

Clinical trial initiative to be launched in Mexico

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

By Norman J. Scherzer
Life Raft Executive Director

At an historic meeting on May 29th arranged by Life Raft Group board member Rodrigo Salas with key officials of the School of Medicine, the Life Raft Group was asked to provide technical and educational support to a new Cancer Center and Clinical Research facility being created in Monterrey, Mexico. After a tour of the construction site board member Salas and myself met with Dr. José Rafael Borbolla, Director of the Department of Clinical Research, and Dr. José Ramos Montmayor, Director of Clinical Services, to discuss the support of cancer clinical trials in Mexico.

Battling gastrointestinal stromal tumor



LIFE RAFT GROUP

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In memory of Roy Barton and Alex Smolyar

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Tec de Monterrey (TEC) Health Science Campus located in Monterrey, Mexico.

The catalyst for this new initiative is Rodrigo Salas whose wife, Cordelia, finally succumbed to GIST after a long and heroic battle. After Cordelia's death,

Rodrigo decided that few Mexican citizens would have had the resources to access medical care in the United States,

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EORTC Study: Progression-free survival improves for 800 mg vs. 400 mg patients

New study shows initial treatment with 800 mg/day Gleevec® significantly improved progression-free survival in group of high-risk GIST patients with exon 9 mutations.

- *Investigation of high-dose Gleevec regimen significantly reduces relative risk of progression by 61 percent in patients with exon 9 mutation*

- *Authors recommend these patients receive 800 mg/day at start of therapy*

East Hanover, May 5, 2006 – A higher, investigational starting dose of Gleevec® (imatinib mesylate) tablets can improve outcomes for high-risk patients

with advanced Kit-positive gastrointestinal stromal tumor (GIST) expressing exon 9 mutation, according to new findings from the largest clinical trial to evaluate the drug's effects by mutation. The study findings are now available online and are expected to be published in May.

The clinical trial, an EORTC (European Organisation for Research

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Learn how to appeal an insurance claim

By Tom Overley
and Richard Palmer

Note: Tom Overley is general counsel and Richard Palmer is the former editor of the Life Raft Group newsletter.

Many oncologists still don't know how to treat GIST. It is wishful and deadly thinking to expect that your health insurance company is going to know how to treat GIST — let alone approve a drug which costs as much per month as a used house trailer.

What can you do?

Appeal. While it isn't fair that people battling cancer must also fight their health insurance company, it's sadly an all-too-often fact of life.

Approximately 1.2 million Americans will be diagnosed with cancer this year, but only 5,000 will have GIST. That's less than one half of 1 percent, or one out of every 240 cancer patients. That's why many — if not most — oncologists aren't familiar with GIST.

You may not have any problems if you have PPO (preferred provider organization) insurance. These give you the flexibility of picking an out-of-network doctor. You can also choose to go to a major cancer center for treatment, though you'll have to pick up travel costs.

HMOs (health maintenance organizations) want you to stay "in group." But it's unlikely any group includes an oncologist truly familiar with GIST. Referrals to a GIST expert are rarely made. This is where problems will likely arise. This is where you'll want to see a GIST expert, but your insurance says it won't pay.

The key to prompt approval is to put the burden — and most importantly, the liability — squarely upon the shoulders of the health insurance company. You must know this stuff if you are to survive.

Insurance companies are very good at making such denials sound like they're written in stone. They aren't. You can always appeal a denial. Even if your first



OVERLEY



PALMER

appeal is denied, you can usually appeal higher up the chain of command. As long as you keep adding new information to your appeal, the insurance company can't refuse to hear it.

You have to educate the insurance company and let them know that their failure to approve the only known treatment for GIST will almost certainly result in your premature death.

Your appeal of any denial must be prompt and in writing. To be safe, fax it to the insurance company, and then mail it to the company. Include the fact that you are mailing a copy of your letter to your lawyer — "cc: Perry Mason, attorney at law." Use your family attorney's name.

But the process is a bit involved. Fortunately, help is just a few mouse clicks away.

One of the best online sources for appealing claim denials, recommended by AARP and others, can be found at the Kaiser Family Foundation Web site, <http://www.kff.org/consumerguide/7350.cfm> There, the foundation and Consumers Union collaborated and posted an online guide to handling disputes with employer-provided or private health plans.

The Web site details what you need to do to appeal a denial. Step-by-step, it tells you what information you should gather, how to begin the appeal process, and how to move things along.

It points out that health plans must follow state and federal rules for handling complaints and appeals within the

Vasella, CEO of Novartis, will appear at Life Fest 2006

Life Fest 2006 is shaping to be an amazing event! Dr. Daniel Vasella, CEO of Novartis Pharmaceuticals has accepted an invitation to join the LRG in Dallas this September. Dr. Vasella was presented with the Life Raft Group Humanitarian Award at its first meeting in 2002.

The LRG's goal for this meeting is to bring together GIST patients, caregivers and medical professionals to exchange strength, hope and knowledge. There will be educational sessions with the LRG Research Team, key medical professionals, and some of our own Life Rafterers who have volunteered to facilitate the flow of life-saving information.

