SPECIAL EDITION

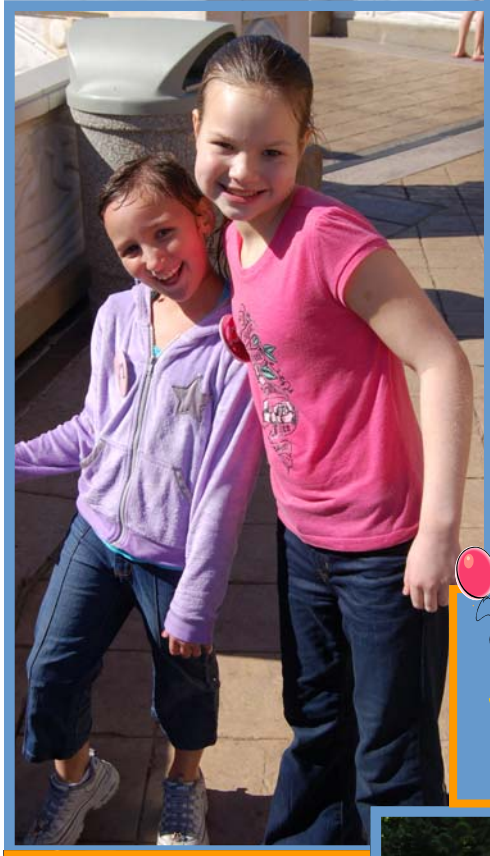
Battling gastrointestinal stromal tumor

LIFE RAFT GROUP

June 2007

In memory of Robert Donohoe, Mary Parker, Robert P. Keefe, Theodore Pantelakis & Marcel Schaddelee

Vol. 8, No. 6



The Life Raft Group 5-Year Anniversary Issue

A word from the executive director...

SCHERZER

The brief history of the Life Raft Group is the unheralded story of ordinary men and women fighting for survival with extraordinary courage and dignity. We set out on this journey from many different places, praying to many gods in many languages and sometimes to none at all. We were mostly afraid and mostly alone.

We had a deadly cancer that almost always was misdiagnosed and labeled with different names like leiomyosarcoma. Traditional cancer treatments made us very sick but did little to slow the relentless progression and inevitable death deemed to be most of our fates. Instead, we bought precious time by surrendering tissue and organs to an endless array of surgeons. Mostly we tried to cope and survive on our own; occasionally we encountered other kindred souls in waiting rooms and sometimes on the internet.

It was the summer of 2000 and an unprecedented series of events would begin to reshape our lives. A new diagnostic test to determine the presence of an enzyme called c-kit ushered in a clinical diagnosis for a cancer called Gastrointestinal Stromal Tumor (GIST). That was the good news: we had our very own cancer. The bad news was that it was particularly deadly and belonged to a family of cancers called soft tissue sarcomas. The next event was a new oral targeted drug called STI571 that a few clinicians thought might help. This drug had just achieved an amazing breakthrough with another rare cancer called chronic myelogenous leukemia. And a clinical trial to test this drug on GIST patients was to begin in Boston, Philadelphia and Portland, Oregon, initially for a total of 30 patients. That confluence of unknown factors-a new cancer diagnosis, a new drug and a new clinical trial was the catalyst for a small number of patients to create an informal organization called the Life Raft Group. Using an internet community called a listserv, run by a remarkable organization called ACOR, we began exchanging information about our cancer and this new drug. Within a few months our new fledgling newsletter reported that about 85% of the first patients in the clinical trial were benefiting from this drug, either through rapid and significant tumor shrinkage or through tumor stability. Both the new treatment and the fact that a patient group was tracking and publicly reporting on its results were unprecedented.

Fast forward to June 2002 to the formal incorporation of the Life Raft Group as a non-profit organization. This newsletter celebrates the five year anniversary of this formation. It is dedicated to the men and women who lost their lives to this cancer and to those still struggling for survival. Some of their stories appear in these pages. All of their stories endure in our hearts.

Drs. Demetri, Druker & Blanke all write articles for the small newsletter of the LRG.

Gleevec is OK'd by FDA

The very first membership meeting of the Rafters occurs in May 2002. This picture serves as our timeline throughout the rest of the issue.

The LRG Prologue (Before June 2002)

**Monthly dates refer to newsletter issues; events may be earlier*

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 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.

Life Raft Office up and running in New Jersey

"The LRG's office opened Monday morning, Sept. 23, the day after Executive Director Norman Scherzer returned from a London symposium on Glivec treatment of gastrointestinal stromal tumor."

2002

2003

September

January

June

July

February

Did You Know?

In 2002, Norman attended a conference at the home of the president of MIT and discussed Medicare reform for oral cancer drugs with Senator Ted Kennedy.

The Life Raft Group becomes a formal non-profit organization on June 10, 2002.

Stan Bunn is elected the first president of the LRG Board of Directors!

Gleevec wins OK for GIST in Europe

BASEL, Switzerland — Novartis announced May 31 that the European Commission (EC) has issued approval, in record time, for the breakthrough drug Glivec (imatinib, or Gleevec in the U.S.) for the treatment of patients with Kit-positive inoperable and/or metastatic malignant gastrointestinal stromal tumours (GISTs).

Jerry Call, LRG Science Coordinator, labels GIST a "model cancer"

"In summary, research of GIST has a high level of interest, and tissue donation will facilitate the pace for discovery about mechanisms of resistance to Gleevec in GIST.

Due in large part to the relative simplicity of GIST, it is a model cancer in several ways…"

LRG member, Kathy Colwell writes a goodbye letter to her "100,000" friends. She died on January 5, 2003, before the letter was printed; she is deeply missed by all.

