

A leader in the battle to defeat GIST

Meet Jonathan Fletcher

By Elizabeth Braun

Dr. Jonathan Fletcher dreams of being able to curl up with a good book in his Berkshire farmhouse in Massachusetts. For that



FLETCHER

matter, he has already started to accumulate a stack of autobiographies and biographies. He also would love to be able to spend more time on his other passions, photography and cooking.

Unfortunately, these dreams will have to wait until he retires. For now, he spends his time keeping current with his research and trying to keep up with his three boys. He loves hiking and swimming with his sons, who are 4, 7 and 11. The boys, in turn, keep him up to date on the latest rap songs, while bouncing along country roads in his old pickup truck. Fletcher and his family try to escape to the Berkshire farmhouse for weekends so they can enjoy the mountains and trees.

Despite the many demands on his time, Fletcher has generously donated a significant amount of time and energy to the Life Raft Group. He has been a vital member of the research team that is developing the grant process to fund studies of Gleevec-resistant GIST. With his help, the process has moved along swiftly and a truly unique paradigm has been developed. The Life Raft hopes to encourage an unprecedented level of cooperation and speed success to the research process.

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Battling gastrointestinal stromal tumor



LIFE RAFT GROUP

November 2005

In Memory of Norma Christian, Don Baney, Fritz Dutro, Diane Henry, Karen Sales

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Resistant GIST may fall to new inhibitor

Young researcher finds way to eradicate the driver of GIST tumors

By Jerry Call

During the 2005 Connective Tissue Oncology Society (CTOS) meeting held Nov. 19-21 in Florida, Dr. Sebastian Bauer was presented with a young investigator award for his research into methods for overcoming Gleevec-resistant GIST. Bauer currently works as a medical oncologist in the interdisciplinary Soft Tissue and Bone Sarcoma Group at the West German Cancer Center, chaired by Professor Seeber, in Essen, Germany. Bauer did his research while working in the lab of Dr. Jonathan Fletcher at Brigham and Women's Hospital in Boston, Mass. Bauer presented the results

of his group's research at the CTOS meeting. The other authors of this abstract include Drs. Lynn Yu, George D. Demetri and Fletcher.

While Gleevec initially works for about 85 percent of GIST patients, Gleevec will eventually fail for many of these patients despite long lasting responses or disease stabilization. The problem of resistance is not unique to Gleevec; it is common in traditional chemotherapy given to patients with metastatic disease.

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Life Raft director Jim Hughes, left, meets Young Investigator Award winner Dr. Sebastian Bauer of Germany.

Novartis presents Life Raft with check for research initiative



With a generous grant from Novartis, the Life Raft Group will coordinate research to overcome Gleevec-resistant GIST by bringing together the top GIST experts from many institutions. Life Raft Executive Director Norman Scherzer accepts a check from Novartis representative Debbie Freire. Also from Novartis are Sarah Boyce, left, and Laurie Letvak, second from right. At right is Sara Rubinoff, LRG program coordinator.

FLETCHER

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As a medical and pediatric oncologist with a long-term commitment to GIST research, Fletcher is an ideal person to lead the LRG's research process. In addition to his experience in clinical oncology, he has developed diagnostic methods to detect DNA and chromosome aberrations in GISTs and other sarcomas. He oversees a clinical lab service in which chromosome abnormalities are analyzed to determine the correct diagnosis and prognosis for each patient. His research group is currently studying tyrosine kinase mechanisms in sarcomas, including KIT and PDGFRA. He has developed novel techniques for rapid profiling of tyrosine kinase activation in frozen human tumors and, using these methods, has identified effective therapeutic targets in several types of sarcomas, including GIST.

Currently, his primary research goals are to identify therapeutic strategies that can synergize with KIT inhibition

to cure GIST. He works as a team with Dr. George Demetri and colleagues in the clinical sarcoma program at Dana-Farber Cancer Institute in Boston to identify laboratory research strategies that can best assist in the rapid development of new clinical approaches for GIST.

Fletcher received his medical degree from Boston University in 1981. He went on to do his internship and residency at the University Hospital in Boston. In 1984 he became their chief resident in medicine. In 1986, Fletcher moved on to become a clinical and research fellow of pediatric and adult oncology at the Dana-Farber Cancer Institute and the Children's Hospital. Fletcher became a research fellow in pathology at Brigham and Women's Hospital in 1988, where he remains today. Currently, he is an associate professor of pathology and pediatrics at Harvard Medical School.