All GIST patients and caregivers are welcome to join the LRG for the weekend, September 15th-17th, at the Adams Mark Hotel in Dallas, Texas.

Check the LRG website, www.liferaftgroup.org, for more details about registration and updates to the agenda and guest list.



Vasella at first LRG meeting in 2002.

MEXICO TRIAL

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particularly clinical trials, as his wife was able to do. In her memory his mission is to support a program in Mexico that will provide cutting edge cancer care, including clinical trials, to Mexican cancer patients. As a first step, Rodrigo—a long term member of the Life Raft Group Board of Directors—was just appointed as a Board Member and a Member of the Institutional Review Board (IRB) of this new Cancer Center and Clinical Research facility in Monterrey.

Located on the TEC Health Science Campus, this new initiative, called CITES (Center for Innovation and Knowledge Transfer in Health) will coordinate the resources of the School of Medicine and the Hospital San Jose with those of the new outpatient cancer and clinical research center. The Tec de Monterrey, better known as the TEC, is one of the most respected universities in Latin America, providing a network of Mexican university campuses.

Traditionally most oncology in Mexico is housed in private practices and at public hospitals. This is the first time that a private cancer center will employ its

own staff of oncologists. Clinical trial patients will be served from throughout Mexico, including those at public facilities. The longer term phase will extend this expert cancer care, research and education throughout Latin America.

The Life Raft Group will provide support and encouragement in several areas.

First, we will utilize our newsletters and websites to provide information about this initiative to cancer patients and scientists around the world. Second, we will link the Monterrey Cancer Center to our new GIST resistance research initiative. Third, we will use our good

offices to advocate on behalf of the Center with pharmaceutical companies and researchers to encourage the conduct of clinical trials at that facility. As medical care is much less expensive in Mexico the end result will be more cost effective clinical trials.



Pictured (from left to right): Life Raft Executive Director Norman Scherzer, Life Raft Board Member Rodrigo Salas, Director of the Department of Clinical Research Dr. José Rafael Borbolla, and Director of Clinical Services Dr. José Ramos Montmayor.

A continued discussion on optimizing therapy for GIST

In the March-April 2006 issue of this newsletter, the first half of a two-part article on "optimizing GIST therapy" appeared. Dr. Jonathan Trent of M.D. Anderson Cancer Center presented the information contained in this article during a recent Novartis sponsored webcast.

In the first part of the presentation, Dr. Trent responded to some of the questions that he typically gets from GIST patients. These questions included:

How do I manage or prevent side effects?

How do I know if Gleevec is helping me?

This month, Jerry Call has summarized Dr. Trent's answer to the second question as he talks about measuring response and answers a number of additional questions about GIST.

Dr. Jonathan Trent as reported by Jerry Call

Agreeing with previous statements by other GIST experts, Trent noted that RECIST (Response Evaluation Criteria In Solid Tumors) substantially underestimates, at least initially, the value of therapy with Gleevec for GIST. At M.D. Anderson, Trent uses modified RECIST (Choi criteria) for assessing response in GIST:

- Tumor size decrease of ≥ 10 percent OR tumor density decrease of ≥ 15 percent by CT scan
 - These were highly correlated with decrease in the standardized uptake value (SUV) by >70 percent to a value of <2.5



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INSURANCE APPEAL

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health plan, known as an “internal review.” Many states have legislated additional procedures outside of the health plan, called “external reviews” or “independent reviews,” to provide an unbiased way to resolve disputes between patients and their health plans.

The Web site offers links to state Departments of Insurance, and summarizes what kind of help you can expect. Some states are better than others at helping consumers appeal a claim denial.

The Web site also talks about external reviews, which is a reconsideration of a health plan’s denial of service done by a person or panel of individuals who are not part of the plan. As of December 2004, external review procedures were established in 43 states plus the District of Columbia.

The U.S. Department of Labor, Employee Benefits Security Administration (EBSA), is charged with overseeing the integrity of pensions, health plans, and other employee benefits for more than 150 million people. The EBSA Web site, www.dol.gov/ebsa/, spells out the rules that employer-provided insurances plans must follow. The site has general information on appealing claim denials.

There are private companies that will help you appeal a claim denial — for a price. One of these is Appeal Solutions (www.appealsolutions.com, www.appeallettersonline.com). According to company co-founder and president Tammy Tipton, insurance companies deny thousands of claims a year. “They do this knowing that most denials are accepted without question or action.”

With all denial appeals, you have to be persistent. “Follow up is absolutely crucial,” said Tipton. “Carriers lose appeals letters left and right because they are processing such a huge volume of accounts. Follow up so that your claims are the ones that get attention. Call them as often as you can. Re-fax your appeal to the person you

talk with on the phone.”

“Remember, tenacity may be your biggest asset when appealing claim denials,” Tipton said. “Do not give up until you are satisfied with the answer you receive.”