I'm lucky, not because of cancer, but because I have one hundred thousand friends. Each of you is a best friend. Every short visit, talk, letter, meeting, and laugh is in my memory, and I think back and smile, and laugh, and sometimes cry.

You all know who you are. My devotion to you never dwindled or faded. My only regret is that I can't write down every little thing — but all of my hundred thousand friends can pull up at least one good time, or thought, and remember for me. Won't those air waves from here to heaven twitch and fizzle, spark and send vibrations skyrocketing up to God and my many guardian angels?

I can hear the laughter increase exponentially. It's all good, positive strength and I want it set loose so that others can share some of the greatest things I have experienced. I have had way more than my fill.

I read something yesterday—that it is not holding on to something that is so hard; it is harder to let it go.

So here it goes.

I have traveled the United States and most of the world. I have met so many wonderful people and pets. I have ridden horses on Carmel Beach. I have spent hours watching my beloved brothers playing baseball, and sometimes just the drive home — with Mom and Dad, Mike, Dave, Steve, Dan and I in the car, with the family dog, navy blue baseball uniform windbreakers snapping in the breeze from the station wagon window — has been the best part of the fading day.

I have the most loving, devoted partner in my husband, Tom. And my three gorgeous healthy, funny, smart, proud, independent kids. A beautiful home in a beautiful state. I've had great jobs, a work ethic I will never let go of. My life could be longer, but in no way could it have been better.

I always seemed to be the one who laughed the loudest, stayed up the latest, ate the most, pushed for just "one more," wanted to win one more game. The leader most times, but recently seeing that it's OK to let others take over and carry the torch for me, even for a little while. I have so much trust in my heart now, which is something I have learned from Tom and Tom's family, and my own family of brothers. And it's great to sit and rest for just a little while. I have been so happy in the Midwest, and something about the change of seasons has touched me, and has given me an understanding of life that I couldn't learn in a book.

COLWELL

A year ago in October, when Tom and I got the initial diagnosis of cancer, I was afraid that I wouldn't have time for a lot of little things that needed to be done — but I do remember asking God if He thought one more year of seasons was too much to ask. I wanted to see the snow and have Christmas with Kate, Tommy, and Mary. I wanted to see my mother-in-law's spring plants in her backyard, and think of the endless orchids my own mother has in tubs at the side of her house in Carmel. I wanted to spend another warm summer with my wonderful friend Marianne, at her house, and go swimming and teach Mary how to swim, and to have margaritas and laugh and laugh. I wanted to see the autumn with my favorite colors, and have a Halloween party, and feel cool fresh air on my face, and wear hats and scarves and sweaters, and eat the extra candy, and think of costumes.

God not only gave me this year of seasons, he gave it to me in a big way. He handed me more than a full year, and it was a beautiful, pain-free year. I could work, I could do things around my house. I spent many extra minutes holding hands with my beautiful baby Mary, and brushing her hair and getting her ready for tea parties, and listening to her stories. I laughed for hours with Kate and Tommy, and went over funny stories when they were little. I was able to write them letters, their own little books, of how they were as babies, and things I want them to remember. Not too sad, because there are so many happy and fun things to think about. I let them know what is important to me, what I want them to keep in mind as they grow up, some good books to read, how to treat others, how to work hard and earn what they deserve.

I'm sorry I won't be around for a lot, but I am also very grateful that I was here at all. Everyone has such a good start on the first part of their journeys — and the seasons help us move the journey into a plan. Every night before I close my eyes, I tell Tom and Kate and Mary and Big Tom how much I love them. But when my eyes close, and I say good night to God, and thank him for my day, and all the good that came from that day. I can really rest, and fall asleep, and trust in anything that happens next.

Sometimes, I even look forward to my next journey — as hard as it is to let go of this one.

I love you all. Remember me, and at least one story. I promise it will find me again, and I will grab the opportunity to recount the story to maybe one angel that hasn't heard it yet — and you will hear us cracking up, maybe sneaking a small glass of champagne behind cloud.

Listen for a little rain on the window sill, the drop of a spring flower on a patio board, a dry leaf rustling across a playground in the wind, a snow flake melting on your eyelash. It's me, laughing, and thinking of you.

2004

April

May

June

July

August

"Mutational analysis of GISTs gives clinicians new tool to predict outcomes" — the first time the LRG mentions the benefits of mutational testing!

Life Fest 2004!

Orlando, Florida hosts the second membership meeting and official first-ever Life Fest

Medicare lottery covers Gleevec for some

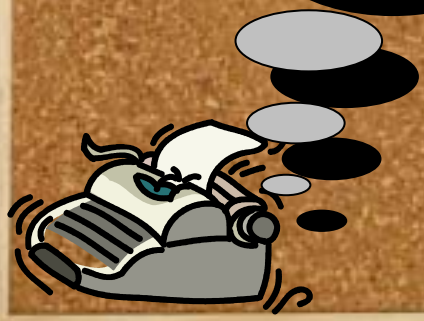
More to come...

NEW

GIST Specialist Directory established!

LRG Relapse Survey

"Norman Scherzer, the Life Raft's executive director, then led a review of the Life Raft's informal relapse poll that surveyed members with metastatic GIST that have been treated with Gleevec for more than a year, and who experienced tumor shrinkage, the informal survey indicated that the higher the dosage, the less likely the chance of relapse."



Going away party forever changes our lives

In the summer of 2001, Mike Matthews is dying. He becomes part of a small group of cancer patients whose GISTs dramatically respond to an experimental drug, STI571.