"Translational research" is where

Fletcher's passion lies. In translational research, the goal is to move new techniques and treatments from the laboratory into patient treatment. He was drawn to it because of the interaction between lab work and clinical practices. It allows him to treat patients while working to affect a greater population and advance science through research.

Even when laboratory techniques don't transfer to clinical practice successfully, the lessons are valuable. Taking those lessons back to the lab leads to valuable insights and knowledge.

The skills he has developed through translational research make him an ideal leader for the Life Raft Group's research team.

The Life Raft is truly grateful for the effort that Fletcher has put in to developing the new research paradigm. We look forward to continuing to work together.

Sile Bao: Growing up with GIST

15-year-old is a fighter determined to make the most out of her life

Editor's note: This article is part of a series on children and teens with GIST, written in their own words.

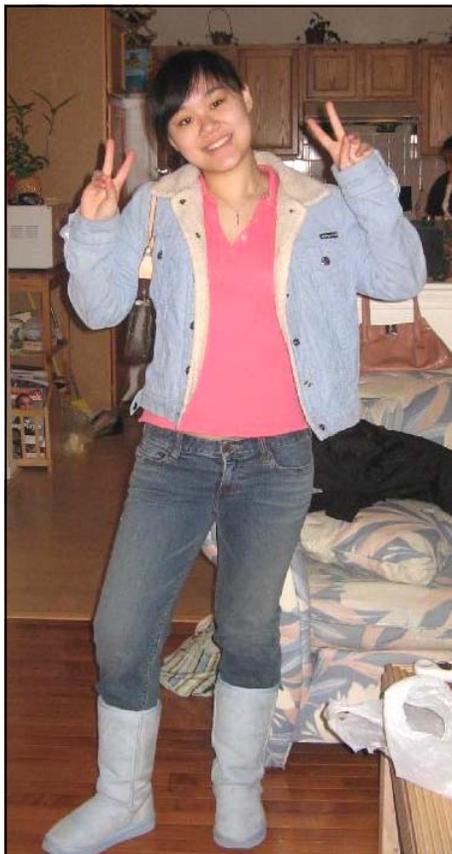
GIST — Gastrointestinal stromal tumor. To doctors, this is a rare tumor that is usually found in the stomach. To me, a 15-year-old girl, it is something that has changed my life in so many ways.

Growing up, I was always a healthy girl. I never got the flu or even a cold. Whenever I even fell and scratched my knee, I would get right back up and put a Band-Aid on it.

One day I had to go to my pediatrician to get a yearly checkup. He noticed that I was abnormally pale and advised me to take a blood test. He asked me how I was doing physically and I told him that I was tired a lot but I did not really take it to heart. The next day my mom came to my school to pick me up and told me that I needed to go to the emergency room. I was alarmed and found out that it was because my hemoglobin had shown up to be only 5.2. At that time, I had no idea what that meant and all I remember was waiting for hours in the emergency room, feeling dizzy and tired. The doctor finally came and diagnosed me with iron-deficiency anemia.

After that, I resumed my normal activities, dancing four days a week and playing in piano competitions. Of course, I had to take iron pills, but other than that, life was good!

Soon after, my stomach started to hurt a lot. My mom and I talked to my doctor about it, but he insisted that it was the iron pills. Then we went away for Thanksgiving. That week, my stomach hurt so much. At first, I thought I it was just the turkey and that



Sile says cancer has been a “blessing in disguise. It has made me stronger in so many ways.”

I was suffering from I-ate-too-much-itis. However, the week following Thanksgiving, I was unable to eat anything. My doctor finally agreed that it was time to bring in another doctor. I went to visit a G.I. doctor and she performed an endoscopy on me.

At that point, the doctors should have realized that something was wrong. There was fresh blood on the site of my endoscopy and there were several masses around my stomach. However, the doctors believed that it was just swelling and ulcers.

I was put on antibiotics. Another couple of months passed and I was scheduled for another scope. That is when the doctors saw that I was still bleeding internally and the mass had grown. That week I was diagnosed with GIST and I was scheduled to

have surgery to remove my 7-centimeter tumor.