More specific advice, including a CD of fill-in-the-blank appeal letters you can send to your insurer, is available at the Web sites. Be advised such help isn’t cheap: a one-year membership to appeallettersonline.com is \$199; downloading their “Power of Appeals” software will cost \$499.

Another online company is HealthSymphony.com, a health insurance Web

site run since 1998 out of Chatsworth, Calif. Their Web site (www.healthsymphony.com) has basic guidelines to filing an appeal. They also have three sample appeal letters that give you a good idea of how to write an appeal.

They also sell a variety of form appeal letters starting at \$9.99 for a single form letter, with discounts if you buy multiple appeal letters covering different situations.

With these resources, you’re ready to appeal your claim denial. With persistence, you may likely prove you can beat the bureaucracy.

Your insurance appeal letter should state:

“Dear Insurance Company:

“I am writing this letter to appeal your decision to deny coverage of a drug treatment plan that will assist in the quality of my life, avoid the additional costs associated with unnecessary surgical intervention, and almost certainly save me from almost certain death.

“As your records will reveal, I was diagnosed with GIST in (date here). GIST is a rare cancer. GIST stands for gastrointestinal stromal tumor. Until five years ago, other than surgical intervention, there was no treatment for GIST. Patients generally died within months of diagnosis. With the discovery of imatinib mesylate (Gleevec), GIST patients have been living longer and enjoying a quality of life heretofore unheard of.

“The U.S. Food and Drug Administration approved Gleevec for treatment of GIST in 2002. I personally know of patients who have lived five or more years thanks to Gleevec. It is the only known treatment for my cancer.

“Every day that your company denies me access to this drug, my chances for survival are reduced. I ask that you act immediately in the resolution of this appeal. Alternatively, I ask that you provide me with a treatment plan that allows me to live.

(I would add the following if you are not satisfied with your current oncologist.)

“Additionally, I have requested an out-of-network approval for treatment of my rare cancer. I have spoken with each “in plan” oncologist in our network and none have had any experience with GIST patients. If you will not, approve an out of network consultation with Dr. (first, last name), I ask that you locate an in-plan physician with expertise in treating GIST.

“Thank you in advance for your time and your anticipated cooperation with my quest for life.

“Sincerely,

“(Your name here)

“cc: Henry Legal Eagle (put your attorney's name here)”

Palmer bids adieu as Life Raft newsletter editor

By Richard Palmer
Former Newsletter Editor

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

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

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

One of the people on that listserv was Gary Golnik of Boxford, Mass. An engineer who worked on complex optical systems like the Hubble space telescope, Gary's wife, Mary, had just learned that

her leiomyosarcoma might actually be variant of LMS called GIST, gastrointestinal stromal tumor. Mary was being treated at Dana-Farber Cancer Institute in Boston. Gary tells of how they found other GIST patients.

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

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

met her.

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

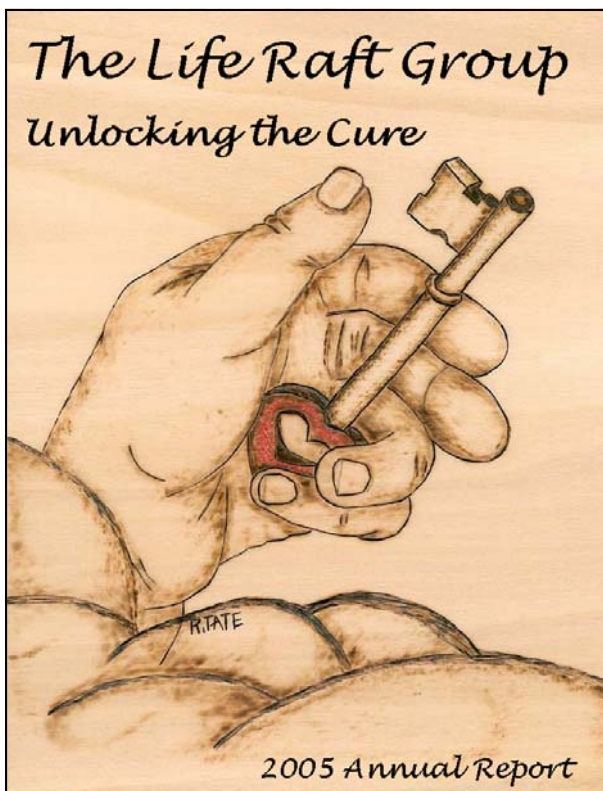
“Mary nervously said yes, and a deep and dear friendship formed in an instant.

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

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

Gary found several such patients on ACOR's LMS list, where news of the STI571 trials was sparking new hope

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Life Raft publishes 2005 annual report

This week marks the release of the Life Raft Group's Annual Report for 2005. The LRG was founded by several GIST patients to facilitate the flow of information amongst a very small community whose mission was survival. The mission has stayed the same but the means to carry it out have grown. A little over five years later, the LRG has reached out to thousands of GIST patients and their

families. The LRG membership continues to grow. This newsletter reaches approximately 5,000 subscribers every issue and the LRG website is visited by patients from over 100 countries. The LRG has also expanded its programs to include Support, Research, Surveillance and Advocacy.