MATTHEWS

...What's left of Mike's tumors remain stable until December 2002 when a new tumor appears. Surgery in March 2003 appears to wipe the slate clean. But nine months later, new tumors are discovered, this time in his liver. It is January 2004. Weeks go by. Mike's tumors continue to grow. He is getting weaker.

...It is July 23. His wife, Valerie calls. Mike's liver enzymes are too high. He asks if I can come to his going-away party.

...We arrive at Purcell's Cove Club outside of Halifax. Valerie greets me and we go inside.

[Mike] has no idea that I was coming and the look on his face is one of complete surprise. Mike gets up from the living room chair that his friends brought from home to make him comfortable, and we hold one another tight, the tears rolling down my face.

...Two moments will forever remain with me. The first is when Mike got up from his chair and danced with Valerie. Only music and heartbeats could be heard as we watched, each of us with the same thoughts and feelings. The second was when Mike had to sit down and take off his shoes. His eldest daughter, Ashley, kneeled by his side and gently massaged his feet.

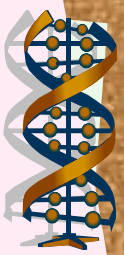
...Tuesday, July 27: At 6:45 a.m., as the sun rises over the Atlantic and tall ships pass by, Mike Matthews' fight ends. The lethal time gap between clinical trials was too much.

Arnie Kwart shares: When the doctor becomes a patient

I frequently consult with patients, they on one side of the desk and me on the other, wearing a long white coat. We have lengthy discussions regarding the nature of their illness, treatment options and how those options apply to their specific problem. I attempt to remain responsive to their individual concerns, be compassionate and informative, always keeping in mind the patient's quality of life.

I have always believed that I will have a lengthy life, as my parents were in their late 80s when they passed away from natural causes. I was quite shocked when I learned I had a rare illness. I could become the topic of medical journals and perhaps grand rounds, the educational forums in hospitals. I will attempt to do the best I can to relate my experience, as I became the patient on the other side of the desk.

Norman presents an award and gets to meet Dr. James Watson—the man who co-discovered DNA!



January

2005

August

November

Life Raft hosts first Pediatric GIST Conference in Montreal, Canada

LRG study presented at CTOS meeting

Starting vs. actual dose significant

A groundbreaking study of cancer patients done by the patients and caregivers themselves was presented at the November 11-13 meeting of the Connective Tissue Oncology Society's in Montreal, Canada.

The study undertaken by the LRG was presented Friday, November 12, to over 300 sarcoma and GIST specialists from around the world. It affirmed preliminary results of a large European study on dose levels of Gleevec for GIST and also tackled the thorny issue of clinical trial patients who begin a clinical trial at a certain dose, but then change that dose.

Norman writes an article entitled, "Time on Fire". He dedicates it to Ara Jelderian and Mike Matthews. "*May their heroic struggles not be in vain.*"

In the past few months we have lost several Life Raft Group members who were not successful in obtaining drugs that were available for clinical trials. Two stories in particular stand out. Both patients are Canadians.

The first patient's GIST was resistant to Gleevec and to Pfizer's Sutent. He tried to get into a phase I clinical trial in Boston for a new drug, BMS354825, but was told there were no available slots. With assistance from the Life Raft Group, he turned to a clinical trial in Scotland. While in the process of joining the trial — the drug was not available on a compassionate use basis — he ran out of time. He died the day he was supposed to be in Scotland to see a doctor about starting the trial.

The second patient's GIST was resistant to Gleevec so he participated in the phase II clinical trial for Sutent. Believing that he was experiencing unacceptable side effects from the drug, he voluntarily left the trial. Later he found he had been on the placebo. The "side effects" were symptoms of his cancer. Because he voluntarily left the trial, he could not rejoin it in order to get the actual drug.

The Life Raft Group tried to get the drug company to provide him with Sutent on a compassionate use basis (the drug was available on such a basis in Boston but not Canada) but again time ran out and the patient died. His wife had died of cancer two years earlier, so their 9-year-old son was left an orphan.

In the latter case, there were two hurdles the patient and the Life Raft Group failed to navigate quickly enough: first, getting the drug company to make the drug available on a compassionate use basis and secondly, getting the local hospital's institutional review board to approve this. The fact that this had been done by another IRB at a major hospital in the United States did not matter.

One could only imagine what would have happened if these patients had a deadly communicable disease. Picture this scenario: Two patients are dying from anthrax. A reporter discovers that there is a drug that might help save them. But both patients die before they are granted access to this drug.

The reporter also discovers that a committee of medical experts at the hospital took three months to decide if the patients should get this drug. This IRB met only monthly and its top priorities were protecting patients against unsafe treatments and of course, protecting the institution against lawsuits. The reporter also learns these experts refused to accept the findings of another expert committee at another prestigious institution, but instead had to duplicate the process.

Imagine the fallout from the ensuing story. Politicians would decry the lack of urgency and inflexibility of the medical bureaucracy, and the absurdity of trying to protect a dying patient from a potentially unsafe treatment.

Protecting a dying patient. Now that is an interesting conundrum.

What could justify not getting a drug to a dying patient in a reasonable period of time, say a few hours or at most a few days?

There is certainly plenty of finger-pointing that could go on. The drug company must produce enough drugs in order for it to be available on a compassionate use basis when the patient is not able to get it in a clinical trial.

Second, a physician at a particular medical facility has to decide that that patient must have this drug and initiate the process of requesting it.