Ever since my surgery, life has been very different. Last year I was unable to attend school. In the beginning of the year, it was due to the side effects of my surgery. My stomach was sore all the time and my body was very weak. However, in January, the cancer reoccurred and they found an almond-sized tumor in my liver and cancer activity in my pelvis. Surgery this time was not an option so I was put on the miracle drug — Gleevec. This drug made my life even more difficult than I ever imagined. I could not sleep at night without pain medication because my joints hurt so much. I was not able to attend school anymore because of the pain, and thus I was put on home instruction. I was losing my friends because I could not see them at school. I was so unhappy.

Since then, I have been off the Gleevec because it was just too toxic for my body. Part of me feels scared because I do not know what will happen to the cancer activity inside me. However, every day I am a fighter.

The hardest part of having cancer is knowing that it is something that I will always have to fight. Because the chance of GIST recurrence is so high, it is often discouraging for me to know that I will have this disease for the rest of my life. However, I have come to the realization that this is and always will be part of my life. And you know what’s amazing about that? I will never stop being a fighter, because as long as I have this disease, I will fight it. For some strange reason, that is very comforting to me.

When people ask me how I feel about having cancer, I tell them that it has been almost like a blessing in disguise. It has made me stronger in so many ways. I used to view life as a routine, as something that had struc-

Kids with cancer take the stage at ArtWorks 2005

By Norman Scherzer

The Montclair Art Museum in New Jersey hosts many works of art, but none of them surpassed the clothes line holding the artistic drawings that were created by the children of the Life Raft group using surgical pants as their canvas.

Hosted by an organization called Artworks, the children's drawings were part of a larger display created by kids with cancer and other serious illnesses in the New York area.

The Life Raft Group drawings were created at our Pediatric GIST Family Weekend this past spring as part of a partnership with Tomorrow's Children, a program that uses art, music



and dance as therapy. The program permits children to use artistic expression to find different ways to express

their feelings and concerns. Nothing the Life Raft Group has done has ever made me prouder.

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BAUER

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In GIST, however, mechanisms of resistance are increasingly well understood, unlike many other cancers treated with classical chemotherapy. The most common cause of "secondary resistance" is the acquisition of secondary mutations in KIT, mostly in the area of the protein where Gleevec binds. Depending where the surface of KIT changes, Gleevec's ability to bind is somewhat to greatly diminished. As a result, some secondary mutations may be sensitive to higher doses of Gleevec, but many resist even the highest doses of Gleevec.

One strategy in targeting secondary mutations is to design drugs that bind to KIT just like Gleevec but that have a somewhat altered structure that fits better into the altered binding pocket of KIT. AMN107, for example, is a modified form of Gleevec that may

inhibit some secondary mutations in KIT that are insensitive to Gleevec.

However, targeting secondary mutations with another KIT inhibitor has some limitations. Since many different types of secondary mutations have been found (and some probably exist that have not been found), the new KIT inhibitor must fit into the binding pocket of as many of these different mutations as possible.

The inhibitor must also retain sensitivity against the original mutation, as many parts of the tumor may still have the original mutation and no secondary mutations.

It is even possible that different parts of a tumor within the same patient may contain different secondary mutations or other mechanisms of resistance. Combining two different KIT inhibitors (as in the current trial combining AMN107 with Gleevec) may therefore

have a broader activity against the different mutations — similar to a broad spectrum antibiotic used to treat strains of bacteria that are prone to resistance against single drugs.

However, whether the combinations will be more effective is not yet clear.

In the research reported at CTOS, Bauer and his associates took a different approach. Rather than targeting the changing KIT protein directly, they targeted a protein that is required to stabilize the KIT protein. This protein, called HSP90 (short for heat shock protein 90), is not known to be mutated in GIST and thus should not be a "moving target."

WHAT IS HSP90?

HSP90 is a member of the "chaperone" family of proteins. It 1) helps proteins to fold into their correct

Second poker tournament brings in \$61,000 for LRG

Host Jerry Cudzil proves he knows when (and how) to hold 'em and fold 'em

By Erin Kristoff

Life Raft Board Member Jerry Cudzil hosted his second Annual Texas Hold'em Poker Tournament on Thursday, Oct. 20. The purpose of the tournament is to raise money for the Life Raft Group and it did just that — totaling more than \$61,169 for the Life Raft Group.

