

# Connecting the Dots: Call offers perspective on GIST trends

By Jerry Call  
LRG Science Coordinator

*Note: This editorial attempts to convey and analyze some of the recent research material, with a focus on genotyping. It is written by a layperson and is for informational purposes only; it is not a substitute for talking to your doctor. Others, including GIST experts, may have a different point of view. This article should not be construed as representing the opinions of any other person.*

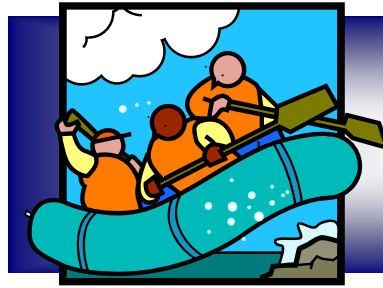
**A**t Life Fest 2006, Life Raft Group Executive Director Norman Scherzer and Science Coordinator Jerry Call gave a presentation, "Connecting the Dots" to try to connect much of the new GIST information. Knowledge about GIST continues to grow at a rapid rate. This knowledge comes from clinicians, researchers, drug manufacturers and from patient groups. With so much new information, it can be difficult to interpret it all.

In the last 6 months quite a bit of new information about GIST has been published and presented at international conferences such as at ASCO (American Society of Clinical Oncology). Eventually the experts will meet and discuss this information and perhaps revise/update GIST treatment guidelines. This editorial is about *survival decision-making*: connecting the dots to survive in the interim.

Much of the new information concerns genotyping. Genotyping is the genetic makeup of an individual, in the form of

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Battling gastrointestinal stromal tumor



## LIFE RAFT GROUP

November 2006

In memory of James Coppede & Omer Cloutier

Vol. 7, No. 9

## Life Fest: A Texas-sized success

### Opening night reception draws 175 guests

By Norman J. Scherzer

**I**t is impossible to choose one memorable moment or even a small number of highlights from Life Fest 2006. As 175 guests gathered for our opening reception and dinner it was striking that one could not pick out who the patients were.

The seamless behind the scenes support and logistics coordinated by Tricia McAleer and the LRG staff made it all seem effortless, but truth is that it was driven by extraordinary energy and skill. Freeze the moment. Late arrivals are signing in at the registration desk. Tricia

and Board Member Rodrigo Salas are heading to the lobby to meet and greet Dr. Daniel Vasella, the chief executive officer of Novartis, accompanied by David Epstein, president of Novartis Oncology and Debbie Friere, vice president of Novartis for Patient Advocacy. The videographer is setting up. A volunteer has been recruited to fill in for the still photographer, a GIST patient sidelined for the evening because he had to be cared for at an emergency room. Drinks are being served at the cash bar. Tee shirts and pins are being sold. New and old friends are greeting one another

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Vasella enjoys a moment with his new friends Leah Knopp and "Jossie" Dunn.

# Researchers give update on GIST Resistance Project

By Rick Ware  
Member of LRG Science Team

One of the highlights of Life Fest 2006 was a presentation of research updates by several members of the LRG GIST Resistance Research Team. Our GIST Resistance Research Team, led by Jonathan Fletcher, M.D., is made up of world-renowned clinical/research medical experts who share a common focus and ultimate goal – *The Defeat of GIST!* Dr. Fletcher and this remarkable team of top international GIST Specialists have committed to helping to successfully lead us into the future of GIST cancer treatment. Development of research methodologies that promote international collaboration along with transparent sharing of individual/collective research excellence and seamless communication between project investigators/laboratories are the guideposts of their novel research paradigm. Everyone works together for success of the project goal – *A CURE for GIST!*



WARE

tance Research Team included:  
1) Dr. Peter Besmer (Memorial Sloan-Kettering Cancer Center) – “Oncogenic Signaling Mechanisms”  
2) Dr. Matt van de Rijn (Stanford University) – “KIT/PDGFR WT GIST”  
3) Dr. Christopher Corless and Dr. Michael Heinrich (Oregon Health and Science University) – “Primary Resistance and Secondary Resistance Mechanisms”  
4) Dr. Maria Debiec-Rychter (Catholic University of Leuven, Belgium) – “Stable Disease”  
5) Dr. Jonathan Fletcher (GIST Resistance Research Team Leader – Harvard/Dana-Farber/Brigham and Women’s Hospital) – “KIT Degradation”  
6) Dr. Cristina Antonescu (Memorial Sloan-Kettering Cancer Center) – “Gene Profiles in Pediatric GIST”

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The LRG Research Team presented at Life Fest 2006 their six-month report on the GIST Resistance Research Project. Pictured from left to right: Dr. Jonathan Fletcher, Dr. Marie Debiec-Rychter, Dr. Brian Rubin, and Dr. Matt van de Rijn.

## 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.). 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.liferaftgroup.org](http://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.

Donations, payable to The Life Raft Group, 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.

# CONNECT DOTS

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DNA. Typically, one refers to someone's genotype with regard to a particular gene of interest. In GIST, it is usually used to describe the common mutations that occur in the KIT and PDGFRA genes usually to the level of the affected exon, e.g., KIT exon 11.

Genotyping can be used for:

1. Determining Gleevec dose levels (Heinrich et al., Debiec-Rychter et al.)
2. Predicting response to Gleevec (Heinrich et al.)
3. Predicting response to Sutent (Demetri, Heinrich, et al.)
4. Generating hypotheses about adjuvant treatment (author's opinion)
5. Helping to evaluate new drugs

Items 1, 2 and 3 were covered in detail in the July and August 2006 editions of The Life Raft Group newsletter. You can review these by visiting [http://www.liferaftgroup.org/news\\_newsletter.html](http://www.liferaftgroup.org/news_newsletter.html).

The following table was developed by myself and is based on data presented by Dr. Debiec-Rychter, Dr. Verweij and colleagues.

As an aid in understanding this table, it is helpful to understand a few terms. Progression-free survival (PFS) is the

length of time from the start of treatment (in this case Gleevec for unresectable or metastatic GIST) until the time treatment fails (significant new growth or new tumors). Median PFS is the time point at which half of the patients have failed treatment and half have not.

In normal English, "significant" means important, while in Statistics "significant" means probably true (not due to chance). A research finding may be true without being important. When statisticians say a result is "highly significant" they mean it is very probably true. They do not (necessarily) mean it is highly important.

P value is a statistical measurement. The logrank test computes a p value that answers this question: If the two populations actually have identical survival curves, what is the chance that random sampling of subjects would lead to as big a difference in survival (or bigger) as you observed? For Table 1, row 1, there is a 2.6 percent probability (p value = .026) of observing a difference this large (between the two curves) if the curves were drawn from the same population (i.e., having the same probability distribution generating curves). An ob-

served difference that large or larger would be expected 2.6 percent of the time.

In the scientific and statistical world, a p value of .05 (5%) is generally the threshold that must be met to be "statistically significant." The second row of Table 1 has a p value of .20 (20%), not statistically significant.