The annual report contains key milestones of the LRG for 2005, Board of Director biographies, a list of LRG donors for 2005 and a summary of expenditures. Thanks to Rachel Tate whose artwork is featured on the front cover.

Look for the 2005 Annual Report in your mailbox.

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on PET scans in GIST patients.

Note: SUV=Standard Uptake Value. It is a measure of glucose uptake into the tumor. In the nearly 50 M.D. Anderson GIST patients, a decrease in tumor size of 10 percent or more OR a decrease in density of 15 percent or more was almost always accompanied by a decrease in glucose uptake during a PET scan. The glucose uptake was almost always decreased more than 70 percent on PET scan (to a SUV value of less than 2.5).

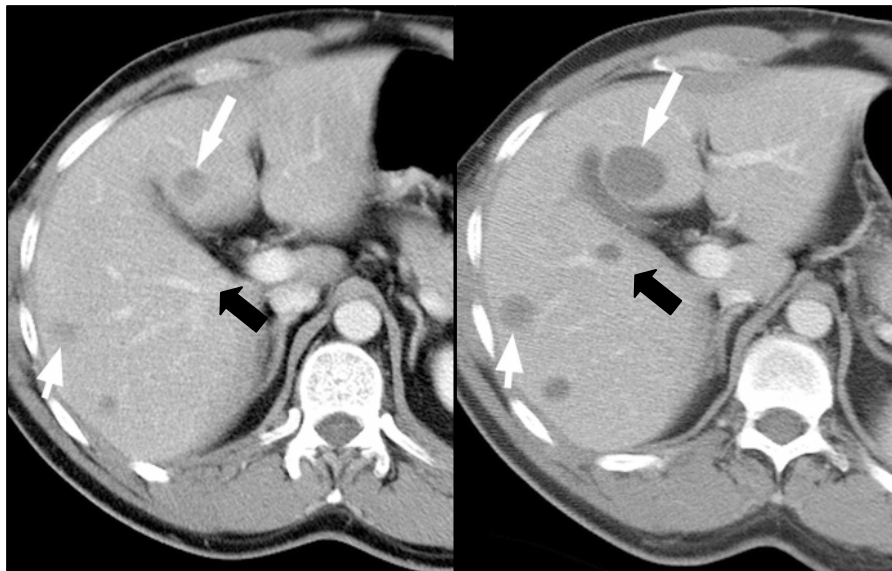
Dr. Trent noted that when the above guidelines are used, PET imaging is not generally needed. He still uses PET in some circumstances, but it's pretty rare.

Another set of slides (Figure 4), presented by Trent, showed another shortcoming of RECIST and a potential diagnosis pitfall. The CT on the left is before treatment with Gleevec. If you look carefully you can see a faint outline of a tumor (Black Arrow). During treatment with Gleevec, this tumor becomes progressively darker and much more visible; in fact, a new tumor appears (Right Panel, Black Arrow). This is the case of an existing tumor that is not apparent before treatment with Gleevec and appears as it responds to Gleevec. This patient was referred to M.D. Anderson after a physician discontinued Gleevec due to progression, when in fact, the lesions were responding to Gleevec. A strict interpretation of RECIST would classify this as a new lesion and therefore progressive disease. Use of the Choi criteria will help prevent the misclassification of patients benefiting from Gleevec.

In the pretreatment CT (left panel), the tumors have the same density as surrounding tissue and do not show up or are very faint. During treatment with Gleevec, the tumors begin responding to treatment and lose density and become much more visible. This can incorrectly be interpreted as progressive disease and is another example of why management by GIST experts is important.

What treatment is there for KIT negative GIST?

Figure 4
Existing lesions that look like new lesions during successful treatment with Gleevec (Black Arrow)



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

GISTs that do not express the KIT protein account for about 5 percent of all GISTs. This type of GIST may still respond to Gleevec according to Dr. Trent, although, as a group, their overall survival is not as long as the KIT positive group of patients.

What is the role of genotyping in GIST?

Dr. Trent is frequently asked about the role of genotyping in GIST. He noted that “it doesn’t play a major role clinically now, but it may in the future. It does appear to play a predictive role, in that patients whose tumors have mutation in KIT exon 11 in general have a greater median PFS (progression-free survival) on Gleevec therapy compared to those with an exon 9 mutation or no mutation.” Trent noted that any individual patient could do better or worse than predicted by genotyping due to other reasons.

Trent noted that genotyping may play an interesting role in the future since patients with metastatic GIST who crossover from a lower to a higher dose Gleevec have an 8-fold better chance of getting benefit from the higher dose of Gleevec if they have a kit exon 9 mutation compared to exon 11 patients. Kit

mutation analysis is available at M. D. Anderson Cancer Center.

What is the role of Gleevec for primary tumors?