The night unfolded at the Park Avenue Country Club in New York City where family, friends and colleagues sat down for an evening of friendly but competitive fun. More than 100 players and spectators came out to join in the fun.

With the chance to help GIST patients in mind, people lined up to pay the \$500 entrance fee. The night went smoothly as players bet their hands and lost, leaving an every smaller number of tables occupied. Soon, just one table of players remained—then the real battle began.

Nicholas Chiara took home first place, a \$10,000 entrance fee to ESPN's World Series of Poker. Oren Bramson came in second — and promptly donated his winnings back to Life Raft Group; Third place went to Mark Bonanni, who went home with a 37-inch plasma television.

A 50/50 drawing was also held and the winner, known only as "Uncle Rippy", donated his winnings back to the Life Raft Group. Many other participants and spectators generously donated their time, talents and good in support of the worthy cause.

Everyone enjoyed the evening and left in good spirits. The Life Raft Group thanks the Cudzil family and all who turned out for the evening of poker. We'll see you next year!



Winners of the second annual Life Raft Group poker tournament were, from left, Oren Bramson, second; Nicholas Chiara, first, and Mark Bonanni, third.



Poker players enjoy the evening as the Texas Hold'em tournament moves toward the final round. More than 100 players and spectators turned out for the second annual event.

LIFE RAFT GROUP



Pediatric

Gastro

Intestinal

Stromal

Tumors

Ensuring that no child has to face GIST alone

This pamphlet will tell you the basics about GIST and its treatment. It is intended to answer some of your questions about the disease, but is not a substitute for your physician's guidance and care.

Pamphlet on pediatric GIST goes to school

Our youngest Like Raft Group member, an 8-year-old girl, came across the Thanksgiving package that had just arrived in her home. Lying there was our brand new pamphlet on pediatric GIST.

She asked her mom if it would be OK to take the pamphlet to school so that her teacher could tell her class about her cancer.

Although no member of the Life Raft Group anticipated this use for the pamphlet, it's hard to think of a better one.



The Life Raft Group participated in the 11th annual Connective Tissue Oncology Society (CTOS) convention held Nov. 19-21 in Boca Raton, Fla. Above, participants look at the Life Raft posters at the conference.

Life Raft at CTOS, sarcoma summit



At the CTOS meeting, the first Collaboration Summit for directors of sarcoma patient advocate organizations was held. Over the past several years, multiple groups and foundations for sarcoma have arisen. The summit was held to support and strengthen the sarcoma community's collective efforts. Participants include, front row from left, Ginger Kyle, Deborah Buks, Sharon Anderson, Suzanne Kurtz, Yvonne Blixt and Tricia McAleer; second row, Beverly Shriver, Marlene Portnoy, Joan Darling, Louise Gallun, Dave Marsh and Ellen Silver; back row, Chris Yates, Susan Erickson, Dave Murphy, Penny Duke, Bruce Shriver, Doreen Trucano, Mike Trucano, Tom Swartz, Andrew Beckert and Mark Thornton.

An overview of CTOS 2005

The Life Raft Group staff headed to Boca Raton, Fla., Nov. 19-21 to attend the 11th annual conference of the Connective Tissue Oncology Society (CTOS). Here is the news of interest to GIST patients.

GENERAL SESSION

The status of two series of patients undergoing surgery after Gleevec was reported at the meeting. While we are going to report those results this month, we hope to do a follow-up story soon in which we will report on other similar series as well as getting some comments from the doctors involved. This is an important topic and one that is difficult to evaluate in clinical trials. For the foreseeable future, it is likely that patients and doctors will have to evaluate the advantages and disadvantages of surgery after Gleevec by considering data from available various sources.

Surgical Management of GIST following treatment with KIT-directed chemotherapy — Abstract 459, Chandrajit P. Raut, et al (Brigham and Women's Hospital, Boston, Mass.

A series of 69 GIST patients had surgery for advanced GIST while receiving KIT-directed therapy. Nine patients had primary tumors only, and 60 had metastatic disease. The groups of patients were:

- 23 patients with unresectable primary/metastatic GIST following maximum drug response (stable disease).
- 32 patients with metastatic GIST with localized progression while still receiving KIT-directed therapy (limited progression).
- 14 patients with metastatic GIST with generalized progression while still receiving KIT-directed therapy (general progression also known as systemic progression).