Third, the hospital's IRB has to approve use of the drug on a compassionate- use basis. The IRB must be able to convene on an emergency basis and to operate under a protocol that defined acceptable risk for terminally ill cancer patients differently than that for other drugs, such as those treating impotence. In the case of a drug like Viagra, the risk of drug side effects may far outweigh the desirability of getting an erection but rarely would that risk-benefit ratio apply to a cancer drug for dying patients.

Fourth, the patient must be able to get to that medical facility, overcoming whatever financial obstacles might exist. Here the issue of financial responsibility is a little clearer: it is the patient's. If the patient is not a citizen of the country in which the medical facility is located, that may involve tens of thousands of up-front dollars.

Fifth and most important, every one involved needs to have a sense of urgency — just as if the patient had anthrax.

I am sure that some bright people reading this would be able to present a rationale of why the current situation has to be —- and we invite anyone who wishes to do so to respond through this newsletter. But it would take an awful lot of illumination from the candles we light when one of our members dies to make that acceptable to the families and friends of these patients.

There is a feeling of helplessness as patients and caregivers try to navigate this institutional landscape to stay alive. It is easy to believe that this system was just not designed to meet the urgent needs of dying cancer patients.

Perhaps we also need to shine some lights on the major obstacles to survival that could be overcome with different priorities.

Maybe a time clock showing how long each part of this process takes. On one side of the clock, the names of IRB members and their photographs. On the other side, a list of patients and their photographs. As the clock ticks and deliberations slowly advance, photos of the patients would wink out.

Perhaps there should be other clocks for the other parts of this process, including expanded drug production to meet compassionate use needs, clinician time to draw up protocols and so on.

Tick-tock, tick-tock. Day three: John Doe has died. Tick-tock. Day seven: Jane Doe has died. Tick-tock. Day 17: The IRB convenes.

Sutent Works!

Trial ends seven months early

Patients on placebo can switch to real SU11248

LRG, Das Lebenshaus & The Association of Cancer Online Resources launch the Global GIST Network

February

September

June

April

$2M pledged for GIST research

Hi my GIST friends, my name is Rachel Gilbert, I am 18 years old and I live in St.Ives, England. I've had Gist for 3 1/2 years, since I was 15; I was diagnosed on the 23rd December.

They announced my diagnosis in a school assembly to make sure that everyone had the facts…I knew about it beforehand and thought it was a good idea, instead of people not being sure about it and making rumors. My friends didn't react very well.

When I started Glivec it hit me very hard, starting on 400mg. Slowly I have been moved up and down and up again and now I'm on 800mg. And stable.

I didn't manage to get to school anymore and didn't complete all my exams. I was upset about not going to school. I felt like I was missing out on having friends and socializing and now years later it upsets me a lot because I feel like I've missed out on my childhood and part of growing up.

I was also very surprised to find out that who I thought were best friends, didn't want to know me anymore. They were upset to start with, but later they didn't know how to talk to me, so I lost touch with some of them. Then when I didn't go to school anymore, I didn't see them either and they never made contact themselves.

I don't see any of my old friends and haven't for 3 years. This has made me lose my confidence.

So, why me? Why a very fit and healthy 15 year old girl? Do you know what? Every time I think that, I think, why not me? What makes me so special above everyone else that I shouldn't get ill? I've always stayed positive; I love life.

Cancer is a big part of me but I'm not going to let it hold me back. My dream is to be a famous singer which I'll try my best to achieve.

I think good things to do when your ill is to stay positive, which I know can be hard and to talk about your fears and worries and if you fancy having a cry, do it, it feels much better when you've had a good cry. Do things that you want to do when you're well enough and live life to the fullest every day. And most importantly: SMILE. I'm doing it right now.

Medical mistakes happen, sometimes in a big way

Most LRG members have learned that there is a high correlation between managing their own health care (either by the patient or a caregiver) and good medical care. While respecting the opinion of their doctors, particularly GIST specialists, members have learned that medical care is quite complex and that mistakes do happen. A recent example: A few weeks ago a GIST patient at one of the world's leading medical centers for GIST was told that (s)he was going to be removed from a clinical trial due to disease progression. The patient's written report stated: "The lesions have increased in size…For example, the dominant lesion...now measures 7.4 cm. x 6.3 cm. …This lesion is ...larger in comparison to prior (report) where it measured 6.3 x 6.1 cm. The concluding impression paragraph stated that "THE LESIONS HAVE INCREASED IN SIZE SINCE THE PRIOR (REPORT). (The caps have not been added; they were that way in the report.) When the report was compared against the actual measurements taken by the radiologist and recorded into the patient's record, quite a different picture emerges. Not only did the other lesions actually decrease in size but the dominant lesion cited changed from 6.3 x 6.1 cm. (that measurement was correct) to 6.1 x 5.0 cm.—not 7.4 x 6.3 cm. In other words, the tumor was smaller, not larger. Fortunately, for this particular patient, the mistake was caught in time to keep her/him from being removed from the clinical trial. The impact upon the patient's emotional wellbeing …well, we will leave that to the reader to evaluate.

The Medicare "Doughnut Hole"

"After you pay the $250 deductible, Medicare will pay 75 percent of all drug costs, up to $2,250. Then there is a gap in coverage — some people call it the 'doughnut hole.'"

Sutent is approved

December — 2006 — January — February

GIST and Gleevec... 5 years of progress

Tania Stutman, Anita Scherzer, Andrea Fuller & Chris Carley are all on five or more years of Gleevec

"...The idea that STI571 might be used to inhibit KIT in GISTs was substantiated in 1999 in essentially simultaneous experiments at OHSU (Dr. Michael Heinrich) and the Brigham & Women's Hospital in Boston (Dr. Jonathan Fletcher). Heinrich showed that STI571 could block the activity of mutant forms of KIT in the test tube, while Fletcher found that STI571 shut down the growth of GIST cells grown in a petri dish.