Dr. Trent often has patients referred with a primary tumor and questions whether or not they should take Gleevec in the preoperative (neoadjuvant) or postoperative (adjuvant) setting. Trent noted that the role of Gleevec in these settings has not been defined by published studies . . . “but that there is compelling evidence to suggest that we need to do something more than just surgery in patients with primary GISTs.”

The rationale for neoadjuvant and adjuvant therapy comes from the historical data on GIST. Trent especially singled out a primary tumor size of over 10cm as a negative prognostic factor for recurrence and survival in the pre-Gleevec era. Historically (before Gleevec) these patients have had only about a 20 percent chance of surviving 6 years.

Dr. Trent talked briefly about several ongoing adjuvant trials: Z9000 and Z9001 and a possible future Z9002 study. Trent also noted the two ongoing combination neoadjuvant plus adjuvant studies: the RTOG S-0132 trial for pa-

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tients with potentially resectable GIST and the M.D. Anderson neoadjuvant plus adjuvant trial, (ID03-0023) combining preoperative imatinib, surgical resection and postoperative imatinib for 2 years.

Dr. Trent noted that the decision to resect the GIST immediately or take Gleevec prior to resection of a GIST is a difficult one. Given the choice between preoperative Gleevec plus postoperative Gleevec or just postoperative Gleevec, many patients prefer to take the drug both preoperative and postoperatively. He noted that patients often prefer to start taking Gleevec as soon as possible and to know whether the drug is working. In the Z9001 adjuvant study, patients don't know whether or not Gleevec is working because they have already had the tumor removed.

Is there therapy for Gleevec-resistant GIST?

Dr. Trent noted that there are really three different types of progression that can be seen on a CT scan: limited progression, progression of a nodule and widespread progression.

Trent noted that patients with limited progression (including progression of a nodule) can be treated differently than patients with widespread progression as shown below:

Limited progression

- Hepatic artery embolization
 - Clinical benefit in about half of patients

Note: Hepatic artery embolization is an alternative palliative therapy for patients with tumors that cannot be resected. Embolization is performed by reducing the blood flow through the hepatic artery, which minimally affects healthy liver cells as they get their blood supply from the portal vein. Embolization may not be suitable for patients with liver diseases such as hepatitis or cirrhosis.

- Hepatic Radio-frequency Catheter Ablation
- Surgical Resection
- Radiation Therapy (special situa-

tions)

Widespread progression

- Increase Gleevec to 800 mg daily
- Sutent
- Clinical trial
 - These clinical trials take two different forms:
 - Agents that don't put pressure on KIT signaling, such as perifosine or RAD001, are given in combination with Gleevec.
 - Agents that bind to KIT with a higher affinity OR inhibit multiple kinases, such as the addition of VEGFR such as dasatinib.

How long do I take Gleevec?

Dr. Trent noted that "... patients with metastatic GIST, for the most part, needed to be on Gleevec for life. We get an idea that this is the proper approach from a discontinuation study that was led by Dr. Blay in France." Patients with metastatic GIST were treated for 12 months and the responders were then randomized to either continue Gleevec or discontinue Gleevec. The patients who discontinued Gleevec were found to progress almost immediately, so discontinuation of Gleevec in a patient that is responding or has stable disease with metastatic GIST is to be avoided. This also raises the question as to whether a kit inhibitor should ever be discontinued in GIST patients.

Is Gleevec cytotoxic or cytostatic?

Note: What are cytotoxic and cytostatic? Cyto=cell. Cytotoxic means toxic to the cell; in this context it means something (Gleevec) that kills the cell. Cytostatic means something that keeps the cell in a static condition; in this case, it means it prevents the cell from dividing (prevents the tumors from growing) but it does not kill the cells (or tumor).

"The answer, of course is, yes", according to Trent. Trent showed pathology slides of a GIST patient before Gleevec and after one month of Gleevec. After Gleevec most of the tumor cells were dead, having ruptured and released the contents of the cell. This dead mix-

ture formed the bulk of the tumor. A few viable tumor cells remained however and these cells may start growing again if Gleevec is stopped.

Are my children at risk for GIST?

Dr. Trent noted that while this is possible, it is rare with only about 17 recorded cases in the literature. Trent presented a family pedigree on one large family with this type of GIST (familial GIST) that he cares for in his practice.

Summary

Dr. Trent made a number of important points in his presentation:

1. Side effects are worse and treatment interruptions and dose reductions occur more often if you start Gleevec at higher doses, but patients that crossover to a higher dose after being on a standard dose of Gleevec for awhile do significantly better in these regards.
2. Tumors do not always shrink even when Gleevec is working. Tumor cells may die but protein debris may linger on and be viewed as areas of low density on CT scans.
3. Gleevec is a life-long treatment for patients with metastatic GIST.
4. Gleevec appears to benefit patients with KIT negative GIST.
5. Genotyping currently plays a predictive role and will probably become more important in the future. Kit mutation analysis is available at M.D. Anderson Cancer Center.
6. Dr. Trent told us of modified RECIST criteria that M.D. Anderson uses in clinical trials for GIST. GIST experts have previously acknowledged that the current RECIST are inadequate for GIST. This new modified RECIST from M.D. Anderson is the first specific proposal that we are aware of (choi criteria).
7. Dr. Trent gave recommendations about the management of Gleevec-resistant GIST noting that patients with limited progression should be managed differently than patients with widespread progression.
8. GIST can run in families, but this is rare.