These three groups of patients were



Research Team members, from left, Dr. Jonathan Fletcher, Norman Scherzer, Dr. Brian Rubin and (backs to camera) Elizabeth Braun and Dr. Chris Corless discuss the priority projects.

also categorized by surgical result: no evidence of disease (NED), minimal/moderate residual disease, and bulky residual disease. Following surgery, 39 percent of patients were NED, 43 percent had minimal/moderate residual disease, and 17 percent had bulky residual disease.

Those patients having stable disease or limited progression prior to surgery were more likely to be NED or have minimal/moderate disease after surgery than those having generalized progression before surgery (89 percent vs. 57 percent).

The median progression-free survival (PFS) was longer for patients who were NED or had minimal/moderate disease versus those with bulky disease (12 months vs. 3 months).

The authors concluded: "Patients with advanced GIST exhibiting stable disease or limited progression on KIT-directed therapy were more likely to have successful debulking procedures. Patients who were NED or had minimal/moderate disease after surgery had improved PFS."

Advanced Gastrointestinal Stromal Tumor: Molecular, Pathological and Clinical Pattern in Post-imatinib Surgery — Abstract 399, A Gronchi, et al, Istituto Nazionale per lo studio e la cura dei Tumori, Milan, Italy.

This study looked at pathological and molecular features of GIST after treatment with Gleevec. Perhaps even more importantly, they looked at how well GIST patients taking Gleevec did after surgery. Thirty-six out of 162 patients in this group underwent surgery. They were then divided into three groups:

Group A had 25 patients whose cancer was still responding to Gleevec. All of the patients in this group were alive 24 months after surgery and 72 percent had not had progression during those 24 months. Gleevec failed four patients 16 to 18 months after surgery (two of three who had stopped taking Gleevec, and two of the 22 who continued taking Gleevec).

Group B had eight patients with either primary progression or secondary

HSP90

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three dimensional shapes; 2) stabilizes a variety of other proteins, among which many are involved in the development of cancer, and; 3) protects them from degradation. Very recent preclinical work by other researchers has shown that some of these mutant proteins can be effectively inhibited by interrupting the HSP90 function. These diseases include cancers such as leukemia (bcr-abl, the other Gleevec target) and lung cancer (EGF-receptor), as well as a rather benign disease of skin cells (mast cell disease) that is driven by a mutant form KIT which usually is highly resistant to Gleevec.

A NEW THERAPEUTIC STRATEGY IN GIST?

Based on these results, Bauer and his associates tested an inhibitor of HSP90, 17-Allylamino-17-demethoxygeldanamycin (17-AAG) against four GIST cell lines. One was sensitive to Gleevec (GIST882) and three were resistant. The resistant cell lines were derived from patient biopsies and represent different mechanisms of resistance just as they can be found in patients: While all cell lines have typical Gleevec-sensitive primary mutations, GIST430 and GIST48 contain two different secondary mutations of KIT; GIST62 lost KIT as a “driver” of tumor growth.

Bauer showed that removing the protector (HSP90) of KIT using 17-AAG completely inhibited KIT function. Unlike Gleevec that just switches off KIT, 17-AAG actually “trashed the whole switch,” causing degradation of KIT. Surprisingly, using a non-GIST cell line that expresses normal, non-mutated and non-activate KIT, 17-AAG did not cause degradation of KIT. This suggests that 17-AAG mainly affects the mutant, activated form of KIT.

Bauer also compared the effects of 17-AAG and Gleevec on the cascade

of “electrical” signals activated by KIT that tell the cell to proliferate and survive. He found that 17-AAG inhibited both KIT and its signaling into the cell in both Gleevec sensitive and Gleevec resistant cells that still expressed KIT. In line with these findings, 17-AAG strongly inhibited growth of these cells and caused cell death at doses that have been shown in clinical trials to be achievable in patients. However, very little effect was seen in the cell line that lost KIT expression, suggesting that HSP90 may not work in GIST with this mechanism of resistance (possibly 10 to 20 percent of patients with Gleevec-resistant GIST). Certainly more work needs to be done to understand the biology of these cells.

