Battling gastrointestinal stromal tumor

LIFE RAFT GROUP

July-August 2005

In memory of Marlies Bruinsma-Bol, Richard Correa, Dale Cross, John Engberg, Ineke de Kejiser, Henry Lange, Peter Morgan, James Olive, Ilkka Ovaska, Carlo Pacquee, Terri Stevens

Overcoming resistance is group's goal

Strategic planning group formed, many of the top GIST researchers sign on

By Norman J. Scherzer
Life Raft Group Executive Director

Armed with a generous $2 million start-up grant from Novartis, the Life Raft Group has begun assembling the best-in-field experts to create a strategic plan that will guide the first phase of our grant funding.

Grant recipients will be expected to work collaboratively with one another and share information on an ongoing basis.

SCHERZER

Several weeks ago we convened a small group to develop a preliminary draft of this strategic plan, to comment on the new infrastructure of a supportive grants management process (which will, among other things, limit administrative overhead costs) and to identify a small number of colleagues who would bring both scientific expertise and synergy to the strategic planning group.

Traditionally, medical institutions

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AMN107+Gleevec clinical trial opens

Testing will be on just 35 patients at six sites, two of them in the U.S.

By Jerry Call and Norman Scherzer

A new phase I trial combining the new Novartis drug AMN107 and Gleevec is opening at four European and two United States sites. This trial is for GIST patients whose cancer is resistant to Gleevec. Patients must have spent two weeks on 800mg. of Gleevec prior to starting the trial.

Currently there are 35 slots allocated for this trial. Although it is expected that all six trial sites will have some slots, it is first-come, first-served. This

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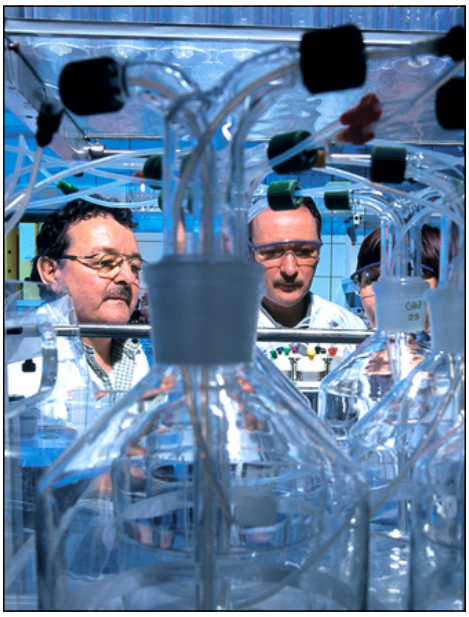

Photo courtesy of Novartis

Drug development at Novartis' headquarters in Basel, Switzerland.

FDA fast-tracks approval process for Sutent

NEW YORK — Pfizer announced Aug. 10 that it has submitted a new drug application for its cancer medicine SU11248 (sunitinib malate), known as Sutent, to the United States Food and Drug Administration.

Pfizer is seeking FDA approval for Sutent as a treatment for gastrointestinal stromal tumor and metastatic renal cell carcinoma among patients whose tumors do not respond to or do not tolerate standard treatment.

The FDA has granted Sutent "fast-track" status since Sutent may provide significant benefit over existing therapy for serious or life-threatening illnesses for which no therapy exists.

Sutent is an oral, multi-targeted cancer therapy that combines anti-angiogenic and anti-tumor activity to simultaneously stop the blood supply to and directly attack tumor cells.

Strategic planners, from left: Drs. Christopher Corless, Cristina Antonescu, Jonathon Fletcher, Michael Heinrich, LRG Science Coordinator Jerry Call, LRG Executive Director Norman Scherzer and LRG Board Research Liaison Jerry Knapp.

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deduct administrative overhead from grants, sometimes as much as 75 percent. Although one could negotiate lower indirect costs on a one-on-one institution basis when donating money to basic research, our intent is to limit our indirect costs as a matter of policy to a maximum of 10 percent for larger grants and 0 percent for smaller grants.

I am pleased to announce that we have now completed that first draft of that strategic plan, and assembled our first strategic planning team. Those who have thus far agreed to join us are, in alphabetical order: Cristina Antonescu, Memorial Sloan-Kettering, New York City; Peter Besmer, Memorial Sloan-Kettering; Peter Blume-Jensen, Merck Research Laboratories, Boston; Julie Cherrington, Phenomix, Australia; Chris Corless, Oregon Health & Sciences University, Portland; Maria Debiec-Rychter, Catholic University, Leuven, Belgium; Jonathan Fletcher, Brigham & Women's Hospital/ Dana-Farber Cancer Institute, Boston; Mike Heinrich, OHSU; Lee Helman, Pediatric Oncology Branch, National Institutes of Health, Bethesda, Md.; Laurie Letvak, Novartis, Florham Park, N.J.; Paul Meltzer, Cancer Genetics Branch, National Institutes of Health; Brian Rubin, University of Washington, Seattle; and Matt van de Rijn, Stanford University Medical Center, Stanford, Calif.

We plan to expand this group in the future and to create a complementary clinical advisory group to help bridge the gap from this pre clinical trial focused group to the clinical trials community.

I have no doubt that this is the most talented, complementary and synergistic team ever assembled to address GIST treatment resistance. The fact that each person has agreed to help create a plan to guide future grants, to share information on an ongoing basis, and to seek excellence over consensus creates a culture that will give us the best chance for success.

Our intention is to create a new research paradigm. An analogy is the Manhattan Project that brought together the nation's best scientists to create the atomic bomb. Although we are not interested in atomic weapons, we are interested in creating a plan that would set priorities on the best research options to finding and overcoming GIST treatment resistance.

This is quite different than the traditional approach of patients and individual benefactors handing checks to prestigious medical institutions for research directed at a disease but not at any specific project.

Instead, we believe that we must leverage our limited resources and direct both where research money goes and how it is used, to control outrageous administrative overhead, to hold each researcher accountable for specific results, to promptly redirect resources when research dead ends, and to insist that collaboration replace competition.

Fortunately other patient advocacy organizations have created research models that we can borrow from. We are particularly interested in the work of the Multiple Myeloma Research Foundation, the Michael J. Fox Foundation (for Parkinson's Disease), the National Organization of Rare Diseases and the Ara Parseghian Medical Research Foundation.

GIST'ers strike just the right note

These three Life Rafters discover healing power, spiritual release in music

By Erin Kristoff
Life Raft Group
Administrative Assistant

Though the people of the Life Raft Group have their cancer in common, they come in different shapes and sizes, backgrounds and cultures. They like different things and have different jobs and hobbies. All have their own way of dealing with the stress of cancer (and life), and all express themselves through something they love. Here are three who do just that, with music.

MEET DAN WISEMAN

Growing up in England, Dan Wiseman met the Partridge Family and the Monkees; this inspired him to get into music … but a different kind of music. He spent five years in a punk band, starting at age 13; he even cut a vinyl, a medley of punk songs. Then he played in a rock band before deciding to pursue his real love, the music of some of his favorite musicians, like Miles Davis: jazz.

"It's more challenging."

For the first time, Dan the musician was nervous. Walking up to that stage can be real intimidating. "They're very friendly but there's often lots of fellow musicians in the audience, that's another thing that makes you nervous, but they're very supportive."