In Table 1, row 1, we see that the p value is .026. Thus, there is less than a 3 percent chance that the data from which the median PFS difference was calculated would have been generated from identical patient populations (for example if both groups had been taking the same dose of Gleevec); the data is considered to be statistically significant. Row 2 of this table is for 377 patients in the same trial that had mutational testing (genotyping). Row 1 and row 2 both contain patients with all of the different types of mutations (exon 11, exon 9, PDGFRA, wild-type, etc). Row 2 is simply a subset of row 1 that has mutational data. Note, however, that when looking at the same heterogeneous group of GIST patients, row 1 is statistically significant (p=.026) while row 2 is not statistically significant (p=.20). Because the PFS difference between dose groups is relatively small, statistical significance was lost when the sample size was re-

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**Table 1-Progression-free Survival (PFS) Differs by Genotype and Gleevec Dose**

	Median PFS		P value log-rank (see note)
	400 mg	800 mg	
<b>All EORTC phase III patients (946 pts)*</b>	21 months	25 months	.026
<b>Patients with mutational data (377 pts)+</b>	21.5 months	24 months	.20
<b>Exon 11 (248 pts)+</b>	25 months	29 months	.25
<b>Exon 9 (58 pts)+</b>	4 months	19.5 months	.0013
<b>Wild-type (52 pts)+</b>	19 months	15.5 months	.07

Median PFS times were *estimated* by Jerry Call from Kaplan-Meier curves. Estimates are rounded to 1/2 month.

NOTE: This type of analysis is not as accurate as examining the numbers.

\*EORTC phase III data; Verweij et al., *Lancet* 2004. The PFS difference estimated from the Kaplan-Meier curve was 4 months; the actual difference (as noted in the article) was 5 months.

+ EORTC phase III data; Debiec-Rychter et al., *European Journal of Cancer*, 2006.

**NOTE:** The p values given are for the *overall PFS curves* (Kaplan-Meier curves); they are not directly related to the median PFS. Median PFS only considers one time point on the PFS curves. The p values given take into account multiple time points on the PFS curves. We have chosen to include these p values because they give an indication of the overall reliability of the PFS curves. From this we can infer something about the reliability of the median PFS data given.



## Over \$85,000 raised at New York City poker tournament

### Jerry's players pony up to lift Life Raft at Park Avenue Country Club

By Tricia McAleer

Once again, Life Raft Group Board member Jerry Cudzil has pulled off a first class event. The LRG's Third Annual Texas Hold'em Poker Tournament was held on October 12 at the Park Avenue Country Club in New York City. Jerry's inspiration for hosting this event every year is his father-in-law Bill Roth (pictured, bottom right). Bill began his battle with GIST in January of 2003. Shortly thereafter, Jerry got involved in fundraising for the LRG.

Over 100 players turned out for the tournament with goodness in their hearts and prizes on their minds. Sitting at the last table were some very serious faces, sweat beading on their brows, hoping to win a \$10,000 seat at the World Series of Poker (WSOP) in Las Vegas.

The final three remained. Lyon Carter III was the first to bow out, taking third place and a 36" plasma TV. Richard Joyce and Harold Kirk Baldwin remained. Harold was holding most of the chips and it seemed as though his fate was sealed but Richard came back in the eleventh hour and won. Still in good spirits, Harold took second place and a 42" plasma TV.

Richard Joyce will be heading to Las Vegas this summer to take his seat at the

main event for the WSOP. Last year's winner, Nick Chiara, gave us a good report on his experience at WSOP this past summer. He went as far as ten hours into the first round. Although not a winner again, he informed us that he is looking forward to coming back next year and bringing along his friends.

Special thanks to all those who attended, Eric Nerse-sian of Balthazar Trading, which offers handcrafted and functional executive gifts, who donated two custom-made humidors for raffle at the event, the staff of Long Island Poker & Casino Rentals and the staff at the Park Avenue Country Club.



Friends gather around cheering on players of the final round.



Baby Sean Cudzil enjoys time with his grandparents.

## Betty Louise Rosenbluth—Celebrating 75 Years (1930-2006)

By Deborah Rinehart

Meet Betty Rosenbluth, an extremely self sufficient, independent Mother, Grandmother (Nan), Great Grandmother, Aunt, Sister, Sister-in-Law and friend to all.

Betty was a very active senior citizen. She spent her time with her family, friends, and church. She was a 47 year

retiree from Danskin, post-retiree part-timer at Kohl's Department Store and an active member of several church and senior citizen social groups.

Betty was first diagnosed with GIST in 1993. After 4 years of utilizing surgical options to beat back the "dragon," she found her way to Dana-Farber and became a participant in the STI-571 trial in November 2000.

When Gleevec ceased to be effective she moved on to Sutent and finally to

AMN107. Due to unstoppable progression resulting in yet another surgery with an extended hospital stay, in June she decided to cease treatment. With her in the lead, our family banded together to bring her home where she rested comfortably until she passed.

Our experiences at Dana-Farber allowed her to meet her last three Great-Grandchildren, other GIST survivors, as well as professionals that have dedicated

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## RESEARCH

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7) Dr. Brian Rubin (University of Washington and The Cleveland Clinic) – “Murine (mouse) Imatinib Sensitive and Resistant Models”

Dr. Jonathan Fletcher, with his commanding presence and distinguished flowing wispy locks, immediately reminded me of “Doc” Emmett Brown from the movie “Back to the Future.” Dr. Fletcher’s compelling and enthusiastic desire to take us all into the future of GIST treatment was mesmerizing. In his opening remarks, “Doc” as I now affectionately think of him, shared that the Research Team Goal is two fold: Elucidation of the mechanisms of GIST treatment resistance and development of novel therapeutic agents to successfully overcome these resistance mechanisms. Dr. Fletcher sincerely believes that through the concerted efforts of our Research Team, GIST as a disease process will be increasingly medically controllable, if not curable, within 4 to 5 years. What a fantastic thought – “Hope for the Future and a Future with Hope.” Way to go Research Team!

Dr. Peter Besmer (Dr. Fletcher presenting) is the group leader of the Oncogenic Signaling Mechanisms Project. Dr. Fletcher and Dr. Besmer, co-discover of the KIT protein and a pioneer in the study of KIT and its oncogenic signaling mechanisms, shared insights into KIT activation and the concept of resistance heterogeneity. Primary KIT mutations in the exon 9 (dimerization domain) and exon 11 (juxtamembrane domain) with secondary imatinib resistance mutations in the ATP binding site and catalytic site were highlighted. Secondary imatinib resistant mutations may activate downstream pathways via abnormal KIT signaling with subsequent effects on GIST cell survival and proliferation. Potential downstream cascades include the JAK/STATs, RAS/RAF/MAPK and AKT/mTOR pathways. Preliminary data from Dr. Fletcher’s laboratory (Dr. Sebastian Bauer, in press) of incubation of

GIST882 (imatinib sensitive) and GIST48 (imatinib resistant) cell culture lines with 17-AAG (an HSP90 inhibitor) showed marked reduction/absence of phosphoKIT (activated KIT), phosphoAKT and phospho-S6 activity in both cell culture lines at concentrations above 0.5  $\mu$ M.