In March 2000, STI571 was tried in a single GIST patient and seemed to halt progression of his/her disease. Phase I and phase II GIST trials were started in July of 2000.

The phase II GIST/Gleevec trial proved to be so successful that it was quickly expanded to include a total of 147 patients at three trial sites. Doctors and nurses were clearly excited about the results they were seeing in early patients, and omitted their typical cautious statements given during clinical trials.

Word quickly spread via the internet and among the sarcoma community that there was a new drug in trials for GIST and that, contrary to previous therapies, it seemed to be working very well. Patients with abdominal leiomyosarcoma were urged to have their pathology slides tested for c-kit, as a positive c-kit test in these patients probably meant they actually had GIST instead of leiomyosarcoma. This knowledge did not spread to the general oncology world until Dr. Charles Blanke presented early results of the phase II trial at a plenary session of the American Society of Clinical Oncology (ASCO) meeting in May of 2001. This marked the beginning of a period of time when many GIST patients were often better informed about treatment options than their local oncologists.

Within a few months of starting the phase II trials for GIST, sarcoma specialists and GIST patients both knew that something special was happening. In the United States and Canada, phase III trials were quickly organized by Dr. George Demetri and started in the record time of five weeks! A European phase III trial was also quickly organized and began accruing patients by February of 2001..."

GIST clinicians and researchers have done a great job in dissecting the biology of GIST. This sarcoma can now be broken down into a few different categories: adult GIST, familial GIST, pediatric GIST and GISTs associated with NF1 (neurofibromatosis).

Some of these categories can be broken down further or in different ways, such as by gene mutation, mutation location within the gene, and by location of primary tumor.

Compared to six years ago, we have an explosion of new information about GIST.

When science advances as fast as it has in GIST, we are often left with as many questions as answers. Even before Sutent was approved, Richard Palmer raised the possibility of doctors/patients combining Gleevec with Sutent. Palmer suggested that we acknowledge this possibility in the newsletter.

The effects of Gleevec as an initial targeted therapy for GIST have been extensively studied in clinical trials. The results are well documented. The most important factor in determining whether a patient is likely to respond to Gleevec appears to be what type of mutation they have.

Patients with exon 11 mutations in KIT typically have the best response rates and the longest time to disease progression. Patients with exon 9 KIT mutations tend to have an intermediate response rate and time-to-progression. Patients with wild-type GIST (no mutations in KIT or PDGFRA) tend to have poor response rates and fairly rapid time-to-progression. Patients with exon 12 mutations in PDGFRA also tend to respond well to Gleevec; while patients with a specific type of exon 18 PDGFRA mutation, D842V, tend to be resistant to Gleevec.

The response rate of Sutent as an initial targeted therapy in GIST has not been well studied. The only results in this setting come from the few patients in the Sutent trials who were unable to tolerate Gleevec as initial therapy. While the response rate in this small group appears to be similar to initial therapy with Gleevec, the numbers are too small to make firm conclusions.

Jerry Call discusses the new information about GIST and how it can help patients better manage their care.

For patients with Gleevec-resistant GIST, the response rate to Sutent *has* been studied extensively. In this group, patients with an exon 9 KIT mutation tend to have excellent response rates, patients with wild-type GIST tend to have intermediate response rates, and patients with an exon 11 KIT mutation tend to have lower response rates.

Many of the questions about Sutent center on the response rates to exon 9 and wild-type GIST. The problem in comparing Sutent rates to Gleevec rates is that it is not an apples-to-apples comparison. The Gleevec rates are for "untreated" GISTs while the Sutent rates are for "resistant GIST."

The "standard approach" would be to start with Gleevec until disease progression, THEN crossover to Sutent. The big unanswered question would be whether the mechanisms of resistance that occur with Gleevec would be likely to emerge as early if you started with Sutent. Similar types of questions apply to neoadjuvant and adjuvant Gleevec as well.

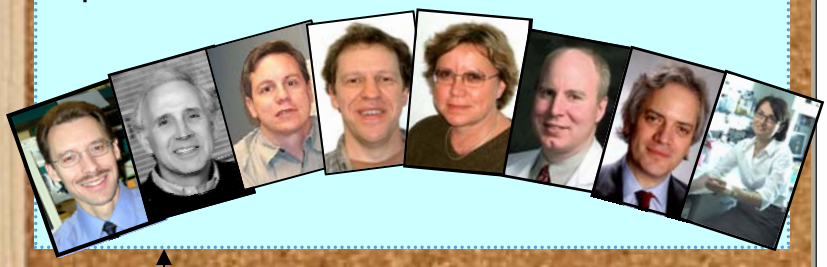
Beyond the issue of initial treatment is the theoretical issue of combining Sutent and Gleevec either for initial treatment or for Gleevec-resistant GIST. The rational for trying this approach is two-fold: broader-spectrum of activity against secondary mutations and additional antiangiogenesis activity due to inhibition of VEGF by Sutent.

While the idea of using Sutent and Gleevec together or with another KIT inhibitor is interesting, the best place to try this would be in the context of a clinical trial. The toxicity profile and possible drug interactions of this combination have not been studied. Other questions, such as dosing schedule, and the optimal setting (initial therapy or resistant GIST) also need answers.

For GIST patients, there are a few options today that did not exist a few months ago. Off-label treatments have many challenges, including unproven efficacy, unknown toxicity (for combinations), and possibly denial of coverage by insurance, but they may represent a last hope for some patients.