That's not to say that Dan doesn't love what he does. For that matter, Dan has few hobbies other than playing guitar. "I'm really all about music."

Sometimes he'll play in a house band at a London pub he likes. Sometimes he enjoys playing with his band at different gigs. Sometimes he likes to practice in the studio he set up in his home.

Dan Wiseman, GIST survivor, Life Raft member, guitar player extraordinaire.

Regardless of how challenging music can be, Dan still believes that it has healing power.

"Yeah, I think making music is very therapeutic and playing with other people, it can be very spiritual, music," he says. "You just forget all the rules and beautiful music comes out of nowhere."

One day, when waiting for the results of his last scan, Dan composed an instrumental he calls "Scanziety." "It's actually pretty good."

But music isn't the only thing supporting Dan during rough times. His wife, Sally, and 19-year-old daughter, Sophie, have been his support system during his time with GIST.

A favorite lyric of Dan's is by Leonard Cohen: *"I'm standing on a ledge and your fine spider web is fastening my ankle to a stone."* That is how he feels about Sally. Besides music, Dan's few hobbies include walking the dog with his wife and spending time with his daughter.

But not every moment has been hopeful and uplifting. "There's a really great Joan Armatrading line, it says, *'Please forgive me if I show no sign of reasoning or consideration in my bleaker times.'"* It's very poetic," he note. "Sometimes you feel like that."

Fortunately, Dan has other ways of getting through difficult moments -- his fellow Rafters.

"The Life Raft Group is a literally that, sort of a lifesaver," he says. "When I first found it I thought I was the only one. The power of realizing that you are not alone is great, there are particularly fantastic people."

His hopes for the future?

"I'd like to live a long time," Dan says. "I would like to release a CD, or at least make one copy, which isn't too difficult, so I can leave my music behind."

MEET GORDON SIMMONS

Gordon's job is a bit different than most people. He works in the "basement" and has no idea what time of day or night it is. During breaks, he walks over to the ballpark and catches an inning of the Detroit

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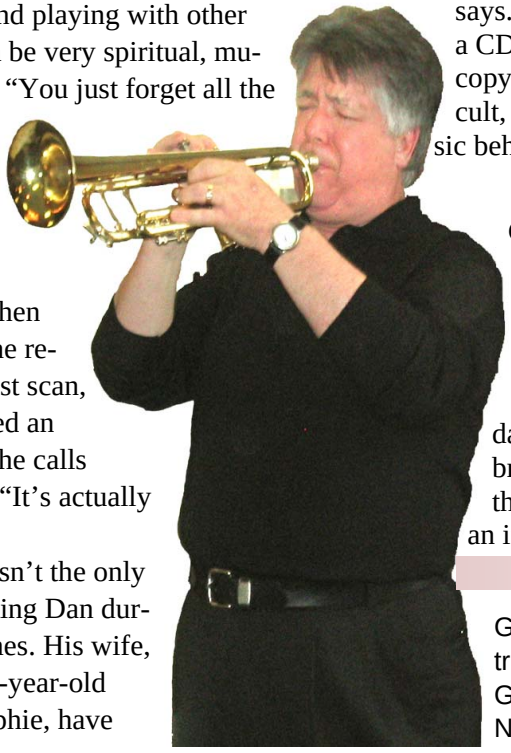

Gordon Simmons plays trumpet at the pediatric GIST family gathering in New Jersey.

New insights to multi-drug resistance

Researchers discover possible reasons why anti-cancer drugs fail

By Jerry Call
Life Raft Science Coordinator

Proteins that move drugs out of cells have been suspected to be a cause of resistance to cancer therapy for many years. "Multi-drug resistance" or MDR is the term used to describe the process where cancer cells are able to "pump" drugs out of the cell before the drug is concentrated enough to kill the cell. The ability of some cancer cells to increase the number/activity of these drug pumps can lead to resistance across a spectrum of drugs, hence the term "multi-drug resistance."

Understanding of multi-drug resistance proteins has largely been limited to their role in pumping drugs out of tumor cells (drug efflux). Recently, several groups have demonstrated that drug transport into the cell (drug influx) and effects on drug bioavailability might also be important factors in multi-drug resistance in patients treated with Gleevec.

One of the largest, and perhaps best studied, families of drug transporters is the ABC transporter family. This family includes seven subfamilies, ABCA through ABCG. Perhaps the most well known member of this family is ABCB1, also known as MDR1 or P-glycoprotein.

Most of the MDR research to date has focused on the ability of drug transporters to pump drugs out of the cell, especially P-glycoprotein. In a recent paper pre-published online in the journal Blood, Julia Thomas et al, of the University of Liverpool, Royal

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AMN107+GLEEVEC

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means that the earliest trial sites may get a disproportionate number of slots.

In the U.S., the investigators and sites are:

— George Demetri, Dana-Farber, Boston. Recruitment has begun.

— Margaret von Mehren, Fox Chase, Philadelphia. Recruitment is beginning.

European investigators and sites are listed below. To the best of our knowledge they have not yet begun recruiting but this information changes constantly.

— Peter Reichert, Berlin, Germany

— Paolo Giovanni Casali, Milan, Italy

— Jean-Yves Blay, Lyon, France

— Patrick Schöffski, Leuven, Belgium

This is a dose escalation trial to determine the maximum tolerated dose. What follows is our preliminary understanding of the intended dose escalation scheme. This is subject to change/modification as information about the combination is obtained.

— The first six patients will receive 800 mg. of AMN107 (400 mg. twice a day) without any Gleevec.

— The next group will receive 200 mg. of AMN107 plus 800 mg. of Gleevec.

— The next group will receive 400 mg. of AMN107 plus 800 mg. of Gleevec.

— The next group will receive 800 mg. of AMN107 plus 800 mg. of Gleevec.

AMN107 was developed to overcome some of the mechanisms of resistance to Gleevec in CML patients. It is 10 to 50 times more potent than Gleevec at inhibiting Bcr/Abl-induced proliferation in cells derived from CML patients. It is able to inhibit almost all of the Bcr/Abl secondary mutations that it has been tested against except the highly resistant T315I mutation.

In contrast, much less has been reported about its effects on GIST cells, or KIT/ PDGFRA mutations. In the few KIT/PDGFRA mutation variants that have been reported, AMN107 has about the same potency as Gleevec.

The phase I trials for AMN107 in CML patients have gone remarkably well. They are in many ways reminiscent of the original Gleevec phase I trials, producing response rates of about 90 percent, but this time in Gleevec-resistant CML patients. Such response rates are almost unheard of in phase I trials.

Regardless, it is much too early to draw any conclusions about the efficacy of this drug with GIST patients.

AMN107 inhibits Bcr/Abl, KIT, and PDGFRA. These are the same targets as Gleevec. The combination of AMN107 and Gleevec has proved to be synergistic in Bcr/Abl cell lines. However, the most compelling reason to use two inhibitors with the same target may be that each has a different mutation inhibition profile.

Using two drugs may provide a broader spectrum of inhibition and hopefully delay or prevent the emergence of resistant clones.

Illustration courtesy of The Fordham Company

Chris Carley's Fordham Spire, center, overlooking Lake Michigan, will be a striking addition to the Chicago skyline.