Dr. Maria Debiec-Rychter, group leader of the Stable Disease Project, has done extensive GIST research into the molecular pathogenesis of imatinib response/resistance mechanisms. Dr. Debiec-Rychter presented research on a GIST xenograft model developed for



Fletcher receives award from Dr. Daniel Vasella.

pre-clinical testing of novel agents. Using this GIST xenograft model (nude mice without hair or immunity that do not reject human tumors), Dr. Debiec-Rychter studied the growth-inhibitory effect of an experimental histone deacetylase (HDAC) inhibitor. HDACs are thought to act in a number of ways, one of which may include degrading KIT, and showed promising results against the murine xenograft GIST tumors. Pathology studies indicated significant effects of HDAC inhibition, as shown by increased apoptotic index (HDAC inhibitor > Imatinib > Control) and decreased mitotic index (Imatinib > HDAC inhibitor > Control). Also, review of the GIST tumor specimens from HDAC treated xenografts showed that HDAC inhibition induced regression with evidence of ischemia, necrosis, arrest of cell growth and induction of cell death. These findings are very interesting but still in the preliminary phase of study.

Dr. Christopher Corless and Dr. Michael Heinrich are group leaders of the Primary and Secondary Resistance Projects. Drs. Corless and Heinrich specialize in development and application of molecular diagnostics for use in the classification of solid tumors. Dr. Corless presented research on an allele specific polymerase chain reaction (AS-PCR) diagnostic assay for the detection of resistance mutations in KIT. This novel diagnostic assay is highly sensitive (1 in 1,000 cells) and will be of use in the detection of low-level resistance mutations in tumor biopsies, and possibly in the analysis of blood samples from patients on imatinib or other inhibitor therapies. Dr. Heinrich is developing a new “library” of cell culture lines that demonstrate mutational resistance to kinase inhibitors. After genotyping and determination of resistance point mutation(s), this new library of resistant cell lines will be cultured for sensitivity testing of combination therapies and new kinase inhibitors.

Dr. Matt van de Rijn, group leader of the KIT/PDGFRalpha Wild-Type GIST Research Project and host of the Adult GIST Tissue Bank has expertise in gene expression profiling, genomic hybridization and tissue microarray analysis. Dr. van de Rijn and his laboratory have developed a new high-through-put gene expression profiling technique that permits the use of paraffin-embedded tumor specimens. Up until now, conventional gene expression profiling methods have required freshly frozen tissue samples for analysis. With Dr. van de Rijn’s new high-through-put gene expression profiling technique, as little as 8 sections of 20  $\mu$ m thick FFPE (formaldehyde-fixed-paraffin embedded) tissue would be needed for analysis. The ability to use FFPE tumor tissue from slides or blocks would allow for almost unlimited availability of GIST research specimens. The key to success of this new high-through-put methodology is use of HEEBO (Human Exonic Evidence based Oligonucleotide DNA Microarray) platform arrays. HEEBO gene arrays are spotted oligonucleotides,



# Relay for Life for Japanese GIST Patients

By Sumito Nishidate  
LRG Japan Representative

It is estimated that there are about 3,000 GIST patients in Japan. Up until now, there has not been a patient group that has existed. The only group efforts have been conversations among patients on the internet.

Last January, I attended a meeting where Hideaki Miura, a lung cancer survivor, spoke about the importance of Japanese cancer patient participation in Relay for Life. While hearing his talk, I got to know that GIST patients share similar problems as other cancer patients.

This meeting inspired me to post an appeal on my Website to encourage people to think about patient participation in Relay for Life, such as:

“Why does treatment change by region?”

“Why is the right treatment not performed?”

“Why don’t patients encourage and support one another more?”

“Let’s all join together and walk for a good cause!”

About ten GIST patients and their family members reacted to my appeal.

I was able to gather participants to Relay for Life and together we formed a group called Cancer Patient Support Project (CPSP). We selected “GISTERS” as the name of our team. We chose this name so that people can



Japanese GIST patients and friends participated on Sept. 2 in the Relay for Life.

recognize that we are a group of GIST patients and their loved ones. This name expresses a team of family and friends.

The day of Relay for Life became the first memorable Japan GIST patient meeting.

In the future, we plan to strengthen cooperation among patients, caregivers, and medical professionals. We would like to continue advocating on behalf of Japanese GIST patients that deserve fair treatment options. We want to work to obtain the same standard treatment of medicine that the United States receives.

Although we are only a small group now, we believe that our power can make a big wave soon.

Relay for life was an event not only to remember the people we have lost in the battle against GIST but also to bless the survivors in the community. In Japan, patients were able to raise awareness about GIST during the Relay for Life event. We intend to change the social consciousness about cancer, GIST, and sarcoma. This is an aim of CPSP and GISTERS.

## Holiday Fundraising Campaign

The Holiday Fundraising Campaign is just around the corner. Keep an eye open for your packet at the beginning of November.

Now, more than ever, the Life Raft Group needs your support and participation in order to continue our life-saving efforts.

If you have any questions, need more materials, or you are not a member and would like to participate, contact the Life Raft Group office at (973) 837-9092 or liferaft@liferaftgroup.org.



*Magic Leaves*

## RESEARCH

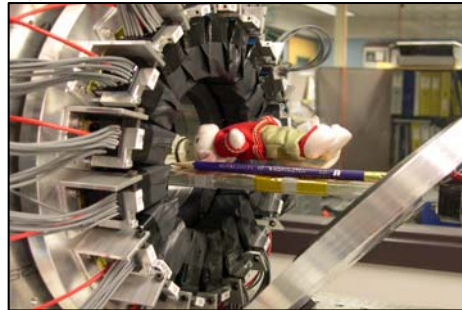
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which allow for analysis of smaller isolated RNA fragments. Dr. van de Rijn has used this new technique to validate Gleevec-sensitive and Gleevec-resistant GIST cell lines as representative models for drug testing. His laboratory demonstrated that immortal GIST 48 and GIST 882 cell lines cluster with known GIST patient samples. This new technology needs further validation, but the early results look very promising.