Life Raft funds 10 research projects

Experts lead studies of imatinib resistance



March

May

June

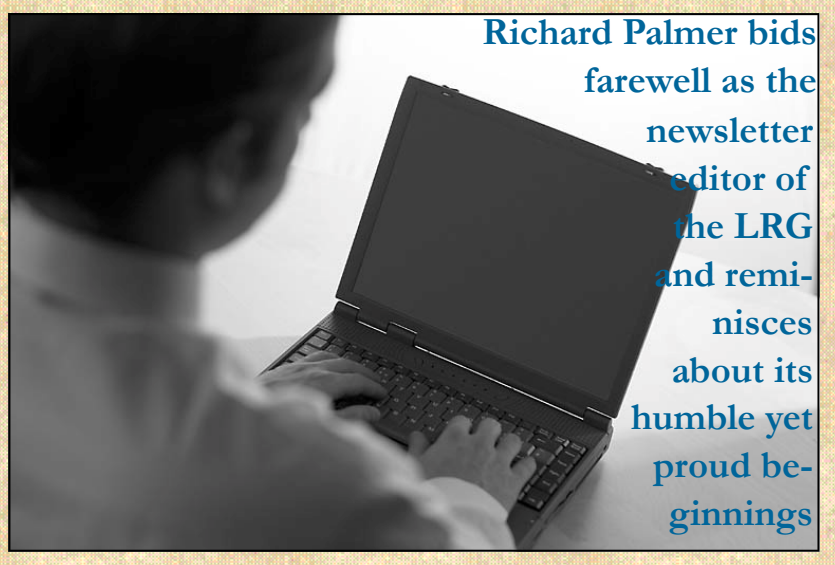
EORTC Study confirms Life Raft Group's original study: Progression-free survival improves for 800 mg vs. 400 mg patients

Life Raft Group forms alliance with the Monterrey, Mexico School of Medicine to support new clinical research center.

Remember to check out our newsletters to see the full articles featured in this issue. You can find them all at www.liferaftgroup.org/news_newsletter.html

E-mail saved my life. Not "e-mail is a life-saver," as in really convenient or really great. E-mail *really, literally* saved my life.

I was diagnosed with leiomyosarcoma in June 2000. A local oncologist advised me to seek treatment at a sarcoma center. My bride spent two days on the Internet, and then announced we were going to M.D. Anderson Cancer Center (MDA) in Houston. That was where my surgeon said I was incurable.



Richard Palmer bids farewell as the newsletter editor of the LRG and reminisces about its humble yet proud beginnings

At MDA I heard about an Internet support group called ACOR, the Association of Cancer Online Resources. After Linda and I got home, I found the ACOR Web site and got on the leiomyosarcoma (LMS) e-mail list.

One of the people on that listserv was Gary Golnik of Boxford, Mass. An engineer who worked on complex optical systems like the Hubble space telescope, Gary's wife, Mary, had just learned that her leiomyosarcoma might actually be variant of LMS called GIST, gastrointestinal stromal tumor. Mary was being treated at Dana-Farber Cancer Institute in Boston. Gary tells of how they found other GIST patients.

"In July of 2000, three patients and two caregivers sat in the waiting room at Dana-Farber Cancer Institute," Gary wrote. "All five were terrified but hopeful, facing fear and pain and the start of a new drug trial. Dr. George Demetri told each of us that 'patient zero' in Finland had GIST that was responding to a new drug, STI571. None of us really believed that a miracle could happen, but one was about to."

A young woman gave the patients a sheaf of consent forms. "After she left," Gary said, "Sandi Merriman came up to Mary. Sandi was pale and thin, her beauty masked by the pain of many operations. She was nearing the end of her battle and desperately needed a solution. Mary was less than a year into her battle and outwardly healthy, but hid her terror in a wry humor that fascinated all who met her.

"I don't remember Sandi's exact words, but this is close: 'I don't want to intrude, but I couldn't help noticing that we seem to have filled out the same forms. I have a GIST and am starting a new drug trial. Are you?'

"Mary nervously said yes, and a deep and dear friendship formed in an instant.

"Then Ken Garabadian walked over and told us he thought he might be in the same boat. We exchanged e-mail addresses and promised to keep in touch." The fledgling group first traded e-mail July 13, 2000. That was the start of the Life Raft Group, even before it had a name.

Demetri said STI571 would be tested at three U.S. cancer centers. "I set out to try to locate people in the other trials," Gary said, "so that we could trade notes and make sure the doctors were telling us all the same thing."

Gary found several such patients on ACOR's LMS list, where news of the STI571 trials was sparking new hope among LMS patients whose tumors were c-Kit positive, which meant their cancer was actually GIST.

I was one of those patients. From the list, I learned of the significance of the MDA pathology report that noted my tumor was c-Kit positive. From the list, I learned about Oregon Health & Science University (OHSU), one of the three trial centers. From the list, I got contact information for Dr. Charles Blanke.

So e-mail *really, literally* saved my life.

Gary reached out through cyberspace and made contact with many other c-Kit positive LMS patients in the summer and fall of 2000. "The first I found were Joyce and Jeff Prichard, and Norman and Anita Scherzer," Gary said. Later he met Jerry and Stephanie Call, Mia and Michael Byrne, Marina Symcox and Trudy Webb. "Trudy was the first

(Continued on next page)

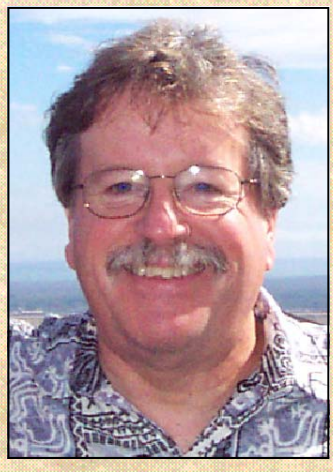
from the OHSU," Gary recalled. To spread the word about STI571, Gary, Trudy and Norman began coordinating efforts. "The three of us worked together to try to figure out what was going on. I started a 'group e-mail' list to keep everyone informed of what was happening.