Life Rafter has sky-high plans

Chris Carley intends to build the nation's tallest skyscraper in Chicago

By Erin Kristoff
Life Raft Group
Administrative Assistant

Life Raft Group board member and GIST patient Chris Carley has far-reaching plans. Being diagnosed with leiomyosarcoma in 1996, later determined to be GIST, it would have been easy to just sit back and feel sorry for himself. Yet Chris persevered, becoming the first GIST patient in the early STI571 (Gleevec) clinical trial. He is still persevering, making headlines with his plans to develop what will be the tallest building in the United States.

To be built in his hometown of Chicago, the "Architectural Capitol of America," the Fordham Spire will be a luxury condo skyscraper. The Spire is set to be 115 stories tall, reaching a spectacular height of approximately 2,000 feet.

Joining the already stunning skyline of Chicago — which boasts soaring skyscrapers like the Sear Tower, Hancock Center and Aon Center, which range from 1,127 to 1,450 feet high, the Fordham Spire will dominate the view from all sides. A New York Times article compared the tower to a drill bit, a blade of grass, a tall twisting tree and lighthouse. If you take one look at the proposed design, you can see why.

Each floor unit of the tower is built out from a central core like a separate box, with gently curving, concave sides. As these boxes are stacked up, each is rotated by a little more than 2 degrees from the one below. The result is that the floors turn 270 degrees around the core as they rise, giving the facade an impression of movement.

Spanish architect Santiago Calatrava designed the $500 million skyscraper. "I know that Chicago is an Indian name, and I can imagine in the oldest time the Native Americans arriving at the lake and making a fire, with a tiny column of smoke going up in the air," he says. "With this simple gesture of turning one floor a little past another, you achieve this form."

CARLEY

A majority of Chicago residents support the project. Chicago Architecture Info reports that 90 percent of its readers like the idea of the Fordham Spire. A Chicago native was quoted on Luxist.com as saying, "The Spire inspires. It will define our city and the lakefront for generations."

Construction won't begin until there are sales agreements for about 40 percent of its units, Carley said in an article on CNN.com, but he would like to break ground in March and complete the building in four years.

For more information about the Fordham Spire, see the Web site at www.chicagoarchitecture.info. To learn more about Chris Carley's story, go to www.livestrong.org.

MDR

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Liverpool University Hospital, U.K., described how another drug transporter, hOCT1, actively transports Gleevec into cells. Further, it is not only drug efflux that determines drug concentration in cells, but that it is the difference between how much Gleevec is transported into a cell and how much is transported out of a cell that determines the concentration.

The past focus on drug efflux, especially P-glycoprotein, has led to studies where P-glycoprotein inhibitors such as verapamil have been used to try to increase intracellular drug levels of chemotherapy. These studies have not been very successful. Munir Pirmohamed, one of the authors of the Liverpool study, speculates that this may be because some of these agents, like verapamil, inhibit not only P-glycoprotein (an efflux pump), but also inhibit hOCT1 (one of the influx pumps). For that matter, verapamil actually decreased Gleevec levels in cells in-vitro studies, apparently because its effects on hOCT1 were more important than its effects on P-glycoprotein.

Using several different cell lines, Thomas et al were able to show that Gleevec is a substrate (a molecule which can be acted on by an enzyme, in this case the transport pumps) for hOCT1, but not the influx pumps hOCT2 or hOCT3. They also confirmed earlier work by Dai, and Mahon that Gleevec was a substrate of P-glycoprotein (ABCB1). There is another study by Ferrao that suggested that P-glycoprotein might not play a significant role in Gleevec resistance. However, this study only used a single cell line, K562, and since this cell line expressed low levels of both P-glycoprotein and hOCT1, it may not have been a good cell line to use for this type study, according to the Liverpool researchers.

After demonstrating that Gleevec was a substrate for hOCT1 and P-glycoprotein, the Liverpool team next showed that several different types of chronic myelogenous leukemia (CML) cells expressed both hOCT1 and P-glycoprotein. They speculated on the clinical implications of their findings. "The net effect of these transport processes may be a decrease in the intracellular concentration of imatinib (Gleevec)." The consequences are that cells might become resistant to Gleevec.

In the laboratory, at least two CML cell lines have been made resistant to

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Michigan Rafters take to the water

Michigan Life Rafters gathered June 18 for a day of boating and a barbecue organized by area coordinator Allan Tobes. Seen relaxing, from left, is Rosemarie and Fred Ekdahl, Nancy Wahl, Matthew Byrne and dad Michael (in back), Ted Wahl (waving), Zarina and Abbas Patni, Allan Tobes and John Kornelsen. The next meeting of the Michigan area group, including northern Ohio and Ontario, will be Sept. 10 at Gilda's Club in Royal Oak, Mich., from 12:30 to 2:30 p.m. Details: contact Allan Tobes, e-mail atobes@comcast.net or phone (248) 932-2977.

All aboard! Life Rafters get settled in on Allan and Kendra Tobes' ski boat at Elizabeth Lake, Mich.

Patient groups gather in Ireland

Knowledge, experience shared by those dealing with GIST and CML

By Tricia McAleer
Life Raft Group
Executive Assistant

While at Dublin patient group conference, Life Rafters enjoyed the ambiance of an Irish pub. From left are Norman Scherzer, Roy Jones of Ireland, Tricia McAleer, Kai Pilgermann of Germany and Dan Wiseman of the United Kingdom.

The Life Raft Group participated in the "New Horizons in Treating Cancer" Conference held June 17-19 in Dublin, Ireland. This was the third international conference for organizations representing people with GIST and CML (chronic myelogenous leukemia) sponsored by Novartis, maker of Gleevec. Like GIST, CML shares in the success of Gleevec. Although GIST and CML are different, the common goal is survival. The goal of the conference is to build networks for patient groups so that everyone can share their experiences with one another.

Life Rafters Roy and Carol Jones of Ireland; Dan Wiseman of the England; Estelle Lecointe of France; Ulrich Schnorf of Switzerland; Kai Pilgermann of Germany; Marlies and Hilbrand Bruinsma, and Carolien Verhoogt of the Netherlands joined U.S. Life Rafters Marina Symcox (also of GSI), Tricia McAleer and Norman Scherzer in the conference as well. Patients and advocates traveled from as far as Israel to join in the exchange of knowledge and experience that flowed back and forth in the working groups.

The meeting was built around a series of focused workshops. The LRG played a key role in moderating these workshops.

Scherzer facilitated a workshop on fund-raising in collaboration with Kathy Redmond, editor of Cancer World Magazine and consultant to the European Cancer Patient Community (ECPC). This workshop focused on the struggle that many organizations face in obtaining funds.

Tricia McAleer, the Life Raft's executive assistant, poses with Ulrich Schnorf, the Life Raft's country representative for Switzerland.

Scherzer also facilitated "Global GIST Network" in collaboration with Markus Wartenberg of Das Lebenshaus, showing how to form a network that can bring all GIST liaisons, patient groups and organizations together. Such exchanges provide support for the groups and ease patient access to precious information and resources in their home countries.

"Survival Issues for GIST Patients" was led by Scherzer. This workshop

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focused on navigating clinical trials, finding the right physician and best care practices.

McAleer facilitated two workshops, "Starting a Patient Group" and "Running a Patient Group" with Wartenberg. These workshops focused on the fundamentals of starting a patient group and cultivating that into an organization with a voice.