Dr. Cristina Antonescu (Dr. Fletcher presenting), group leader of the Pediatric GIST Project and host of the Pediatric GIST Tissue Bank, is investigating pediatric GIST and its imatinib resistance mechanism(s). Dr. Antonescu and her laboratory are developing strategies to successfully treat Pediatric GIST. Dr. Antonescu has shown that most pediatric GIST patients lack KIT or PDGFRA mutations (wild-type) and, according to gene expression profiling, group together (are biologically related) with adult wild-type GIST. Also, KIT is strongly activated in pediatric GIST and demonstrates both activity levels and signaling mechanisms very similar to those observed in adult GIST. Genes that are uniquely upregulated in pediatric GIST include FGF4 (fibroblast growth factor 4), PLAG1 (pleomorphic adenoma gene1) and IGF1R (insulin growth factor 1 receptor). An observed 10- to 20-fold increase in expression of these genes may have direct effects on cellular proliferation. Dr. Antonescu and her Research Team are also developing lab models for testing and evaluating novel KIT inhibitors for activity against wildtype KIT, some of which may inhibit wildtype KIT better than imatinib.

Dr. Brian Rubin, group leader of the Mouse Imatinib and Resistant Models Project has expertise in genomics and proteomics of sarcomas and in the development of mouse sarcoma models. Dr. Rubin working in conjunction with Dr. Besmer is constructing murine (mouse) models that mimic the development and biology of human GISTs as closely as possible. These genetically engineered

mouse models will be used to evaluate novel GIST therapies and assist in prioritizing the most promising new GIST drugs for clinical trials in human patients. GIST mouse models would have corresponding KIT and PDGFRA activating mutations similar to those observed in human GIST. In addition, Drs. Rubin and Besmer are also constructing GIST mouse models that harbor secondary resistance mutations. These new GIST mouse lines with secondary resistance will be used to expedite development and testing of novel drugs or combination therapies for imatinib-resistant GIST. “Stuart Little,” Dr. Rubin’s able-bodied lab assistant, served as the model for the newly developed mouse PET Scanner. This new PET Scan methodology will allow for “mini-clinical GIST



“Stuart Little” tries the new PET scan.

mouse trials” that permit both time-dependent evaluation of drug therapies and harvesting of tissue specimens for additional gene expression profiling and pathologic studies. Stuart was quite the Mouseketeer!

On behalf of our Life Fest 2006 participants, as well as all the members of our extended GIST Family who were unable to join us in Dallas, we extend our personal gratitude and a “very special thank you” to Dr. Daniel Vasella and Novartis AG for their generous financial support and to each member of the GIST Resistance Research Team for helping make this gathering a complete success. Your altruism and compassion, your selfless commitment to each individual patient and your unwavering dedication to research excellence have built a strong foundation upon which “Our Hope for the Future” now stands. Let us all continue to link arms together and pledge to complete our noble task — *A Cure for GIST.*

## LIFE FEST

From Page 1

as patients, scientists, caregivers and physicians mingle happily, their Hawaiian shirts and Texas jeans contrasting with sleek cocktail dresses, suits and tuxedos. Stunning.

Earlier in the day the LRG Board of Directors has met and reviewed all the plans for the meeting, and the scientists of the LRG Research Team have gotten together to coordinate their very first report on their research effort.

The pictures in this Newsletter and on our website will help fill in the story. I will let those who attended pick their own meeting highlight. Perhaps it was high energy Pam Barckett, LRG staffer, leading Leah and Josalin around the next door skating rink. Or maybe it was the sight of David Epstein conducting a marathon hug-a-thon as he presented a certificate to each long term (5-year) GIST survivor—there were over 20 there. The heart stealer of the meeting could have been the introductions of Dr. Vasella by Anita Scherzer and Josalin Dunn. Anita thanked Vasella and his

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Life Raft Group Board Member Silvia Steinhilber enjoys a small chat with David Epstein, president of Novartis Oncology, who just handed out the five-year survivor awards at Life Fest.



## LIFE FEST

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Life Fest attendees enjoy meeting one another Friday evening over a Texas-style barbecue dinner. Pictured from left to right counterclockwise: Dr. Jonathan Fletcher, Stan Bunn, Debbie Freire, Jerry Cudzil, Rodrigo Salas, David Epstein, Javier Baldor, Dr. Daniel Vasella, Norman Scherzer, and Anita Scherzer.

work with Gleevec for allowing her to know her seventh grandchild. Josalin, age nine, then took to the podium, standing on a milk crate, and told the guests that her best friends call her Jossie and then turned to Dr. Vasella and pointedly told him that “he could call her Jossie and that he was her new best friend.” Another end of the emotional spectrum was the candle ceremony conducted by LRG Board Member Bob Book for the many Life Rafterers who are no longer with us. The fact that the park we all met in was called “Cancer Survivor’s Park” added a special poignancy to the occasion.

### Research

In so many ways research turned out to be the thematic thread of the meeting. We began with a Friday afternoon meeting of our research team led by Dr. Jonathan Fletcher of Dana-Farber Cancer Institute and Brigham and Women’s Hospital, to review the Research Team’s five-month progress report and work out some wrinkles in coordination. Fletcher was joined by Dr. Maria Debiec-Rychter of Catholic University in Leuven, Bel-

gium, Dr. Brian Rubin of the Cleveland Clinic, Dr. Chris Corless of Oregon Health and Science University, and Dr. Matt van de Rijn of Stanford University. In his Friday evening keynote address, Vasella took considerable time to recognize and compliment the research done to date by the Life Raft Group’s review of patient medical records, particularly noting that we were the first to report on the relationship between Gleevec dosage level and efficacy and that an initially skeptical Novartis later came around to acknowledging that we were right. He also acknowledged and praised the research effort that we initiated to find the reasons for GIST resistance and then called our research team leader, Dr. Fletcher, to the stage to confer upon him our Scientist of the Year Award.

At a special breakfast meeting the next morning the LRG

Research Team got to meet with David Epstein to discuss early findings and the direction they were headed. The meeting also presented an opportunity to discuss moving mutational testing from a research test to a routine clinical tool. Also present at this meeting were LRG staff members Jerry Call, Norman Scherzer and Elizabeth Braun; Dr. Alberto Pappo from Texas Children’s Cancer Center; Dr. Laurie Letvak from Novartis; and Drs. Jerzy LaSota and Markku Miettinen from the Armed Forces Institute of Pathology.

On Saturday the research team presented a coordinated and patient friendly report at the morning’s plenary session. The team then joined Drs. Alberto Pappo and Jonathan Trent for an afternoon expert panel to respond to dozens of questions from the audience.

The keynote address on Saturday was given by David Epstein and once again the LRG research effort was singled out for praise, this time in commenting on the next AMN107 clinical trial for GIST patients that it was likely that Novartis would hear about the results first from



Trent gives medical update on GIST therapies.



## LIFE FEST

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the LRG patient surveillance system.

### Awards

Awards were a pleasant part of the meeting. In addition to the Scientist of the Year Award given to Dr. Fletcher, the LRG took the occasion to honor Richard Palmer for our Volunteer of the Year Award for his work as our Newsletter Editor. Like Fletcher, Richard was clearly moved and went on to describe how important it was to tell the stories of the GIST patients' lives and struggles. Richard's award was presented by LRG Board member Jerry Cudzil who noted that "what Richard

uniquely did was to put a human face on the story of GIST and the struggle of patients and caregivers...and that he did so with a compassion for the human spirit and a personal artistry with words and pictures."