As the e-mails went back and forth, it was apparent that STI571 worked incredibly well for some patients. "Ken wrote one of his usual wry notes, and said that we were like a group in a life raft," Gary said. "The name resonated, and we were the Life Raft Group."

Besides putting together the first Life Raft newsletter in November 2000, Gary would also build the Life Raft's first Web site. Both would help hundreds of patients. But not Mary. Gary later wrote of the "dark December of 2000 when Mary became the first (I think) person to be kicked off the trial, my resulting collapse, and Norman's courageous leap forward to grasp the reins and get many of our current volunteers to take up their positions."

Gary and I jointly put out the third newsletter in January 2001, then Gary resigned to focus on Mary's care. He remained aboard the Life Raft, organizing the groups first gathering held May 3-4, 2002, in Boston. A high point of the gathering was a speech by Dr. Dan Vasella, president and CEO of Novartis, the company that developed STI571, now marketed as Gleevec. Sadly, Gary hosted the gathering without his bride of 27 years. Mary, 50, had died two weeks earlier.

Triumph and tragedy. That's been the history of the Life Raft. The shattering discovery that you have cancer, the hope that surgery or Gleevec will keep it at bay, the joy of scans that show dramatic tumor shrinkage, dismay at cancer's recurrence, the renewal of hope with new drugs like Sutent.



PALMER

I share this bit of history as I write the end of my own chapter as newsletter editor. I need to thank the dozens of Life Rafters who've willingly shared their stories in the hope of encouraging others. I've spent one weekend a month hunkered over the computer, assembling the parts into a hopefully cohesive whole. It's no great sacrifice when Hilo's torrential rain is falling, but the newsletter is burdensome when the tropical sun is shining and the surf is just right for body boarding. And though she's very patient, I know my bride has missed the time we could have spent together. Indeed, her contributions to the newsletter have been considerable. For the first couple of years, Linda maintained the newsletter mailing list, which grew to more than 500 names. She'd also print and snail-mail dozens of newsletters to computer-challenged Life Rafters around the U.S. and in Canada, Australia, Iran and China.

For the past several months, the Life Raft staff has taken on more and more newsletter tasks, which I've gladly relinquished. Sara Rubinoff has become builder of the newsletter, following Norman Scherzer's architecture, while I've merely added the trim and paint.

Tomorrow my bride and I will head to the mainland to visit family, friends and celebrate our 30th anniversary. On the way home we'll check in with Dr. Blanke, and see good friends we've never met before at the GIST Cancer Research Fund presentation at OHSU. This column will be my only contribution to this month's newsletter, and my last as newsletter editor.

Thanks for your patience, your tolerance when errors reached print, and your encouragement. I look forward to seeing you in cyberspace, and someday meeting you face to face.

Richard Palmer, Hilo

dx LMS/GIST 6/2000, surgery 7/00, immediate recurrence, started 400 mg. Gleevec 1/01, 80% shrinkage/stability as of 1/04, elective surgery 2/17/04, all visible disease gone

July

Norman Scherzer & Jerry Call meet with the Centers for Disease Control & Prevention Director, Dr. Julie Gerberding and Chief Operating Officer William Gimson, and discuss LRG programs.

December

LRG Firsts

The first wedding in the LRG was between pediatric GIST patient Meredith Simmons and her longtime beau Brad.

November

Life Raft Group holds its 2nd annual Life Fest in Dallas!

Speeches were given by Dan Vasella, David Epstein, Rafters Josalin Dunn & Anita Scherzer. Richard Palmer received the Volunteer of the Year award; Jonathan Fletcher received the Researcher of the Year award and the five-year survivors were honored.

Dr. Jonathan Fletcher of Brigham & Women's Hospital, Dana Farber Cancer Institute writes the first article in a series written by each of the key research team members. He is the lead coordinator of the research team.

Trial confirms Gleevec reduces recurrence

On April 12, the National Cancer Institute (NCI), the American College of Surgeons (ACOSOG) and Novartis pharmaceuticals announced that a phase III trial studying Gleevec use to prevent recurrence in patients whose primary Gastrointestinal Stromal Tumor (GIST) had been removed by surgery would be ended early because it had met its primary endpoint of increasing recurrence free survival with a statistically significant hazard ratio of 3.1.