Life Rafter Schnorf facilitated the "Living with a Chronic Disease" workshop which focused on disease management as well as how it affects other areas of a patient's life.

It is rare to meet such a large group of knowledgeable and friendly people and even rarer that most share a deadly disease in common. Over the course of the weekend, it was easy to see that this was not just a patient meeting; it was an army of survivors assembled in one camp, to share visions and hope that rejuvenate and encourage others to continue the fight.

The meeting was a great success. It gave the patient community the opportunity to access a wealth of knowledge and experience in establishing and maintaining a voice to ensure survival.

Note: One of the participants, GIST patient Marlies Bruinsma-Bol, active in the Life Raft and in forming its Dutch counterpart, Life Raft Group Nederland, succumbed to her disease. GIST patients worldwide extend their condolences to her husband, Hilbrand.

Following a workshop, a mini-meeting took place to discuss the progress of international listservs. Pictured are, from left , Hilbrand Bruinsma, Norman Scherzer (back to camera), Markus Wartenberg (seated, gesturing), Carolien Verhoogt (back to camera), Marlies Bruinsman-Bol and Ulrich Schnorf. A particularly poignant footnote is that Marlies died two months later following the conference.

MORE MDR

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Gleevec by culturing the cells in Gleevec at lower-than-optimal concentrations. In one case it led to an increase in BCR-ABL protein expression, causing one cell line to become resistant to Gleevec. The second cell line developed a resistant clone that had a secondary point mutation in BCR-ABL.

Lucy Crossman, Brian Druker, and Michael Deininger extended the laboratory work of the Liverpool team to CML patients. In a letter to the editor of the journal Blood, they gave a short report on their experience with a small group of CML patients. They divided the patients into responders (achieved a complete cytogenetic response to Gleevec within the first year) and non-responders (remained at least 65 percent Philadelphia-chromosome positive during the first 10 months of Gleevec). In general, responders (n=15) and non-responders (n=15) were closely matched except that the median time from diagnosis to starting Gleevec was 20 months for responders and 41.7 months for non-responders.

The Crossman team found that baseline expression of hOCT1 (the influx pump) was variable and not significantly different from healthy bone marrow donors. Interestingly however, the pre-Gleevec expression level of hOCT1 in non-responders was one eighth that seen in responders (P=.005). Once on Gleevec, six of the non-responders had a further twofold decrease in the expression of hOCT1 compared to baseline. The implications were that in the non-responders, not as much Gleevec was being pumped into the tumor cells.

In contrast to hOCT1, the pre-

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A too-many-to-name group of Life Rafters gathered at The Wellness Place in Palatine, Ill., for the Chicago area meeting.

Big turnout at Chicago area meeting

LRG board meeting held in Windy City coincides with patients' gathering

By Tricia McAleer
Life Raft Group
Executive Assistant

The Chicago Chapter of the Life Raft Group met June 12 at The Wellness Place in Palatine, Ill., to share support and good spirits.

LRG board member Jim Hughes chaired the meeting, which drew more than two dozen GIST patients and caregivers. Executive Director Norman Scherzer, Executive Assistant Tricia McAleer, Robert and Jeanne Book, and Allan and Kendra Tobes also attended the meeting after being in town for a Life Raft board meeting.

Scherzer gave a presentation on the recent pediatric GIST family meeting. Introductions were made all around and then discussion began, ranging from not knowing exactly what GIST is to battling resistance and long term survival.

Druing a break, everyone enjoyed wine and cheese. Newcomers were welcomed and friends caught up on the latest gossip. It was certainly a pleasure to once again experience the close knit GIST community that shares such a remarkable bond.

The next Chicago area meeting will be held Sunday, Sept. 11 at 12:30 p.m. at the Wellness Place. Special guest Dr. George Demetri will be calling in from Dana-Farber Cancer Institute in Boston to talk about clinical trials and discuss patient concerns.

MDR III

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Gleevec expression levels of the efflux pumps ABCA2, ABCG2 and ABCB1 were similar for responders, non-responders and normal bone marrow patients. After starting Gleevec, six, five and three non-responders had at least a doubling of ACBA2, ABCG2 and ABCB1 expression respectively, but when the whole group of non-responders was considered, the results for the efflux pumps were not statistically significant.

Crossman noted in her correspondence to the editor, "Since hOCT1 actively transports imatinib (Gleevec) into cells, patients with low baseline expression of hOCT1 may be unable to achieve adequate intracellular concentrations of imatinib, and hence fail to achieve a cytogenetic response. Although our study is small, our observations add weight to Thomas et al's proposal that differential expression of hOCT1 may affect patients' responses to imatinib. We believe that further work is warranted to explore the interaction of hOCT1 and other drug transporters as a cause of primary cytogenetic resistance to imatinib."

In the same issue of Blood, the Liverpool group also reported their own experience with a larger group of 67 CML patients in whom expression of hOCT1 varied between responders and non-responders.

The research team of Herman Burger, Kees Nooter, et al is investigating the effects of multi-drug resistance proteins on the bioavailability of Gleevec. Their work was recently reported in a paper published in the July edition of Cancer Biology & Therapy. MDR proteins are not limited to tumor cells. They also exist on other cells in the body and have a variety of effects. For instance, MDR proteins may play a part in preventing many drugs from reaching the brain -- i.e., crossing the "blood-brain barrier" -- or in reducing drug absorption from the intestines.

The Burger team of primarily European researchers has demonstrated that chronic exposure to Gleevec can "induce" the ABCG2 and ABCB1 drug efflux pumps, and that this has the potential to affect the oral bioavailability of Gleevec. The Burger team had previously demonstrated that Gleevec was a substrate for ABCG2.

In an earlier study for the European Organisation for Research and Treatment of Cancer, Ian Judson et al, found that Gleevec levels in the body tended to decrease over time. This retrospective pharmacokinetic study was small, so not statistically conclusive, but the results were interesting. The Judson team found that apparent Gleevec clearance increased by 33 percent from day one to 12 months and exposure to Gleevec decreased by 42 percent. An article about this study can be found in the January issue of the LRG newsletter. The Burger study provides a possible explanation for the decreased levels of Gleevec over time.

Oral bioavailability refers to the percentage of an oral drug that reaches the systemic circulation. It is a comparison of the blood level of a drug given orally versus the same amount of drug given via an intravenous injection. An oral drug with 50 percent oral bioavailability would reach half of the concentration in the blood compared to the same amount of drug given intravenously.

The oral bioavailability of Gleevec is about 98 percent, which is excellent. But the studies that determined Gleevec bioavailability were given in healthy patients who were only exposed to the drug for a short time. Long-term Gleevec bioavailability is, to our knowledge, unknown (or at least unpublished). Oral bioavailability is highly dependent on gastrointestinal absorption and first-pass drug clearance.

Burger and his team used a Caco-2 cell line model to examine the long-term effects of Gleevec on the expression of intestinal drug pumps. Caco-2 cell lines have been widely used as an in vitro model for studying drug transport across the intestinal epithelial barrier. They found that continuous exposure with Gleevec (up to 100 days) specifically up-regulates the expression of both of the multi-drug resistant proteins, ABCG2 and ABCB1. Although the degree of up-regulation varied over time, in both cases it tended to eventually stabilize at five-fold higher levels of expression compared to starting levels. The hypothesis of the Burger team is that "… chronic use of imatinib may induce enhanced expression of intestinal drug transport pumps and drug-metabolizing enzymes, which may then limit the bioavailability and efficacy of imatinib. Moreover, this may eventually lead to decreased drug uptake and lower drug plasma levels, development of cellular resistance, and subsequent treatment failure."