A third (and surprise) award was given to Tricia McAleer, LRG executive assis-



Richard Palmer, right, accepts Volunteer of the Year Award from Life Raft Group Board Member Jerry Cudzil.

tant. Following his Friday evening closing remarks, Norman asked Tricia to join him to go over the meeting's logistics. When Norman asked Dr. Vasella to come up to the stage to join them, Tricia started getting really suspicious. When he asked the entire Board of Directors to also come up, she was getting really

nervous. And when he pulled the Employee of the Year Award out of his briefcase to the applause of all, she finally smiled. We cannot do justice here to the other plenary session and workshop presentations so we will try to get as many as possible up on our website, [http://www.liferaftgroup.org/members\\_lifest.html](http://www.liferaftgroup.org/members_lifest.html). The meeting ended for most on a note of happy exhaustion. For the LRG staff it will take some time to absorb everything that took place, make sure all

the bills get paid, and follow-up promises are honored and to start planning the next Life Fest.

Many thanks to the following companies that helped contribute to our meeting: Bristol-Myers Squibb, Build-A-Bear Workshop, Genentech, Infinity Pharmaceuticals, Novartis, and Pfizer.



A moving candle ceremony was held on Saturday in honor of all those we have lost to the battle with the GIST dragon.

# November 2006 clinical trial update

**By Jim Hughes**  
**Member of LRG Science Team**

## **AZD2171 (AstraZeneca International)**

This investigational drug is in early trials for a number of cancers. It inhibits KIT and VEGFR-1, VEGFR-2 and VEGFR-3. This Phase II trial is being sponsored by the maker, AstraZeneca, in the United Kingdom. The clinicaltrials.gov website lists a site recruiting in London. GIST Patients progressing on Gleevec are given AZD2171 45mg daily without Gleevec. Biologic tumor activity is evaluated by FDG/PET response at eight days and four weeks.

## **OSI-930**

OSI Pharmaceuticals has begun a Phase I trial of the compound OSI-930 at two locations in the US and one in Europe. The trial is for patients with advanced solid tumors, but will admit GIST patients. Locations include:

- Dana Farber Cancer Institute- Boston, Massachusetts (Dr. George Demetri, Principal Investigator)
- Colorado University- Denver, Colorado
- Royal Marsden Hospital- London, UK (Dr. Michelle Scurr, Principal Investigator)

OSI-930 is a new small molecule tyrosine kinase inhibitor. It inhibits c-Kit, VEGFR and PDGFRb. The trial began in August. Up to 60 patients are expected to be accrued.

## **Sutent**

In the United States, Canada, the United Kingdom and the European Union countries Sutent is now approved for patients failing Gleevec or those who cannot tolerate Gleevec. In addition, Sutent continues to be available to patients via the "Treatment Use Protocol," which is "four weeks on/two weeks off" (50 mg). There are many sites open throughout the world. Site information changes frequently; for the most current information, contact EmergingMed at 1-877- 416-6248 (outside the United

States) or at 1-800-620-6104 (inside the United States). If international patients have problems with the listed number, use email at: sutent@emergingmed.com.

In September Pfizer posted a new Phase III trial on the NIH website. This study will compare 37.5mg daily of Sutent with 800mg daily of Gleevec for patients progressing on 400mg of Gleevec. Anticipated enrollment is 212. Site information has not yet been announced. According to the listing this trial is not yet recruiting and is scheduled to start November 2006.

## **AMN107 + Gleevec**

The combination of AMN107 and Gleevec may have a broad spectrum of activity against primary and secondary mutations in GIST. The generic name for AMN107 is nilotinib and our understanding is that the brand name will be Tasigna. The Phase I trial is now closed at all sites. A Phase III trial is planned. In the meanwhile, access to AMN107 is available through a compassionate use process provided by Novartis.

## **IPI-504**

The IPI-504 phase I trial is open for patients resistant to prior therapies and is accruing patients at Dana-Farber Cancer Institute. It undergoes fairly frequent start/stop periods as cohorts accrue.

IPI-504 is an inhibitor of Heat Shock Protein 90 (HSP90) and has been the subject of articles in the November 2005 and January 2006 editions of the Life Raft Group newsletter. This is an intravenous drug which is administered twice a week for two weeks followed by a one week off period. HSP-90 is administered without Gleevec.

## **Genasense + Gleevec**

A phase II trial testing the combination of Genasense plus Gleevec in patients with Gleevec-resistant GIST recently opened.

Genasense (Genta Inc.) is an antisense drug that inhibits bcl-2. Bcl-2 is a protein involved in cellular survival. This

drug is administered intravenously. It is hoped that Genasense may help Gleevec kill tumor cells by making them more sensitive to Gleevec.

This trial is currently open only at M.D. Anderson. Several other trial sites are planned including: Dana-Farber Cancer Institute, Boston, Massachusetts; University of Michigan Comprehensive Cancer Center, Ann Arbor, Michigan; Mayo Clinic Cancer Center, Rochester, Minnesota; and Memorial Sloan-Kettering Cancer Center, New York, New York.

## **Perifosine + Gleevec**

Perifosine is an oral drug that inhibits the AKT protein. AKT is an antiapoptosis protein. It is speculated that inhibition of AKT might enhance therapy. Apoptosis is a form of controlled cell death, a type of cellular suicide where the cell issues its own death warrant.

The phase II trial, which combines Perifosine with Gleevec, is open at M.D. Anderson Cancer Center and accruing Gleevec-resistant GIST patients.

## **RAD001 + Gleevec**

Both RAD001 and Gleevec are manufactured by Novartis. RAD001 is an mTOR inhibitor that may improve the effectiveness of Gleevec

The phase II portion of the trial is completing its initial enrollment; the decision to expand the trial will be made in the coming months.

Additional sites are being opened in anticipation of the future work. Current sites are: Dana-Farber in Boston; Fox Chase Cancer Center in Philadelphia; Oregon Health & Science University (OHSU); University of California in Los Angeles; Berlin, Germany; and Leuven, Belgium.

## **PTK787/ZK222584**

This is a phase II study being conducted at the University of Helsinki in Finland and in Milan, Italy. This trial is for patients progressing on Gleevec.



# CONNECT DOTS

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duced.

When the difference in survival curves is relatively small, it takes large numbers of patients to reach statistical significance. Also note that the method used to construct this table can introduce error. This is evident in the first row where the PFS estimated (by the author) from the survival curves (not shown) is 4 months; the actual PFS calculated from the data (by the EORTC) was 5 months.

## Exon 9

From Table 1 we can see that the difference in PFS for (KIT) exon 9 patients is quite large; patients on high-dose Gleevec have about 15.5 months of additional (median) PFS vs. low-dose Gleevec. In addition, the p value (.0013 for the entire exon 9 PFS curve) is quite low. Because the difference is so large, it doesn't take as many patients to reach statistical significance. Based on the data, we can see that:

1. The difference between dose groups is large. PFS is almost 5 times as long in the high-dose group.
2. High confidence that the data is accurate.