Nonetheless, Bauer summarized his work as a proof of concept for a new strategy to treat KIT positive Gleevec-resistant GIST. Targeting KIT indirectly via HSP90 inhibition might help to overcome resistance by inhibiting activated KIT regardless of its mutations, unlike direct KIT inhibitors such as Gleevec and Sutent that are unable to inhibit all forms of mutant KIT.

SIDE EFFECTS?

As mentioned in the introduction, HSP90 has been shown to protect more than a hundred other “client” proteins besides KIT. Many of the “client” proteins are crucial for the function of normal cells. This naturally raises the question as to the side effects that could be expected by 17-AAG. Several phase I trials have already been conducted in patients with other types of solid tumors and side effects have been rather mild, compared to effects usually seen with classical cytotoxic chemotherapy. This can be explained by the fact that HSP90 apparently exists in two different states, a native form found in most normal cells and a form bound in a “super-chaperone complex” that is found mostly in cancer cells. The native form has a low affinity for 17-AAG, while the super-chaperone

complex has a high affinity for 17-AAG. Thus, there could be a “therapeutic window” where HSP90 inhibitors are able to affect cancer cells more than normal cells.

CLINICAL TRIALS FOR GIST IN SIGHT?

17-AAG is the HSP90 inhibitor that is furthest along in clinical development. It is entering or near phase II trials even though it is not an ideal drug as it only exists in an IV formulation and has very poor solubility. Therefore, it must be given with “carriers” like DMSO or Cremaphor, both of which have side effects of their own and limit the dosing of 17-AAG. However, HSP90 inhibitors are advancing fast and newer, synthetic, small molecule inhibitors of HSP90 are in development that will be available as oral drugs in the near future.

IPI-504, a modified 17-AAG, is an intravenous drug from Infinity Pharmaceuticals based in Cambridge, Mass., which is water soluble and does not require carriers such as DMSO.

Bauer and Fletcher presented a pre-clinical evaluation of IPI-504 in GIST cell lines at the joint National Cancer Institute-American Association of Cancer Researchers-European Organization for Research and Treatment of Cancer meeting on targeted therapies held Nov. 14-18 in Philadelphia, PA, showing that IPI-504 is as effective as 17-AAG at shutting down Gleevec-resistant GIST.

Based on this data, a clinical trial of IPI-504 for GIST has been developed by Dr. George Demetri and is awaiting institutional review board approval at Dana-Farber Cancer Institute in Boston. This phase I trial will be for patients with Gleevec-resistant GIST.

Bauer and the Dana-Farber team are cautiously optimistic that this new method of indirectly targeting KIT through inhibition of HSP90 may provide a broadly relevant therapy for Gleevec-resistant GIST.

Dr. Sebastian Bauer contributed to this article.

BAO

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ture. Now, life is something that I can enjoy and have fun with! As a result of my illness, I have become an active member of my church and closer to those people whom I consider to be my “real friends.” I use the term “real friends” because this disease has really helped me recognize those who really care about me. When I was sick, there were certain people who always visited me and made sure I was feeling well. Other people just simply did not want to hear about my situation anymore. Thanks to my illness, I now have certain people I can count on.

These people keep me sane through those hard days. There are some days when I just want to yell and scream at the world because I feel yucky, and those loyal friends keep me grounded. They talk to me, take me out, make me laugh, and pray for me. I really do not know what I would do without my family and friends.

I guess this whole ordeal has been extremely hard on my family as well. Sometimes I tell my mom, “Why are you getting so upset? This is my ill-



Sile shows that she is not camera shy.

ness and it has nothing to do with you.” Then I realize how cruel I am in saying those words because everything that happens to me affects her in more ways than I will ever know. Yes, having cancer has broken this family up a

bit but it has also made us so much stronger. I cannot help but feel that every time I get sick, it gets more and more frustrating for my parents.

Last year, I had no goals for myself and I just let GIST take over my life. However, this year I am determined to live a normal life. I have missed days of school but I will make them up and ace this year. My dream is to go to a good school and become like a person I met at the Cancer Institute of New Jersey. Her name is Christine and she fights for kids’ rights at school and is also there for us to talk to her. She is my inspiration in so many ways and I would love to have a job like hers where I can help kids like me.