The conclusions of the Burger team were "… our in-vitro data suggest that, at the systemic level, these drug pumps may play a role in acquired [pharmacokinetic] resistance to imatinib by lowering the bioavailability after oral dosing. Furthermore, these in vitro data and the clinical data discussed above (the EORTC pharmacokinetic study which showed that Gleevec levels decrease over time) suggest that it is of great importance to address the question whether in vivo exposure of imatinib will indeed result in enhanced expression of ABC transporters in the epithelial cells of the gastrointestinal tract of cancer patients. In that case, it might have far reaching consequences for the clinical use of imatinib and a different dosing approach may be the ultimate outcome."

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PERSPECTIVE

First Gleevec class marks 5th anniversary

By Norman J. Scherzer
Life Raft Group Executive Director

Traditional graduation ceremonies were not held for the class of 2005, Gleevec-GIST University. Of the 30 patients who entered the first Novartis clinical trial for GIST in the summer of 2000, we do not have current statistics as to how many are still enrolled at the five year point nor whether we can confer graduation status on those who remain in this trial.

But as the husband of student No. 27, I would be remiss if I did not pause to celebrate her five-year milestone. I know that she is not alone in this distinction. I also know that many have not made it to this clinical trial anniversary — some continued on Gleevec but have dropped out of the trial; many have developed resistance and are trying other drugs; many have died.

But the miracle of Gleevec as the first oral targeted cancer drug that worked so dramatically for most GIST patients, and after five years continues to work for some, should not go unheralded. And we should not forget that prior to Gleevec there was absolutely no drug that worked for this deadly disease.

The history of Life Raft Group closely parallels the story of Gleevec. We began as part of an Internet-based listserv for leiomyosarcoma patients hosted by ACOR, the Association of Cancer Online Resources). In the spring of 2000, a new pathology test for an enzyme called c-kit began to separate out GIST patients as a quite different cancer, and the leiomyosarcoma diagnosis no longer applied.

The distinction between LMS and GIST was crucial, and lifesaving. An experimental drug called STI571, then used only for CML patients, appeared as a blip on the GIST Internet horizon. In the summer of 2000, the first of 30 patients began enrolling for a clinical trial in Boston, Philadelphia and Portland. A new Internet-based listserv for GIST patients quickly followed and the Life Raft began evolving as a patient organization.

STI571 proved incredibly effective against GIST, and was approved by the United States government in February 2002. Novartis, the manufacturer, gave it a brand name: Gleevec, or Glivec outside the U.S.

In the spring of 2002, 80 of the survivors and caregivers of this trial — which had quickly expanded due to the drug's remarkable results — traveled to meet one another at an historic gathering in Cambridge, Mass. A few weeks later, the Life Raft was incorporated as a formal 501-C-3 nonprofit organization.

Norman Scherzer gives a keynote address at the first "New Horizons in Treating Cancer" conference held in May 2003 in Switzerland.

Thus the summer of 2005 marks two anniversaries, the fifth birthday of the first Gleevec-GIST clinical trial and the third birthday of the formal founding of the Life Raft Group.

What an adventure this has been. A few highlights can help capture a small part of this journey:

- On June 24, 2000 my wife and I had gathered our family and friends at my son's home and renewed our wedding vows on the occasion of our 39th anniversary. Anita was bald and emaciated from her latest unsuccessful chemotherapy and was not going to be here for our 40th, and not likely to even make the fall of that year. Weeks later she became patient no. 27 on STI571. Ten days into the trial, a liver tumor that was being used as a marker had shrunk dramatically. By 30 days all her tumors had shrunk more than 50 percent and they were beginning to liquefy.

Her story was like a bolt of lightening over the Internet and desperate patients all over the world scrambled to find a spot on the clinical trial. Fortunately, Novartis managed to increase drug production and decided to keep expanding the trial to accommodate these new patients. More and more miracle stories appeared with patients literally walking out of hospice care and getting out of deathbeds. Nothing like this had ever happened in the treatment of cancer.

- In October 2002, two weeks after opening our first office, we are robbed. All our computers and our server are taken.
- I find myself in London, England giving a keynote address to the first international meeting convened for more than 500 medical experts
- I am asked to share the podium with Senator Ted Kennedy at a May 2002 press conference held at the home of the president of the Massachusetts Institute of Technology. The conference marks the opening of the Novartis Institutes for BioMedical Research, Cambridge Research facility.
- The Life Raft Group publishes its

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Life Raft board meets in Chicago

Photo by Tricia McAleer

Posing during a break in the action at the June meeting of the Life Raft Board of Directors held in Chicago are, from left, Silvia Steinhilber, Melinda and John Poss, Christopher Carley, Nancy Carley, Norman Scherzer, Allan Tobes, Jerry and Susan Knapp, Margi and Jim Hughes, and Jerry Cudzil.

MDR IV

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As Berger acknowledges, there is still more work to do to verify whether oral bioavailability actually changes over time in patients. Patients currently taking Gleevec are still left with questions about the optimal dose of Gleevec. This study adds a little more weight to the side that suggests higher doses of Gleevec may work better in the long run. It also seems to support the concept of starting Gleevec at a lower dose and, in the absence of unacceptable toxicity, escalating the dose as Gleevec blood levels drop and side effects diminish over time. Previous GIST studies that have supported the theory that higher Gleevec doses may produce better results include the Phase III EORTC randomized clinical trial, the EORTC pharmacokinetic study on Gleevec blood levels, and the Life Raft Group relapse survey that found that Life Raft Group patients actually taking higher doses of Gleevec reported few relapses than patients actually taking lower doses of Gleevec.

The work of the researchers mentioned in this article is an example that demonstrates how CML/GIST and Gleevec are models for molecularly targeted therapies. The tremendous focus that results from having one target and one drug being so important to controlling CML and GIST results in a more thorough inquiry into every aspect of what can go wrong. In the case of multi-drug resistance, this has resulted in looking at an old problem in new ways. Additional work is needed to translate these initial findings into clinical benefit.

PERSPECTIVE

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first major research effort in its own newsletter, a study on the side effects of Gleevec from the perspective of patients. Other cutting-edge research efforts follow, including the efficacy of Gleevec and the relationship between Gleevec dosage levels and the onset of resistance.