Laughter helps sisters battle the GIST dragon

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

By Erin Kristoff

Leigh Borland was at her lowest point. On November 14, 2005 she had gone into the hospital for a hysterectomy. The doctors thought they had found a mass on her ovaries, what they actually found was a 5-6 cm primary tumor on her colon and two smaller tumors nearby; the pathology report listed it as "unknown malignant potential." The oncologist decided to send slides out to the Cleveland Clinic and got a GIST confirmation. From that moment on Leigh's life became more and more confusing. The Chief of Surgery at Good Samaritan Hospital in Illinois approached Leigh and told her that she needed a second opinion; he explained he knew little of GIST. That night the gynecologist she



Pam Broadus, left, and Leigh Borland, right, visiting Loch Ness in Scotland.

had been seeing called to tell her not to worry, that she was fine and the tumor was "benign." In mid-December she finally had an appointment with an on-

cologist who came highly recommended. Leigh thought that he would know exactly what was going on and

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EORTC REPORT

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and Treatment of Cancer) Phase III study, compared two doses of Gleevec in patients with unresectable and/or metastatic Kit (CD117) positive GIST. While the majority of patients derived benefit from taking 400 mg/day of Gleevec, the study showed that patients whose tumors expressed a mutation on a certain gene segment called exon 9 had significantly superior progression-free survival ($P=0.0013$) when administered Gleevec at the investigational dose of 800 mg/day.

"This latest study provides further evidence that Gleevec is a highly effective therapy for patients with advanced Kit-positive GIST, and offers insight into potential ways to improve long-term outcomes for these patients," said Diane Young, Vice President and global head

of Clinical Development at Novartis Oncology. "These data also highlight that the investigational dose of 800 mg/day may be more effective for high-risk patients expressing the exon 9 mutation."

In this study, investigators analyzed data from a recent randomized EORTC Phase III trial comparing two doses of Gleevec (400 mg/day vs. 800 mg/day) in patients with unresectable and/or metastatic Kit-positive GIST, to assess whether tumor genotype correlated with the dose-dependent clinical response to Gleevec. Pre-treatment samples of GISTs from 377 patients enrolled in the clinical trial were analyzed for mutations of Kit and platelet-derived growth factor receptor alpha. The presence of a Kit exon 9 mutation was the strongest ad-

verse prognostic factor for response to Gleevec, increasing relative risk of progression by 171 percent ($P<0.0001$) compared to Kit exon 11 mutations. In patients whose tumors expressed a Kit exon 9 mutation, treatment with the high-dose regimen resulted in a significantly superior progression-free survival ($P=0.0013$), with a reduction of the relative risk of 61 percent.

Note: This is a very important paper that has been published by the European Journal of Cancer. There is more relevant information in this article than just the link to progression-free survival and exon-9 mutations. We plan to discuss this paper with some key people and we will provide more in-depth coverage in a later issue.

PALMER FAREWELL

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among LMS patients whose tumors were c-Kit positive, which meant their cancer was actually GIST.

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

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

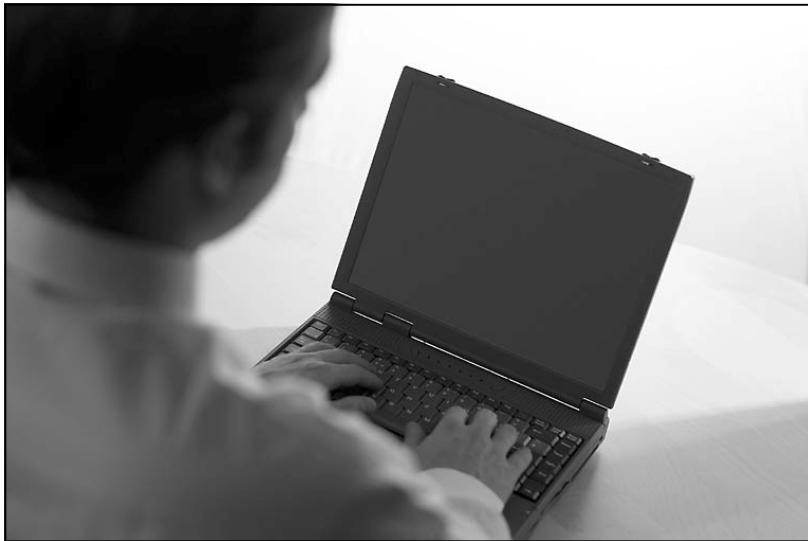
Gary reached out through cyberspace and made contact with many other c-Kit positive LMS patients in the summer and fall of 2000. "The first I found were Joyce and Jeff Prichard, and Norman and Anita Scherzer," Gary said. Later he met Jerry and Stephanie Call, Mia and Michael Byrne, Marina Symcox and Trudy Webb. "Trudy was the first from the OHSU," Gary recalled. To spread the word about STI571, Gary, Trudy and Norman began coordinating efforts. "The three of us worked together to try to figure out what was going on. I started a 'group e-mail' list to keep everyone informed of what was happening.