2007

January

March

May

An anniversary is a time to celebrate the joys of today, the memories of yesterday, and the hopes of tomorrow. ~Author Unknown

The LRG institutes a new way to inform readers of clinical trial changes

CLINICAL TRIAL

From Page 13

United States Clinical Trial Table (continued)

Therapy	Title	Trial #	Phase	For
IPI-504	Safety Study of IPI-504 for GASTROINTESTINAL Stromal Tumors (GIST)	NCT00276302	I	GIST
	U.S. Locations & Contacts: Dana Farber, Boston, Mass., Michael T Quigley, RN, 617-632-5117, Michael_Quigley@dfci.harvard.edu; Univ. Of Mich., Ann Arbor, Mich., Rashmi Chugh, M.D., 734-936-0453, rashmim@umich.edu.			
LBH589	A Phase IA, two-arm, multi-center, dose escalating study of LBH589 administered intravenously on two dose schedules in adult patients with advanced solid tumors & non-Hodgkin's lymphoma.	NVCI	I	Advanced Solid Tumors
	U.S. Locations & Contacts: Nevada Cancer Institute, Las Vegas, Nev., Donna Adkins, 702-822-5173.			
Oblimersen (G3139, Genasense) + Imatinib (STI-571, Gleevec/Glivec)	Oblimersen and Imatinib Mesylate in Treating Patients With Advanced GASTROINTESTINAL Stromal Tumors That Cannot Be Removed By Surgery	NCT00091078	I	GIST
	U.S. Locations & Contacts: Dana-Farber Cancer Institute, Boston, Mass., 617-582-8480; University of Michigan Ann Arbor, Mich., 800-865-1125, Mayo Clinic Cancer Center, Rochester, Minn., 507-538-7623, cancerclinicaltrials@mayo.edu; Memorial Sloan-Kettering Cancer Center, New York, N.Y., Robert Maki, M.D., Ph.D., 212-639-5720; M.D. Anderson Cancer Center, Houston, 792-3245.			
OSI-930	Dose Escalation Study of Daily Oral OSI-930 in Patients with Advanced Solid Tumors [illegible] coma	[illegible]	[illegible]	Advanced Solid Tumors [illegible]
	U.S. Locations & Contacts: [illegible] Mass., Michael T Quigley, RN, 617-632-5117, Michael_Quigley@dfci.harvard.edu; Colorado University, Denver, [illegible] Dr. Ross Camidge.			
Perifosine + Sunitinib (RX-0447, SU11248, Sutent)	Perifosine + Sunitinib Malate [illegible] Advanced Cancers	NCT00399152	I	GIST/RCC
	U.S. Locations & Contacts: [illegible] Online Collaborative Oncology Group, 415-946-2410, ocogtrials@ucsf.edu; Gainesville, Ala.; Tower Hematology and Oncology, Beverly Hills, Calif.; Pomona, Calif.; Santa Monica, Calif.; Kalamazoo, Mich.			
XL820	Study of XL820 Given Orally Daily to Subjects With Solid Tumors	NCT00350831	I	Cancer/Solid Tumor
	U.S. Locations & Contacts: The Cancer Institute of New Jersey, New Brunswick, N.J., Pamela Scott, 732-235-7459, scottpo@umdnj.edu, Mark Stein, M.D., Principal Investigator; Cancer Therapy and Research Center, San Antonio, TX, Pat O'Rourke, 210-616-5976, porourke@ddd.org, Kyriakos P. Papadopoulos, M.D., Principal Investigator.			

CLINICAL TRIAL

From Page 14

International Clinical Trial Table

Therapy	Title	Trial #	Phase	For
Sutent SU11248 Sunitinib	A Treatment Protocol for Patients With Gastrointestinal Stromal Tumor (GIST) Who May Derive Benefit From Treatment With SU011248	NCT00054029	III	GIST
	International Contact: EmergingMed 1-877-416-8248, sutent@emergingmed.com Locations: Chile, Colombia, India, Turkey, Spain, Finland, Taiwan, Singapore, Rep. of Korea, Hong Kong			
AZD2171 Recentin	The Biological Activity of AZD2171 in GIST	NCT00383203	II	[illegible]
	International Contact: information.center@astrazeneca.com Locations: The Royal Marsden NHS Foundation Trust, Liverpool Christie Hospital NHS Trust In Manchester U.S. Contact: AstraZeneca Cancer [illegible] Network, 866-992-9276,			
PTK787 Vatalanib	PTK787/ZK222584 [illegible] Metastatic Gastrointestinal Stromal Tumors [illegible] to Imatinib	NCT00117286	[illegible]	[illegible]
	International Contact: Heikki Joensuu, M.D., +358-9-471 73208, heikki.joensuu@hus.fi; Mia Viskari, +358-9-471 [illegible] Locations: [illegible] Central Hospital, Helsinki, FIN-00029, Finland			
BMS-354825 Dasatinib Sprycel	A Phase I Dose Escalation Study of BMS-354825 In Patients With Refractory Solid Tumors	NCT00099606	I	Neoplasms
	International Contact: THIS TRIAL IS NOW LISTED AS NO LONGER RECRUITING. BMS Call Center Outside the United States & Canada, 941-906-4711, Ext. 131 Locations: Glasgow, Strathclyd, United Kingdom US Contact: BMS Call Center, 1-866-592-15MS Ext. 131; Boston, Mass.; Detroit, Mich.			
BMS-354825 Dasatinib Sprycel	A Phase I Study of BMS-354825 In Patients With Solid Tumors	NCT00339144	I	Tumors
	International Contact: BMS Call Center Outside the United States & Canada, 941-906-4711, Ext. 376 Locations: Toshima-Ku, Tokyo, Japan US Contact: BMS Call Center, 1-866-592-15MS Ext. 376			
LBH589	LBH589 In Adult Patients With Advanced Solid Tumors or Cutaneous T-Cell Lymphoma	NCT00412997	I	Advanced Solid Tumors
	International Contact: Novartis +81-3-3797-8748 Locations: Tokyo, Japan			
OSI-930	A Phase I Dose Escalation Study of Daily Oral OSI-930 In Patients with Advanced Solid Tumors	EmergingMed	I	Advanced Solid Tumors
	International Contact: Dr. Michelle Scurr, Principal Investigator, Royal Marsden NHS, Sutton, United Kingdom Locations: Royal Marsden NHS, Sutton, United Kingdom			

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