- Tricia McAleer (the secret weapon of the Life Raft Group, and my executive assistant) and I carry our display on our backs to set up a booth at the annual meeting of the American Society of Clinical Oncology that begins May 31, 2003, in Chicago.
- The family of a young woman who died of GIST comes to a Life Raft Group board meeting in January 2005 and offers to donate $6,000 a month for five years if directors will increase their own donations to match that grant. The board does.
- In late summer of 2004, I have lunch with James Watson, the Nobel laureate who co-discovered the makeup of DNA. We discuss the genetics of GIST. I am awestruck at the thought.
- A Life Raft Group clinical trials advisory group meets to discuss the issue of a placebo in a clinical trial and tearfully puts aside its own fears that formal opposition might jeopardize their participation or that of others in a "better than nothing" trial protocol. Instead, the group unites to oppose the use of a placebo in this situation because it is the wrong thing to do. Within months, two members of this advisory group have died. This was not a theoretical discussion.
- In November 2004, the Life Raft Group convenes the first international pediatric GIST scientific meeting in Montreal, Canada.
- In May 2005, the Life Raft convenes the first pediatric GIST family meeting in New Jersey and families from as far away as London and Seattle, Wash., gather for the first time.
- I chair a workshop in Warsaw, Poland, with the Amazonski, a breast cancer advocacy group in Poland consisting of women rewriting patient support history in their country.
- General membership meetings of the Life Raft Group are held in Cambridge, Mass. and Orlando, Florida
- Corporate Cultures Clash: The CEO of Novartis agrees to write an article for our fledgling newsletter. The CEO of another major pharmaceutical company (better unnamed to keep this article on a positive note) asks us to take him off of our newsletter distribution list.
- Lastly, I remember being invited to Nova Scotia to attend the "going away" party of Life Raft Group member Mike Matthews. I arrive at a community center to join over 250 of Mike's family and friends; it turns out I am the surprise his friends arranged. We meet and hug, then Mike goes back to his chair, his energy waning. There is a '60s rock band playing and it is one hell of a celebration with lots of music and lots of noise. Suddenly the noise stops. Mike has gotten up and asked his wife to dance. Everyone knows it's their last dance and that thought binds every heart in that room as one. Later that evening, I am invited to Mike's home for dinner. Mike is very tired and retires to bed. I'm asked to join him and I sit on the side of his bed and we talk. I don't remember everything we talked about but I do remember holding his hand and looking out the window at the incredible beauty of the ocean and the inlet outside. I catch a very early flight home; Mike dies the next day.

The onset of resistance, although not unexpected, is particularly cruel to those patients who cheated death while responding to Gleevec. Although a number of new drugs are making their way through the clinical trial process, none has yet emerged to match the initial success of Gleevec once resistance has occurred. The loss of innocence when a fatal disease reappears after a period of successful treatment is hard to explain to those who have not experienced it.

Thus, at our third year, the Life Raft Group undertakes its newest and biggest challenge, to find the key to overcoming GIST treatment resistance. Although we will also continue to expand our efforts at information, education, patient support, and advocacy, nothing is more important than the GIST treatment resistance project that we have just launched. (See Page 1).

Register online for GIST research fund's Oct. 2 Walk for a Cure

The GIST Cancer Research Fund's fifth annual Walk For A Cure will begin at 10:30 a.m. Sunday, Oct. 2, at Rockland Lake in Congers, N.Y. Registration is from 9:30 to 10:15 a.m.

GIST patients from around the U.S and Canada have already made plans to attend. Several widely known GIST experts plan to attend as well, including Drs. Margaret von Mehren and Andrew Godwin from Fox Chase Cancer Center in Philadelphia; Drs. Robert Maki, Ronald DeMatteo, Cristina Antonescu, David D'Adamo and Ephraim Casper from Memorial Sloan-Kettering Cancer Center in New York, and Dr. George Demetri from Dana-Farber Cancer Institute in Boston.

A dinner will be held the evening before the walk, and anyone wishing to attend should contact Chairperson Tania Stutman, phone (845) 634-6060 or e-mail gistcancerfund@aol.com. Registration forms are available online at www.gistinfo.org.

"We need your continued support to help eradicate this devastating cancer that has afflicted so many and claimed to many lives," says Tania. "Please join us and let's make the difference."

MUSIC

From Page 3

Tigers. Every day his work must be just as good as the last. There is no room for mistakes at Gordon's job.

Plus, there are "divas" to contend with.

"We deal with a lot of singers. Like Pavarotti — talk about a prima donna. He has a guy there just to adjust his mike stand."

Then there are the conductors. "There's an adversarial relationship between orchestras and conductors. But we have ways of dealing with them. One day you'll find them floating in the Detroit River with a baton between their eyes," he joked.

Gordon, you see, is a professional trumpet player. He plays with the Michigan Opera Theatre Orchestra (the orchestra pit is his "basement") and at a host of other venues, teaches at a university, and is one of Detroit's most sought-after trumpet instructors.

Gordon and his fellow musicians also have to contend with stereotypes. "There's a misconception that we're uppity and nauseatingly intellectual. That's not true, at least in the orchestra," he says. "We go mow our lawns after we're done."

Gordon has always wanted to do this. "I remember as far back as the first grade wanting to play the trumpet even though there was nobody around who played it," he says. "That never changed."

So music is what Gordon loves, regardless of the pressures or people he may have to deal with.

"Sometimes you're just swept away in the mass of sound and great music is going on all around you. It's a way for me to escape, get beyond some of the frustrations I'm feeling. It soothes the soul."

"Music is a language that doesn't necessarily use words, sometimes playing just helps me release."

Dealing with the stress of daughter Meredith's illness, Gordon finds support from all kinds of places, "My wife had breast cancer, so she'd gone through some of these things. We're also very involved in the church and get wonderful support from the church families on different level, financially and emotionally."

Tom Overley gets in some hot licks playing with his group, the Plat III band, at a venue in Toledo, Ohio.

But there's always the music.

"I'm a romanticist by nature, I love ballads and melodies, so those things by nature help me."

At the Life Raft's recent pediatric GIST weekend, Gordon was able to experience another blessing — playing "Amazing Grace" on his trumpet as GIST patient Rachel Gilbert sang.

"Playing with Rachel was the highlight of my life," he says. "That was a privilege."

As was the weekend. "That was a huge thing, a dream that was coming true," he says. "For 10 years we fought so hard to find anyone and then, there they were."

Gordon's ready for more in the dreams-coming-true department. "Dream No. 1 was realized when we got all the parents and kids together" for the pediatric GIST weekend. "Dream No. 2 will be a cure. I would love to see [Meredith] for one day when she feels good for at least 24 hours, to see her well, without it being on her mind."

But Gordon will always keep his spirits up. "We mustn't give up hope," he says. "It comes and goes, that's why we have each other."

MEET TOM OVERLEY

Tom Overley's life is pretty straight-laced. He's a lawyer who lives in Ohio, he takes care of his kids, and occasionally women take off their bras and throw them at his feet.

Well, that last bit may happen only in Tom's imagination. Regardless, "the guitar is a chick magnet, that was the appeal," says Tom, who started playing in 1962.

Lately, however, he's noticed something a little odd.

"I play elevator music. Go on an elevator and listen, they play rock from the '60s and '70s. That's what I play, elevator music.

"Oh my God," Tom says in mock alarm. "Rock has been relegated to elevator music."

When he's at home TomO (as most folks call him) can be himself.

"If no one's home I can play loudly and experiment with new sounds," he says. "If the kids come home, they yell, 'Dad, turn the music down.'"

All his life people have been telling him to turn the music down. So, why *does* he need it so loud?

"Sometimes I like to play music I can feel rather than hear," he says. "I like to feel the air coming from the amplifier. Once my daughter came home and said, 'I heard you all the way down the block, I'm home now, turn the music down.'"

From rock, Tom progressed to bluegrass in college. "I lived with hillbillies for 10 years," he jokes.