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

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

forward to grasp the reins and get many of our current volunteers to take up their positions."

Gary and I jointly put out the third newsletter in January 2001, then Gary resigned to focus on Mary's care. He remained aboard the Life Raft, organizing the groups first gathering held May



3-4, 2002, in Boston. A high point of the gathering was a speech by Dr. Dan Vasella, president and CEO of Novartis, the company that developed STI571, now marketed as Gleevec. Sadly, Gary hosted the gathering without his bride of 27 years. Mary, 50, had died two weeks earlier.

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

I share this bit of history as I write the end of my own chapter as newsletter editor. I need to thank the dozens of Life Rafterers who've willingly shared their stories in the hope of encouraging others. I've spent one weekend a month hunkered over the computer, assembling the parts into a hopefully cohesive whole. It's no great sacrifice when

Hilo's torrential rain is falling, but the newsletter is burdensome when the tropical sun is shining and the surf is just right for body boarding. And though she's very patient, I know my bride has missed the time we could have spent together. Indeed, her contributions to the newsletter have been considerable. For

the first couple of years, Linda maintained the newsletter mailing list, which grew to more than 500 names. She'd also print and snail-mail dozens of newsletters to computer-challenged Life Rafterers around the U.S. and in Canada, Australia, Iran and China.

For the past several months, the Life Raft staff has taken on more and more newsletter tasks, which I've gladly relinquished. Sara Rubinoff has become

builder of the newsletter, following Norman Scherzer's architecture, while I've merely added the trim and paint.

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

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

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

SISTERS

From Page 8

that he had been researching GIST this whole time. When she began speaking to him she knew he hadn't looked at her file. He told her she looked fine and to return in six months for a CT scan; he didn't know she had not had an initial scan yet. Leigh left the office feeling disheartened and alone, she decided to call her sister, Pam Broadus.

"When she told me what had happened she said, 'We've got to figure out what to do.'" Even though the sisters lived miles away from each other (Pam lives in Virginia while Leigh lives in Illinois), they were partners in this ordeal, and spoke daily. Pam picked up the phone and started making phone calls for her. "We sort of teamed up together to figure out what to do, it's been she and I together."

Pam called Memorial Sloan-Kettering and was referred to Dr. Evens of Northwestern University. She flew out for the first appointment without hesitation. "The first thing [Leigh] said was, 'Do I have cancer?' he said 'Yes, you do' and we went from there. From the minute we got there we thought, 'This is so great', it's just night and day from the

terrible experience she had had before. When you're in good hands you can just breathe a little bit."

Pam is mindful of the twists and turns this GIST path has taken, "It's kind of like a roller coaster, when she was at a low point I kicked in."

One support system for the ladies came when a high school friend of Leigh's told her about her mother being misdiagnosed with GIST, though it could offer no information for her mother, she told Leigh about the Life Raft Group. Leigh wasn't ready for that yet so Pam took the reins, "I decided to be her information line, her conduit to everything."

Besides her family (which includes her husband Barry; son Matthew, 9; daughter Allison, 15 and older daughter Emily, 19) and the LRG, Pam finds additional support at her church, where she is the church secretary.

She also finds enjoyment in reading and spending time with friends. But mostly Pam enjoys spending her time with her kids and talking to her sister, "She's wonderful and like a best friend to me."

She admits that there are times that are difficult, but on one occasion, when she was feeling really down, her pastor told her, "Don't borrow trouble from tomor-

row because today has enough of its own."

"I repeat that to myself whenever I feel overwhelmed. I focus on each day and what I can do that day for her."

Pam is careful in remembering the pastor's words, "I found it important to focus on the present. I really don't worry about 5 or 10 years from now. I just decided that I was not going to entertain terrible thoughts, I would literally take it each day and I was able to do that, but it's hard to do."

Despite this steadfast mantra, "living in the now" is not the only way Pam faces her challenges, "Laughter is what really get us through, my mother, my sister and I laugh all the time, we try to find the humor in everything."

All in all, Pam is optimistic for the future. "I just think that every family and every person is going to have something they have to face, some worse than others, and through our loved ones and organizations like LRG is how we get through it. One thing that amazed me is the connections and the support. It really helps me to see the connection between all of this and how people really pull together—when you do it you can get through it, it makes it bearable."

**Global GIST Network
adds
new
representatives**



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Visit the Global GIST Network
at www.globalgist.org

Roy Barton, 69, battled GIST for five years

Roy Barton Jr., 69, a GIST "slayer" since early 2001 lost his battle with GIST and died on May 15 in his home, surrounded by family. Some of the GISTers out there may remember that Roy was a five-year survivor and that those five years were like a rollercoaster, with his health constantly going up and down. But, as his wife of 48 ½ years, Mary, stated recently, "There are a lot of things people didn't know about Roy."