Now I am back in school enjoying every day. I consider myself to be a regular teenager who fights with her mom, does not clean her room, and does not do her homework (of course, only occasionally). Yes, I get sick occasionally, but I guess that just makes me a little more extraordinary than everyone else.

CTOS

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progression. All had disease progression at 12 months and only half were still alive.

The authors concluded: “This series suggests not to discontinue imatinib after surgery, even if complete. Prognostic advantage from surgery of residual disease in response is left to elucidate by combining available series. Neoadjuvant imatinib in bulky primary disease is beneficial. Progressive disease should be treated with second-line molecular-targeted therapies, surgery being likely of minimal benefit.”

ONGOING TRIALS REVIEWED

A very short summary of ongoing

(mostly adjuvant Gleevec) trials was presented by a number of different organizations. The general trend seemed to be that adjuvant GIST trials continued to accrue patients at or above expected rates.

The ACOSOG (American College of Surgeons Oncology Group) Z9000 trial is closed. The first interim analysis is expected in 2006.

The Z9001 has been expanded from 489 patients to 732 patients. This was required because they were recruiting more patients in the lower risk categories than expected.

The Spanish sarcoma group Grupo Espanol de Investigacion en Sarcomas (GEIS) has opened a sarcoma and

GIST registry at www.registrokeis.com. They have a doxorubicin-plus-Gleevec trial for refractory GIST, and are also participating in the European Organization for Research and Treatment of Cancer (EORTC) 62024 adjuvant Gleevec trial.

The Scandinavian group has an adjuvant trial (SSG XVIII) for high-risk GIST. This trial compares one year of Gleevec versus three years of Gleevec and is being conducted in cooperation with the German group.

The Italian Group has an “observational” study called GIOTTO (GIST Optimal Treatment and Therapy Outcome). They also have a phase II trial

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of PTK787 (a KIT/VEGF inhibitor made by Novartis) for GIST patients refractory to imatinib. Ongoing Italian clinical protocols can be found on the web at: www.istitutotumori.mi.it/INT/struttura/pdf2004/Protocolli.pdf.

The Radiation Therapy Oncology Group S-0132 trial is almost full (accrued 55 of 63 patients). This phase II trial is for neoadjuvant/adjuvant Gleevec for primary and recurrent operable GIST expressing CD117. More information about this study can be found at: www.clinicaltrials.gov/ct/show/NCT00028002?order=1.

The large EORTC 62024 trial continues to accrue patients. Many different centers are participating in this adjuvant Gleevec for GIST trial. Further information about this trial can be found at www.eortc.be/protocol/Details.asp?Protocol=62024.

SARCOMA COLLABORATION SUMMIT

On Saturday, Nov. 19, several sarcoma patient advocacy organizations met for the first time to collaborate on a shared mission: to find a cure for sarcomas.

Representatives learned about each organization's unique role, efforts and contributions; established a communication network between all groups; discussed the most current developments, issues and needs for advocates; and defined mutual goals and collaborative strategies.

At the end of the meeting, the group decided on a name — iSPAN, short for International Sarcoma Patient Advocate Network — and two task forces were established. One will address patient education, support and outreach, the other will undertake legislative lobbying. Each task force set up an action plan for the next six months.

The following organizations were represented: Amschwand Foundation, STS Patient Advocate Committee of



Clockwise: Dr. Robert West (back) and LRG Board Members Jerry Knapp and Dr. Arnold Kwart listen at the meeting of the Life Raft Group Research Team.



LRG Board Member Bob Book, left, and Dr. Chris Corless watch the research presentation.

Children's Oncology Group, Desmoid Tumor Research Foundation, GIST Support International, Jennifer Hunter Yates Sarcoma Foundation, Karen Wyckoff Rein In Sarcoma Fund, Liddy Shriver Sarcoma Initiative, Life Raft Group, National Leiomyosarcoma Foundation, Sarcoma Alliance for Research through Collaboration, Sarcoma Alliance, and the Sarcoma Foundation of America.

The summit would not have taken place if not for the help of Sharon Anderson, whose dedication as a patient advocate made it possible.