Now, he plays with his band, Plat 3,

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Questions and answers from our members

What follows are a few recent questions-and-answers from members posting to the Life Raft listserv. The intent is to share this information more generally and to make the quality of such layperson discussions available for public scrutiny. As always, comments or corrections from readers are welcome.

The following questions were answered by Jerry Call, the Life Raft's science coordinator

Does Gleevec change what the pathologist sees in a GIST biopsy? That could become important for me next week.

J.C. :Yes, treatment with Gleevec can sometimes cause a change in what the tumor cells look like. A recent paper by Pauwles, et al, discusses this issue. In this study, they describe three cases (of 35) that change phenotype. In the cases described, the tumor cells changed from spindle shaped -- about 70 percent of GISTs are spindle cells, the rest are either epithelioid (more common with PDGFRA mutations) or mixed spindle/epithelioid) to epithelioid. They also lost expression of KIT, and two of three lost expression of CD34.

My impression is that some of the tumors are possibly differentiating to a different phenotype. Importantly, two of the three also no longer responded to Gleevec.

The most accurate way to verify that suspect tumors are still GIST and not a new second cancer is probably to have a biopsy and have it tested for KIT mutations.

Even though the new/changed tumors don't express KIT, they still harbor the same KIT mutation (all of these cases had KIT mutations) as the original primary tumor.

The question that comes to mind is, how does this translate into preventative or proactive treatment? My father in law is down to four tumors in his liver, three identified as "dead" but one inexplicably lives on.

Should we be looking at having these tested for c-kit and then ...? What are the potentialities of looking at the tumors like this? Is there something that can be done that logically makes sense but perhaps is in an untested state?

J.C.: The most practical use of this information is when a new tumor appears in a location that is unusual for GIST. When GIST metastasizes, it usually goes to the liver. It can also spread to other areas in the abdomen. In rare cases it can spread to other areas including the lungs, bones, the brain, and the extremities (as two of our LFG members have reported GIST tumors of the arm). There is one case in the literature of subcutaneous GIST metastases.

When a new tumor appears in one of these unusual places, the question that arises is whether it is GIST or a second type of cancer (do you have two different types of cancer at the same time)? It can become confusing for the pathologist if this new tumor has "changed its type" so that it no longer looks like GIST. The definitive way to tell if the new tumor is GIST is to have it analyzed to see if it has the same mutation (in KIT or PDGFRA) as the original primary tumor.

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MORE MUSIC

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at a winery, at bars or private parties.

"We usually play for people in their 40s and 50s. They like to dance. For younger people we do Sheryl Crow, Norah Jones."

Tom recently purchased a guitar neck on eBay. "It showed up and I thought, now what do I do? So I said, well, OK, and I built a guitar."

How's the guitar coming along?

"It's a bit nerve-wracking, I keep wondering when the wiring is going to go haywire."

Beside music, poetry lets Tom give voice to his feelings.

"The ability to write the poetry I write, put it on the listserv and be open to people."

But music is where his heart is, and his mischief. "There's a lyric I like from the Allman Brothers' 'Live at the Fillmore East' disc and was written by Blind Willie McTell. It is called 'Statesboro Blues:' "*I'm goin' to the country, baby do you want to go? If you can't make it, baby, your sister Lucille said she'd want to go.*"

"What this line says to me is that hope can spring eternally in the heart and mind of an old/young man."

So what are Tom's plans?

"I want to see the sun rise tomorrow, I want to see all three of my girls graduate from high school (he's seen one so far) and I'd like to marry a rich, good-looking woman willing to put up with all my zanias and have complete freedom … with all her money."

But seriously, Tom does have one wish, "What I would hope is for everybody, with whatever time you have left, to do something to make the world a better place."

— Erin Kristoff is administrative assistant of Life Raft Group.

Henry Lange Jr., farmer, veteran, outdoorsman, was 69

Henry William John Lange Jr., 69, of Cole Camp, Missouri, died Tuesday, July 19, 2005, at Harry S. Truman Veterans Hospital in Columbia.

He was born on March 16, 1936, at Yuma, Colo., a son of Henry and Martha Cordes Lange Sr. On June 17, 1962, he was married to Carol Jean Kreisel at Mount Hulda Lutheran Church of rural Cole Camp.

Mr. Lange was a member of the Trinity Lutheran Church in Cole Camp. He served on the MFA Producers Board and Oil Board, and was a member of the Cole Camp Jaycee's. He enjoyed being outdoors, farming and raising cows. He loved to fish with his buddies and entered crappie contests sponsored by the Cole Camp Chamber of Commerce and Jaycees, winning twice. He enjoyed hunting with his friends, children and grandchildren. He loved to collect and restore old tractors, and he especially enjoyed pulling his Oliver tractors. Over the years, he traveled to several towns to pull and won many trophies. He loved listening and dancing to his German accordion music. He was an Army veteran.

Henry Lange is shown raising a pair of pry bars like a victory salute during deer-hunting season this past fall. Though all his family was there, Henry didn't feel up to going hunting with the younger guys. However, he looked out the window one morning and saw a deer, got his gun, and bagged it in the yard.

In addition to his wife, Mr. Lange is survived by two daughters, Nancy Balke, and her husband, Bryan, of Lenexa, Kan., and Christel Harms, and her husband, Darin, of Cole Camp; a son, Bruce Lange, and his wife, Jeanene, of Lincoln; a sister, Mary Ann Adolph, of Independence; a brother, Robert Lange, of Gladstone; and five grandchildren, Derek and Johanna Balke, Tray and Tory Lange and Sara Harms. He was preceded in death by a grandson, Kyle Balke.

Services were held July 23 at Trinity Lutheran Church, Cole Camp, with the Rev. Todd Kollbaum officiating. Pallbearers will be Arthur Hagen, Wilbert Meyer, Detlef Heumann, Larry Stoermer, Anthony Kreisel, Larry Meyer, Tray Lange, Derek Balke and Jason Lange. Burial will be in Trinity Lutheran Cemetery, Cole Camp.

Memorial contributions to a favorite charity are preferred.

Q&A

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The classic example of this was patient A. After a year on Gleevec she had growth in a long dormant nodule in the lung (remember it is rare for GIST to go to the lung). Several centers got involved in testing the tumor with somewhat different results, particularly over the issue of whether it was c-kit positive or negative GIST. Finally it was determined to be c-kit negative.

But it was GIST. The single tumor was removed with a less invasive type of surgery, and patient A remained on the phase II trial (even though they could have kicked her off if they had strictly interpreted the protocol). A was one of the earliest GIST patients to take Gleevec and remains on the trial.

Even though the GIST trials were only one year old, A's example demonstrated at least two principals of excellence in GIST management. First, the suspect tumor was analyzed for c-kit mutations, which proved that it was indeed GIST and not a second new cancer. Second, since only one tumor was progressing (local progression), the single resistant tumor was surgically removed and she continued on Gleevec.

Should we be looking at having these tested for c-kit and then what? What are the potentialities of looking at the tumors like this?

J.C.: No I don't think you should have those tumors tested for c-kit. This should generally be reserved for when there is a question of whether the tumor is GIST or something else.