In addition to the PFS data, Dr. Michael Heinrich presented data at ASCO (2005) that exon 9 patients on high-dose Gleevec had 8 times as much chance of responding to Gleevec (significant shrinkage) as those on low-dose Gleevec. Even though the data had a low p value (.03) it was not considered statistically significant at the time because it was an interim analysis.

From the data by Debiec-Rychter and Heinrich it is easy to conclude that exon 9 patients should be on high-dose Gleevec. In fact, this was recommended in the paper by Debiec-Rychter et al. (*European Journal of Cancer*).

In fact, the response of

exon 9 patients to low-dose Gleevec is so poor that one wonders if any exon 9 patient, including patients taking Gleevec as adjuvant treatment, should be on low-dose Gleevec. Patients that are not able to tolerate high-dose Gleevec (even with a dose-escalation period) have the option of taking Sutent, which has very good activity against exon 9 GIST tumors.

## Wild-type

Early data from the phase II GIST trial suggested that wild-type GISTs did not do as well as other GIST patients. They did not respond as well to Gleevec and they did not live as long. This data was based on only 9 patients, however. Recent data from both phase III trials show that wild-type patients have much better survival times than previously thought. In fact, the survival times are similar to exon 9 patients. This raises some questions:

- Is the response of wild-type GIST to Gleevec better than we thought?
- OR**
- Does wild-type GIST just have a slower natural course than other types of GIST?

It is difficult to interpret the dosage data on wild-type GIST. With a somewhat better initial response on low-dose

Gleevec vs. high-dose Gleevec and 83 percent of patients getting significant benefit from crossover to high-dose Gleevec, it is difficult to justify starting patients at higher doses. Wild-type GISTs also have a relatively good response to Sutent with a median PFS of 20.9 months after failure on Gleevec.

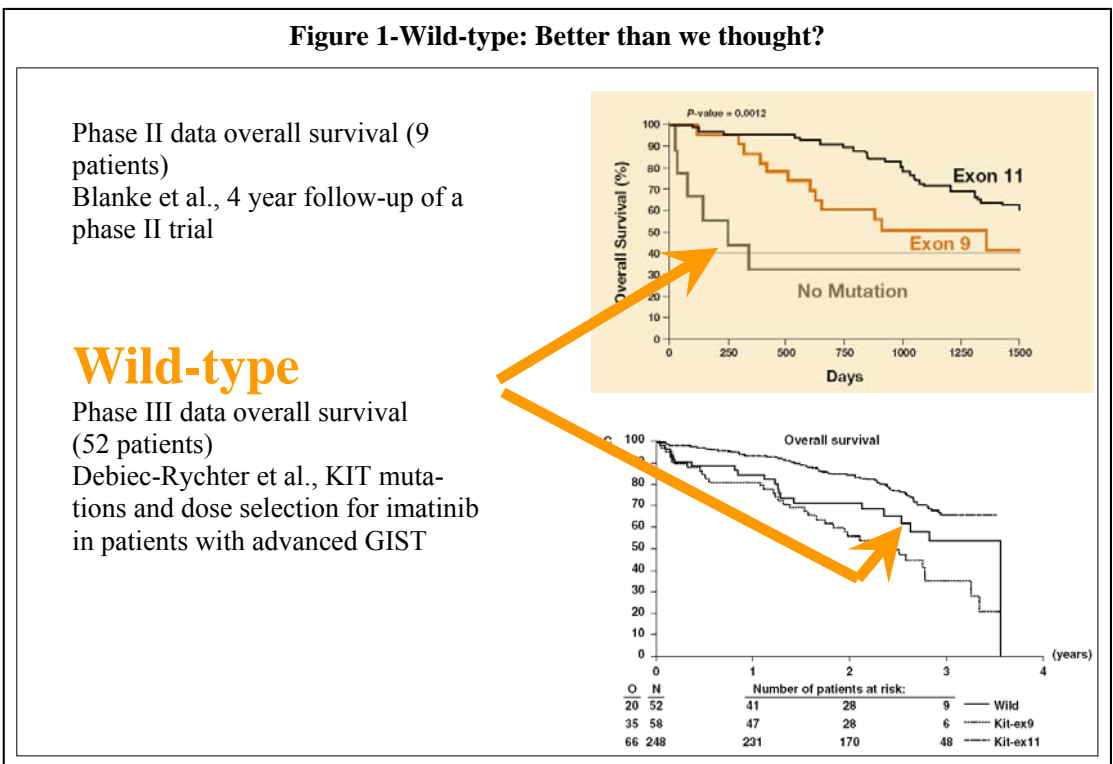
## Exon 11

In contrast to exon 9 and wild-type GIST, the data for exon 11 GISTs are not as clear-cut. If we were to only consider the EORTC data and we were to use strict scientific criteria, then we would conclude that no significant difference in PFS has been demonstrated. With a p value of 0.25, there is a 25 percent chance of getting as big (or larger) a difference as shown by the survival curves (from which the 4 months PFS advantage was calculated) even if both groups were exactly the same.

The exon 11 data is potentially subject to the same loss of significance (due to a reduction in numbers) as the overall data. Remember that the overall difference in PFS went from a statistically significant p value of .026 to a not statistically significant p value of .20 when the number of patients in the analysis was reduced from 946 to 377. Smaller

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Figure 1-Wild-type: Better than we thought?



## CLINICAL TRIALS

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PTK787 is administered without Gleevec. A seven day washout period is required.

PTK787/ ZK222584 was synthesized and developed by Novartis AG and Schering AG. It is a tyrosine kinase inhibitor and inhibits VEGF receptors as well as KIT and PDGFRB. See the July 2006 Life Raft Group newsletter for an article about this trial.

### BMS-354825 (Dasatinib)

BMS-354825 is a tyrosine kinase inhibitor of Src, abl, KIT, and PDGFR.

Dasatinib is available in a phase I trial at Dana-Farber and Glasgow, Scotland. In June the Karmanos Cancer Center in Detroit, Michigan also began recruiting patients. Future plans include a SARC phase II trial. We will update trial sites and the scope of the trial as this information becomes available.

This trial is for patients with progression on Gleevec. The BMS drug is administered without Gleevec.

### BAY 43-9006 (known as Sorafenib and by trade name Nexavar)

This drug was approved in December 2005 for kidney cancer. BAY 43-9006 inhibits several kinases including KIT, VEGFR-2, VEGFR-3, PDGFR-β, RAF, FLT3, and RET.

The phase II trial for BAY 43-9006 is open and recruiting patients. Three trial sites are open in Illinois and one in New York:

- University of Chicago- Chicago, Illinois.
- Decatur Memorial Hospital- Decatur, Illinois.
- Oncology/Hematology Associates of Central Illinois- Peoria, Illinois.
- Memorial Sloan-Kettering Cancer Center-New York, New York.

