (Response Evaluation Criteria In Solid Tumors). To qualify for a “partial response,” RECIST requires a 30 percent or greater decrease in the sum of the largest diameter of all measurable tumors and an absence of any new tumors. Trent noted that for GIST, the RE-

CIST criteria is misleading at times and doesn’t make for the best design of clinical trials — at least when using drugs like Gleevec.

Trent gave examples of why RECIST is inadequate to measure response of GIST tumors to Gleevec. Figure 1, above, shows two CT scans. In the scan at left, a large GIST tumor is shown before treatment with Gleevec. The variation in gray is characteristic of a GIST. The lighter areas indicate viable (alive/capable of growing) tumor and the dark areas represent non-viable (dead) tumor. The scan at right shows the same tumor after eight weeks on Gleevec. The tumor now is a darker shade of gray. This uniform, dark color and density change are characteristic of GIST that is responding to Gleevec.

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**Global GIST Network  
adds  
New  
Ireland  
representative**



**Carol Jones**  
roycal@eircom.net

Visit the Global GIST Network  
at [www.globalgist.org](http://www.globalgist.org)



### Locks of Love

Michelle Mattioli, granddaughter of Life Raft Executive Director Norman Scherzer, decided to donate her hair to Locks of Love as a way to show her support for her grandmother Anita and other cancer patients. Locks of Love is a nonprofit group that provides hairpieces for disadvantaged children under 18 suffering long-term medical hair loss.



## MANSFIELD

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like the swamps of Louisiana and the climate of India, and we would see when they break and how they break. It was fun.”

Nonetheless, when they finally decided to retire, the two were happy to leave it all behind and devote time to each other. But in early 2004 Tim began to feel the flu-like symptoms returning. That’s when GIST started becoming very real to Gail.

“It’s the fear of losing him, of not having him there,” she says. “We’re very close, we always have been, we’ve done everything together. It’s the fear of loving somebody so much and seeing them die. He’s the only one who knows what it feels like. I try to feel with him and for him.”

The Mansfields didn’t know what was causing the sickness but they supported each other as best they could. “It’s always just been Tim and I, we have no children, and we have few friends,” Gail says. “We didn’t even tell anyone when the metastases came back. Our support system is just the two of us.”

They found solace in talking with each other about the situation. “We would sit on the front porch and talk. It’s hard. We don’t like to take our troubles to others, we’re very independent. So we talked to each other a lot.”

But as a caregiver it was hard for Gail. When Tim felt the pressures of sickness, he leaned on her. Gail had only Tim. “Sometimes I would get really bothered and go to sleep and silently cry, others times I would talk about it.”

“Tim actually thought he might have hepatitis from the blood he was given in 1994, until the ultrasound showed the mass in his liver. His internist then ordered a full body scan and a needle biopsy which confirmed it was metastatic GIST that was c-kit positive.”

Tim received the news on his 62nd birthday, 10 years after the original diagnosis. “Needless to say, birthdays will never be the same.”

Tim started Gleevec on Sept. 1, 2004, just a few months after they heard the bad news. He had a PET scan just 10



Gail Mansfield displays one of her beautiful quilts.

days after starting Gleevec and it showed dramatic results. Since then, Tim’s six-month scans have shown shrinkage followed by stability.

Normalcy has almost returned to the Mansfield home and the couple is enjoying their retirement.

Though Gail and Tim are grateful for their good fortune, GIST is also about the opportunities they don’t have. “One of the frustrating things is the things we wanted to do in retirement that we can’t do,” Gail says. “We’ll never buy that condo in the mountains or go on the vacations we want. It’s the disappointment of having something like this and putting away your hopes and dreams.”

Gail is still looking toward the future, despite these worries. “I hope that the Gleevec works for him for a really long time and on the horizon that there’s a new drug that will kill [GIST]. I just want to grow old together.”

Whatever the circumstance, Gail is aware of how lucky they both are for Tim’s restored health. “We feel blessed, we have freedom, every day is our own.”

## GRANTS

From Page 1

### TISSUE BANKS CREATED

The Life Raft has created two tissue banks, one at Stanford University Medical Center for adult GIST, together at Memorial Sloan-Kettering for pediatric GIST. A common protocol has been adopted for submitting tissue. Each of the principal investigators has agreed to participate in testing and annotating frozen tissue samples that will be collected by the appropriate tissue bank and distributed to each individual institution.

An article by Dr. Jonathan Fletcher describing the 10 priority research projects begins on page 4. The research team members are on pages 6-7.

The complete GIST Research Plan can soon be found on the Life Raft Web site, [www.liferaftgroup.org/research](http://www.liferaftgroup.org/research).