RESEARCH TEAM MEETING

The Life Raft Group Research Team met Saturday, Nov. 19 for several hours prior to the start of the CTOS general session. Joining the LRG Research Team were several members of the Board of Directors. Dr. Jonathan Fletcher led the discussions. In a matter of a few hours, priority allocations were made for the components of projects that have been given priority over the past few months.

The LRG is working with a truly amazing group of researchers. There is an unprecedented environment of collaboration and cooperation. The process is moving forward with exceptional speed; the first grants will be awarded in early 2006. By capping the amount of funds that may be used for indirect costs at 10 percent, the Life Raft Group is ensuring that more money is available to researchers. In contrast, indirect administrative costs can consume 50 percent or more of the grants institutional researchers receive. This could well become a model for other organizations.

Online Q&A from the Life Raft Group

What follows are two 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 two questions were fielded online by Richard Palmer, the Life Raft's newsletter editor.

Question: What's the deal with sun exposure and Gleevec?

RP: This is Richard's rant on sun sensitivity, offered to new Gleevec gulpers so they can avoid becoming human lobsters.

If you loved the sun and liked to sport a nice tan, well, those days are behind you. Besides stopping cancer cell growth, Gleevec apparently inhibits melanocytes, the cells that produce melanin, the pigment your body makes to keep it from absorbing harmful so-

lar radiation. It's this pigment that gives you a golden glow.

I grew up in a Southern California beach town and spent summers in the sun. Always tanned easily and fast. Today if I go out in the sun, I simply turn red. And Gleevec makes it possible to get the most amazingly painful sunburn. I found that out once, a couple of years ago, and vowed never again.

I still boogie board, but I wear a wet-suit, even in tropical waters. It's for sun protection.

As for eye protection, I've worn eyeglasses for 15 years now and they have 100 percent UV protection. If I didn't wear glasses, I'd probably be more concerned. If the sun is bothering your ability to see, you need to do something. Draw the drapes, close the blinds, and wear cool sunglasses.

As for vision, Gleevec causes periorbital edema (water retention/swelling around the eyes). This can put pressure on the eye, squeeze it, and this can change the eye's focal length and af-

fect vision, for better or worse. I've been hoping it will give me X-ray vision, but so far ...

May I ask why some people call it Sugem and others call it Sutent?

RP: The Pfizer drug Sutent was initially developed by another firm, Sugem. In early clinical trials the drug was called SU11248, as early drugs often have alphabet soup names. Gleevec (Glivec outside the U.S.) was initially called STI571.

Because SU11248 is a mouthful, patients simply called the drug "Sugem." Now that Sugem is nearing U.S. approval and Pfizer is getting ready to market the drug, they're calling it Sutent (generic name: sunitinib malate).

Why funny names like Gleevec and Sutent? Two reasons: 1) a new brand name must be different from all existing brand names; 2) when spoken, it can't sound like a lewd, crude or obscene word in any language.

ATTENTION to Medicare-eligible Gleevec patients

Medicare eligible Gleevec patients who are currently receiving assistance from Novartis will need to sign up for a Medicare Part D Prescription Plan. If a patient finds they are unable to pay for the cost of Gleevec, they may contact the Novartis Medicare Prescription Drug Plan Assistance line (1-800-942-3424) to determine if other assistance is available. Other information resources include:

1-877-GLEEVEC
www.gleevec.com
www.medicare.gov



Thanksgiving Campaign

Thank you to our members and their families and friends for sending contributions for our 3rd Annual Thanksgiving Campaign.

We are still accepting donations so please do not hesitate to contact us if you

have any further questions or you need any additional materials. We have had a positive response about our pamphlets so if you need more, please contact our office.

Don't forget to check out our web site for an updated list of our donors!

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Who are we, what do we do?

The Life Raft Group is an international, Internet-based, non-profit organization offering support through education and research to patients with a rare cancer called GIST (gastrointestinal stromal tumor). The Association of Cancer Online Resources provides the group with several listservs that permit members to communicate via secure e-mail. Many members are being successfully treated with an oral cancer drug Gleevec (Glivec outside the U.S.A.). This molecularly targeted therapy represents a new category of drugs known as signal transduction inhibitors and has been described by the scientific community as the medical model for the treatment of cancer. Several new drugs are now in clinical trials.

How to join

GIST patients and their caregivers may apply for membership free of charge at the Life Raft Group's Web site, www.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
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Disclaimer

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