A GIST tumor losing expression of c-kit is just one of several ways that GIST can become resistant to Gleevec. The data is based on small numbers (so subject to change), but from what I have seen, I think that it might account for somewhere

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Terri Stevens, restaurateur and 15-year GIST survivor

Terri L. Stevens of Colchester, Conn., a 15-year survivor of GIST, succumbed to the disease July 19, 2005. She was 42.

Born in Hartford, Conn., she was the youngest daughter of Josephine and the late Walter Remillard. She grew up in Hartford and East Harford, and had resided in Colchester for the past 13 years.

TERRI STEVENS

Terri owned The Doc Stop restaurant in Hartford since 1995. She loved the challenge of operating a business, creating recipes, and engaging new people every day.

"You couldn't help but eventually learn some degree of acceptance, patience, and perseverance in her presence," a friend recently remarked, "… all the while being nurtured with great pasta sauce, soups, desserts and turkey melts."

Terri always believed in doing the little things in life well and with great love. Among her many passions were gardening, cooking, flowers, family, friends and entertaining, as well as raising her many roosters, chickens, goats, dogs, rabbits and maras.

Joe Stevens says he and his wife rarely spent a day apart in the past 22 years, "and we never went a day without at least talking to one another. Terri remained my confidant, teacher, my friend and above all, my family."

Those who knew Terri knew her to be endlessly passionate, creative, driven, nurturing, tireless, positive, enthusiastic and generous to a fault. She was never one to sit on the fence with an issue or her feelings.

She loved family, had an eagerness to laugh, and a willingness to embrace life. She had the courage to pursue her dreams, love unconditionally, and consistently challenged herself and those around her to become better people.

In addition to her mother and husband, Terri is survived by her six brothers and sisters: Carol Sirois, Jo-Ann Gagne, Laverne Devin, Walter L. Remillard Jr., Francis X. Remillard, Richard A. Remillard; and many nieces and nephews.

"She touched the lives of those that knew her and left her fingerprints upon all our hearts," says Joe. "While we mourn her passing, we also celebrate her wonderful life."

Daniel Raymond Hoffman, 58, was a decorated veteran

Daniel Raymond Hoffman of Mechanicsburg, Penn., died Sunday, June 19, 2005. He was 58.

He was born Oct. 23, 1946, in Harrisburg, a son of Ruth E. Hoffman Sheibley of Camp Hill, Penn. He retired in November of 2004 after 23 years of service with Naval Sea Logistics, Department of the Navy, in Mechanicsburg. He was a decorated Vietnam War veteran awarded the Purple Heart, Bronze Star and the Combat Infantry Badge while with A Company, 1st Battalion, 27th Infantry of the 25th Infantry Division, also known as the Wolfhounds.

He was a lifetime member of the Military Order of the Purple Heart, a member of the Mechanicsburg Presbyterian Church, Linglestown VFW, Mechanicsburg Club and loved to travel.

In addition to his mother, he is survived by his wife, Kathleen Wright Hoffman; a daughter and her husband, Alicia and William Deardorff of Hummelstown, Penn.; half brother, Milton Keith Sheibley of York Haven, Penn; half sister, Debra Ann Wheeler of Boiling Springs, Penn.; and a grandson, Kyle D. Shemory.

Funeral services were held June 24 in Mechanicsburg, with the Rev. Dr. Richard D. Sweeney officiating. Burial with full military honors was in Gettysburg National Cemetery.

Contributions may be made to Life Raft Group, 40 Galesi Drive, Wayne, NJ 07470.

MORE Q&A

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around 10 percent of resistant GIST.

As for those "dead" tumors; even in tumors that respond very well to Gleevec, there are almost always at least a few residual cells that are still alive.

Is there something that can be done that logically makes sense but perhaps is in an untested state?

J.C.: In my opinion, the two main choices that you have right now are to continue the Gleevec until resistance OR, if surgery is feasible, to remove all tumors and continue the Gleevec. I am not advocating either position. This is something to be discussed with GIST experts (surgeon and oncologist).

The Life Raft Group

Executive Director	**Norman Scherzer,**	nscherzer@liferaftgroup.org
Executive Assistant	**Tricia McAleer,**	tmcaleer@liferaftgroup.org
Administrative Assistant	**Erin Kristoff,**	ekristoff@liferaftgroup.org
IT Director/Web Master	**James Roy,**	jroy@liferaftgroup.org
Research Assistant	**Pamela Barckett,**	pbarckett@liferaftgroup.org
Science Coordinator	**Jerry Call,**	jerry.call@comcast.net
Special Assistant	**Matthew Mattioli,**	mmattioli@liferaftgroup.org

Contact the Life Raft Group
40 Galesi Drive
Wayne, NJ 07470
Phone: 973-837-9092
Fax: 973-837-9095
Internet: www.liferaftgroup.org
E-mail: liferaft@liferaftgroup.org

Life Raft volunteers

Chief Financial Officer	**Allan Tobes**	atobes@comcast.net
General Counsel	**Thomas Overley**	guitarman335@msn.com
Accountant	**Allan Tobes**	atobes@comcast.net
List Manager	**Mia Byrne**	mebmcb@wowway.com
Newsletter Editor	**Richard Palmer**	richardpalmer@hawaii.rr.com
Web Designer	**Tami Margolis**	tami@comcast.net
Fund-raising co-chairs	**John Poss**	john@celeritylogistics.com
	and **Gerald Knapp**	gsknapp@winfirst.com

Life Raft country representatives

Australia	**Greg Ladbrooke**	lad57b@bigpond.com
China	**Ruijia Mu**	ru_ruijia@yahoo.com
France	**Bertrand de La Comble**	bdelacomble@oreka.com
Iran	**Negar Amirfarhad**	negaraf@sympatico.ca
Italy	**Anna Costato**	anna.costato@virgilio.it
Mexico	**Rodrigo Salas**	rsalas@maprex.com.mx
Netherlands	**Ton de Keijser**	tdk@lrgnederland.nl
Poland	**Bartosz Szczesny**	bsz1974@yahoo.com
Switzerland	**Ulrich Schnorf**	ulrich.schnorf@bluewin.ch
United Kingdom	**David Cook**	D.Cook@sheffield.ac.uk

Life Raft area groups

Arizona	**Linda Martinez**	linda.martinez1@cox.net
Chicago	**Richard Kinzig**	rjkinz@aol.com
Detroit	**Allan Tobes**	atobes@comcast.net
Los Angeles	**Floyd Pothoven**	floyd@keralum.com
New York	**Dan Cunningham**	Daniel.Cunningham2@pseg.com
Texas	**Kerry Hammett**	yaloo@gvtc.com
	and **John Poss**	john@celeritylogistics.com

Board of Directors

Executive Committee

Stan Bunn, President	SBunn@BSTGlobal.com
Allan Tobes, Secretary-Treasurer	atobes@comcast.net
John Poss, Fund-raising	john@celeritylogistics.com

Directors

Robert Book	RMBook2@aol.com
Mia Byrne	mebmcb@wowway.com
Chris Carley	ccarley@fordhamco.com
Jerry Cudzil	jerry.cudzil@csam.com
Jim Hughes	tjhughes43@comcast.net
Gerry Knapp	gsknapp@winfirst.com
Dr. Arnold Kwart	amkbmp@aol.com
Rodrigo Salas	rsalas@webtelmex.net.mx
Silvia Steinhilber	nswplas@mb.sympatico.ca

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.
Wayne, NJ 07470

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