Several sites are also pending.

This trial is for patients progressing on Gleevec. BAY 43-9006 s administered without Gleevec. A fourteen day washout period is required before trial drug start.

### Sarcoma trials that also allow GIST patients:

The last two trials listed are sarcoma trials that allow GIST patients. There are several ways to attack GIST tumor cells with drugs. The most common method is to inhibit KIT and/or PDGFRA signaling. The protein is still present; it is just inhibited by the drug. This is the method used by Gleevec, Sutent and most of the other new inhibitors being developed (dasatinib, AMN107, etc).

Another way to target GIST is to destroy the KIT or PDGFRA protein. IPI-504 targets GIST tumors in this manner.

A third way to target GIST is to try to prevent (or reduce) the formation of KIT or PDGFRA proteins. The following two trials take the approach of inhibiting the formation of a large number of proteins including KIT and PDGFRA.

### Doxorubicin + Flavopiridol

This is a phase I trial to determine the maximum tolerated dose of the combination of doxorubicin (a traditional cytotoxic chemotherapy) with flavopiridol (an inhibitor of the cell cycle and an inhibitor of transcription). This trial is for sarcoma patients (including GIST patients) that are 18 years old or older. Patients must have a performance status of ECOG 0-2 or Karnofsky 60-100 percent. Projected accrual is 3 to 36 patients.

The trial is being conducted at Memorial Sloan-Kettering Cancer Center in New York, New York.

### FR901228

This is a phase II trial for sarcoma patients, including GIST patients, with metastatic or unresectable disease. FR901228 (depsipeptide) belongs to a new class of chemotherapy drugs called histone deacetylase inhibitors (HDAC inhibitors). This is a class of drugs that works at a higher level within the cell-acting on the genome, which is like the master control room for all of the genes in a cell.

Patients must be at least 18 and have a Performance status of ECOG 0-2 or Karnofsky 60-100 percent. Projected accrual is 18 to 36 patients.

Trial locations include:

Phoenix, Ariz.; Oakland, Calif.; Rome, Ga.; Decatur, Ill.; Louisville, Ky.; Columbus, Ohio; Greenville, S.C.; Spartanburg, S.C.; Danville, Va.; Burlington, N.C.; Greenville, N.C.; Goldsboro, N.C.; Winston Salem, N.C.; High Point, N.C.; Elkin, N.C.; Goldsboro, N.C.

## New websites launched for Italy and France LRG Groups

French LRG representative Estelle LeCointe



launched a GIST organization in France called "Association Française des Patients du GIST: Ensemble contre le GIST" in May 2006. Educational materials have been produced in the French

language and a website has been created. For more information, please contact Estelle LeCointe at [info@ensemblecontrelegist.org](mailto:info@ensemblecontrelegist.org) or visit [www.ensemblecontrelegist.org](http://www.ensemblecontrelegist.org) (which will be up at the end of November).

Italian LRG representative Anna Costato just founded and announced on October 19 the new GIST organization in Italy called "Associazione Italiana GIST." Costato hopes to reach nearly



one thousand GISTers identified in her country. For more information,

please contact Costato at [info@gistonline.it](mailto:info@gistonline.it) or visit [www.gistonline.it](http://www.gistonline.it).

One can view other organizations in the growing Global GIST Network by visiting [www.globalgist.org](http://www.globalgist.org).



## CONNECT DOTS

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differences in PFS require larger numbers of patients to prove that a real difference exists. The EORTC data is designed to be combined with the U.S./Canadian phase III trial. When this occurs, the exon 11 picture should become clearer as the power of the study will increase.

When considering clinical results, it makes sense to evaluate all of the available information. The EORTC data is very valuable and will become even more valuable when it is combined with the other phase III data. But it is not the only information available. Would limited effective treatment options after failure of low-dose Gleevec lend more weight to the argument for higher-dose Gleevec? What are the options (and how effective are they) after Gleevec failure?

- Crossover to 800 mg after progression was only effective (as measured by the growth modulation index) in 7 percent of exon 11 patients in the EORTC study.

- With Sutent, the median PFS is about 5 months and only about 35 percent of exon 11 patients get 6 months of stability (significant shrinkage is fairly rare).

Other arguments favoring higher doses for exon 11 patients include:

- The dilution of data from dose reductions using intent-to-treat analysis. In the

EORTC trial, 60 percent of patients assigned to 800 mg had permanent dose reductions (to 600 mg, 400 mg or below) but are still counted in the high-dose arm. This type of analysis (which is the gold standard) may tend to estimate the *minimum* potential benefit of the high-dose arm (in this case).

- An internal LRG study found that when comparing actual dose to intent-to-treat dose, a greater difference in PFS was observed, with higher doses showing a greater benefit. This study has limitations including possible selection bias and subjective progression criteria (patient-reported data). The effect may be that this study estimates the *maximum* possible benefit of the high-dose arm.

- Gleevec levels may fall as much as 33 to 40 percent over time (several possible reasons have been cited). This may be riskier for patients who are on lower doses.

With exon 11 GISTs, an argument can be made for either low-dose Gleevec or high-dose Gleevec. Low-dose proponents can cite the data has failed to show statistical significance and the PFS difference is relatively small. High-dose proponents can cite the lack of efficacy of crossover to high-dose Gleevec and Sutent and that 4 to 5 months PFS benefit (which may exist) for high-dose Gleevec is equal to the benefit they might get from Sutent.

Gleevec produces side effects which can be significant. These side effects are worse at higher doses. The long-term effects of Gleevec are not known and could be worse at higher doses. With exon 11 patients, there seems to be a wider therapeutic range of Gleevec dosing especially compared to exon 9. Patients that might be more suitable for low-dose Gleevec (400 mg) might include:

- Those with more significant side effect issues.
- Those that have less confidence that the data shows a difference that is significant *to them*.
- Those that are willing to accept a little more risk of progression.
- Patients with good adherence to taking Gleevec (they don't forget, reduce or skip Gleevec).

Patients that might be more inclined to want higher doses of Gleevec might include:

- Patients with less side effects.
- Patients that believe the overall data shows a difference between doses that is significant *to them*.

To summarize exon 11 patients and their physicians appear to have a lot more flexibility. The wider therapeutic range appears to allow more fine-tuning to balance side effects against the possibility of longer PFS.

## Coppede was an avid golfer and gardener

James Coppede, 80, of Kersey, northeastern Pennsylvania, died Wednesday evening, Sept. 27, 2006, at the Elk Regional Health Center after a lengthy battle with GIST.

He was born July 15, 1926, in Kersey, son of the John and Dina Gavazzi Coppede.

He was a lifelong resident of the Elk County area and attended Kersey schools. He retired from the Brockway Glass Co. in 1989 after 15 years of service. He was a member of the St. Boniface Church and a veteran of World War II, having served in the Army. He was a

member of the Dagus Mines American Legion, Knights of Columbus, and was an avid golfer and gardener who loved to hunt.