## Help keep the Life Raft afloat!

The Life Raft Group would like to thank everyone who participated in the Thanksgiving Fundraising Campaign. It was exceptionally successful. We are grateful for all of your support of the Life Raft’s programs.

For those unable to participate due to the holiday craze, donation envelopes will soon be sent out with our first Annual Report and you will have the opportunity to contribute again.

Additionally, you are still able to donate to the Life Raft Group throughout the year by going to our Web page, [www.liferaftgroup.org](http://www.liferaftgroup.org), or by calling us at (973) 837-9092.

Thank you to everyone who chooses to participate. Every contribution makes a vast difference.



## Deep in the heart of Texas

GIST patients and caregivers enjoyed lunch together after the March 25 meeting of the Southwest chapter of the Life Raft Group at Gilda's Club, North Texas. From left are Ronnie and Betty Arnett, Kerry Hammett, Kurt Molitor, Tricia McAleer, John Poss, Betty and Jim Avant.

## TRENT

From Page 10

"We've found that tumor cells have been replaced by myxoid degeneration in this setting, despite the fact that the size of the tumor hasn't markedly changed," according to Trent, "solely monitoring the size of tumor in GIST patients treated with Gleevec can be misleading if one doesn't consider the changes in radiodensity of the tumor."

In Figure 2, at right, the CT scans on the top show a tumor increasing in size but the majority of the tumor is turning a dark uniform color.

This is evidence of Gleevec response with only a smaller rim of tumor on the right side which appears to still be viable. The PET scans on the bottom confirm the response to Gleevec.

"GISTs treated with Gleevec can stay the same size when a patient is receiving incredible benefit," said Trent. "In fact in some instances, the tumor can actually increase in size. This type of increase in size can be due acutely to intratumoral hemorrhage, but it may also be due to increased osmotic pressures after tumor cells rupture within an encapsulated mass (many GISTs are confined by a very thin surrounding pseudocapsule)."

Another example of patients getting excellent benefit from Gleevec in spite of limited tumor size reduction can be



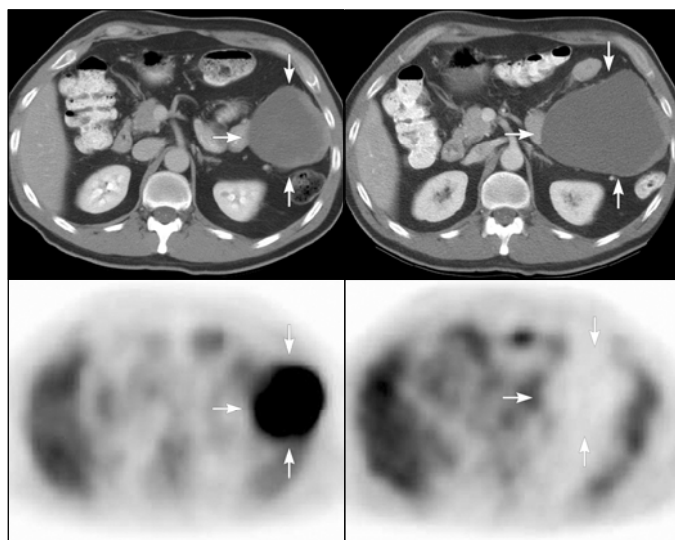
TRENT

seen from the graph of overall survival by best response (see the "Patient status ..." article, Page 9 Figure 1). In this trial, patients with stable disease had survival rates that were very similar to patients achieving a "partial response."

### SUMMARY

Gleevec-related side effects improve significantly over time. It has been suggested that this may be due to drug levels that tend to fall over time in GIST patients. A European study found that Gleevec levels may fall by 40 percent during the first 12 months of treatment (see the January 2005 edition of this

**Figure 2:** Imatinib's effects on GIST, as shown via CT and PET scans



Choi et al, Radiographics. 26:481-495, 2006

newsletter).

Trent noted that for patients needing a higher dose of Gleevec, he slowly raises the dose over a period of several weeks or even months. This approach is known as dose escalation or a "run-in" period. It has been advocated by some GIST specialists, especially some European specialists. Patients seem to be able to tolerate this approach much better than starting at 800 mg.

*The second half of this article will be featured in our May 2006 newsletter.*



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## 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.). This molecularly targeted therapy represents a new category of drugs known as signal transduction inhibitors and has been described by the scientific community as the medical model for the treatment of cancer. Several new drugs are now in clinical trials.

## How to join

GIST patients and their caregivers may apply for membership free of charge at the Life Raft Group's Web site, [www.lifteraftgroup.org](http://www.lifteraftgroup.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.

Donations, payable to The Life Raft Group, should be mailed to:

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## 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.