He was married to the former Mary Sicheri. They would have celebrated their 50th wedding anniversary Oct. 13.

In addition to his wife, he is survived by two daughters, Laurie (David) Pasi of Kersey, a Life Raft Group member for nearly four years, and Darlene Schlimm of Palm Harbor, Fla.; six grandchildren, Brooke Pasi, Kyle Pasi, Morgan Pasi, Chelsea Schlimm, Kaila Schlimm and Danielle Schlimm; a sister, Irene

Coppede of St. Marys; and a brother, Mario Coppede of Buffalo, N.Y.

Besides his parents, he was preceded in death by three sisters, Angeline Morrow, Marie Coppede and Loretta Carrara.

A Mass of Christian burial was celebrated Sept. 30 at the St. Boniface Church in Kersey with the Rev. John Kuzilla officiating. Burial was in the Holy Cross Cemetery in Brandy Camp. Full military rites were accorded by the Fox Township Servicemen's Burial Detail.

# GIST Walk in memory of Peter Thomas

By Richard Palmer  
Newsletter Editor Emeritus

From the California coast to the shores of Rockland Lake in New Jersey, GIST cancer patients, family and friends collectively walked hundreds of miles Sunday, Oct. 15, to raise money for research.

And raise money they did. Robert Stutman, who with his wife, Tania, began the Walk for a Cure six years ago, said the fund-raising effort should easily top last year's total of \$147,000 – and could break \$200,000.

“The donations are still coming in,” Robert said a few days after the event. “I don't know if we can get \$200,000 but I know we can get \$175,000. And every penny is going to research.”

Chances of a record-high tally this year are virtually assured for two reasons. One is the first Walk for a Cure West that took place the same day in Ventura, Calif. Second is the financial boost from the GIST e-2-e 2006 Cycle Ride held in England this past July.

This year's walk was in memory of Peter Thomas of Woking, U.K., a GIST patient who died Aug. 22. Thomas battled GIST through four surgeries and various treatments, and came up with the idea of raising money for research via a bicycle ride – not just any ride, but a 10-day endurance trek from Lands End to John O'Groats in the U.K., a distance of approximately 1,000 miles.

Peter motivated, inspired and persuaded a varied group of people and companies to participate and give support, time and money to the ride. He wanted desperately to do the ride himself but was sidelined by failing health and had to monitor the riders' progress from the sidelines.

The ride started July 10 and ended, as Peter planned, 10 days later – a scant month before his death.

Traveling from the U.K. to New Jersey to participate in the walk – and present a check for \$85,000, proceeds of the GIST e-2-e ride – were Peter's wife, Riëtte, his

son, Dylan, and daughter, Lauren, as well as his brother, Wayne, and the three Americans who participated in the ride, John Hebert and Debbie Mockler-Hebert, and Bob Murray. The Thomas family was presented with a plaque recognizing their contribution, and certificates were given to the three American riders.

They were greeted by close to 500 people who turned out for the walk, coming from such distant points as Sweden and Belgium and across the United States.

Basketball great Walt Frazier was on hand again, signing T-shirts and photos and posing for pictures.

Robert Stutman introduced the impressive roster of GIST experts who attended this year's walk: Dr. George Demetri of Dana-Farber Cancer Institute, Dr. Chris Corless of Oregon Health & Science University, Drs. Margaret Von Mehren and Andrew Godwin of Fox Chase Cancer Center, Drs. Ronald DeMatteo and David DAdamo of Memorial Sloan-Kettering Cancer Center, Drs. Anette Duensing and Stefan Duensing of the University of Pittsburgh.

The Stutmans and the GIST Cancer Research Fund were recognized the week before the walk by New York Gov. George Pataki. He wrote a letter commending the Stutmans for bringing together the GIST community to raise public awareness of GIST, and the efforts of patients to encourage doctors and researchers to pursue more effective treatments and a potential cure for GIST.

Even as the walkers at Rockland Lake were settling down to a luncheon feast, walkers on the other side of the United States were gathering for the first Walk for a Cure West happening in Ventura,



GIST patients and families participated in the GCRF Walk for a Cure Oct.15 in New York and California.

Calif., organized by Michele Scheiper-peter, her husband Carl, family and friends.

About 85 GIST patients, family and friends enjoyed meeting, talking, walking, sharing information and taking pictures.

“Thank you to everyone who was able to attend,” said Michele the day after the walk. “It was such a pleasure to meet so many patients, caregivers, family and friends of the GIST community.”

“I want to say thank you to Tania and Robert for all they have done and for all the help and support they gave me in organizing this West Coast walk,” Michele said, also singling out Ken Schou for his support and help.

In New Jersey, after the walk, and after the lunch, as the participants were disbanding, Wayne Thomas approached Robert. Peter, he said, had wanted to attend the walk and be a part of the event. That wasn't possible, but something else was.

Wayne, Riëtte, Dylan and Lauren then went down to the water's edge and carefully scattered some of Peter's ashes into Rockland Lake. So Peter did make the walk – and will make more walks in the years to come.



## ROSENBLUTH

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their lives to fighting GIST.

We had the opportunity to learn about GIST and experience the launch of the Life Raft Group. She and I attended the Life Fest in Boston as well as the local events in Lancaster. I monitored the list and offered what I could.

Every day was a “good” day for Mother; some were just better than others. Even the less “good” days she always met with a smile. Betty was truly thankful for every day and tried to make

the very most of all of them.

As her primary caregiver, I could not have asked for a better patient. She was my mother who set an example of how to make the best out of a life fraught with challenge. She made me a better person. Although I wish her and I could have experienced the relationship that we grew into through this battle without GIST, I know that would not have been possible. Thanks Mom....



BETTY ROSENBLUTH

## LRG member John Leary raises money for GIST research

By Janice Leary

September 17th was a remarkable and significant day for John Leary. It was a beautiful summer day in Boston where John's family and friends joined him for the Jimmy Fund Walk and the celebration of his son, Christopher's first birthday. About one hundred adults and children participated in the Jimmy Fund

Walk as official and unofficial members of Team John Leary.

Concurrently, GIST patients and family members as well as Dana-Farber Sarcoma Team staff joined John to help make a difference for GIST. John's team fundraised exclusively for Dana-Farber's GIST Research Fund. All money raised by Team John Leary is allocated for GIST research.

The support Team John Leary has received has been overwhelming. The

Team has successfully raised over \$65,000 dollars to date. This incredible success is thanks to the generosity of family and friends across the nation.

With the help of all the amazing people who have contributed to Team John Leary, John's Team is making a difference for GIST patients everywhere. To check out the Team's fundraising website, go to [www.jimmyfundwalk.org/teamjohnleary](http://www.jimmyfundwalk.org/teamjohnleary).

## Leary family gathers supporters for Jimmy Fund Walk



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