Roy was a man who appreciated creation and the beauty of life. In his retirement he spent a good deal of time painting in oils. These paintings touched the hearts of those around him. An excellent gardener, Roy built his family a pond in back of their home complete with water lilies, reeds, fiddle leaf plants

and a lotus which he maintained day after day. He was also an excellent cook and worked at various restaurants during his life.

"He could do anything," that's what Mary Barton thought was the best way to describe her husband. If Roy didn't know how to fix or do something, he just read up on it. Everyone in the Barton family would agree that once Roy set his mind to something there was no stopping him.

Roy is survived by his wife, Mary; daughters Loretta Ann Harris and Mary Ellen Barton; sons Roy Eugene Barton III and Steven Barton; his 16 grandchildren and 2 great-grandchildren. A Memorial Service was held on May 24 at Cohasset Neighborhood Church.

June 2006 clinical trial update for GIST patients

By Jerry Call

Sutent

In the United States, Sutent is now available by prescription for patients failing Gleevec or those who can't tolerate Gleevec. In addition, Sutent continues to be available to patients via the "Treatment Use Protocol," which is "four weeks on/two weeks off" (50 mg). There are many sites open throughout the world. Site information changes frequently; for the most current information contact EmergingMed at 1-877-416-6248 (outside the United States) or at 1-800-620-6104 (inside the United States). If international patients have problems with the listed number use email at: sutent@emeringmed.com.

The phase II trial testing Sutent given on a continuous basis has met its accrual goals and is now closed.

AMN107 + Gleevec

This Phase I trial is open for accrual. The U.S. sites are:

- Dr. Demetri in Dana-Farber Cancer Institute in Boston, Massachusetts
- Dr. von Mehren in Fox-Chase Cancer Center in Philadelphia, Pennsylvania.
- International trial sites include:
- Dr. Patrick Schöffski in Leuven, Belgium
- Dr. Jean-Yves Blay in Lyon, France
- Dr. Peter Reichardt in Berlin, Germany
- Dr. Paolo Giovanni Casali in Milan, Italy

The current intention is to evaluate doses as high as 800 mg of AMN107 and 400 mg of Gleevec. A total of about 45 patients are expected to be enrolled in the phase I trial and 200 to 300 patients are expected for the phase II trial. The phase II portion of the trial has a projected start date of mid-September.

The combination of AMN107 and Gleevec may have a broad spectrum of activity against primary and secondary mutations in GIST. The generic name for AMN107 is nilotinib and our understanding is that the brand name will probably be Tasigna.

IPI-504

The IPI-504 phase I trial is open and accruing patients at Dana-Farber. IPI-504 is an inhibitor of Heat Shock Protein 90 (HSP90) and has been the subject of articles in the November 2005 and January 2006 editions of The Life Raft Group newsletter. This is an intravenous drug which is administered twice a week.

RAD001 + Gleevec

Both RAD001 and Gleevec are manufactured by Novartis. RAD001 is an mTOR inhibitor that may improve the effectiveness of Gleevec. This trial is moving into phase II.

The phase II trial will have two strata:

- 1) Patients progressing on Gleevec
- 2) Patients progressing on Sutent (2nd-line).

In the U.S., only the Dana-Farber site (Boston) is open at this time.

The additional sites planned are:

- Dr. Blanke-Oregon Health & Science University- Portland, Oregon
- Dr. Hecht- University of California- Los Angeles- Los Angeles, California
- Dr. Trent- M.D. Anderson- Houston, Texas
- Dr. Taub- Columbia University-New York, New York
- Dr. Von Mehren- Fox Chase Cancer Center- Philadelphia, Pennsylvania

Sites participating/recruiting in Europe are:

- Dr. Patrick Schöffski- Leuven University Hospital- Leuven, Belgium
- Dr. Peter Reichardt- Charité University-Berlin, Germany
- Dr. Marcus Schlemmer- Univ.Klinikum Grossharden- Munich, Germany

We also understand that Dr. Jean-Yves Blay in Lyon, France will participate and that additional sites in Germany (not yet known) are also planned.

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

This drug was approved in December 2005 for kidney cancer. BAY 43-9006 inhibits several kinases including KIT,



CALL

VEGFR-2, VEGFR-3, PDGFR-β, RAF, FLT3, and RET. The phase II trial for BAY 43-9006 is open and recruiting patients. Three trial sites are open in Illinois and one in New York:

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

Sites are pending in the following places:

- Univ. of Southern California/Norris Comprehensive Cancer Center- Los Angeles, California
- City of Hope-Los Angeles, California
- Univ. of California at Davis/Davis Cancer Center- Davis, California
- Central Illinois Heme/Onc Center-Springfield, Illinois
- Univ. of Maryland- Baltimore, Maryland
- Univ. of Michigan- Ann Arbor, Michigan (This site may be delayed more than others)
- Duke University Medical Center-Durham, North Carolina

Highlights from the American Association for Cancer Research meeting

Editor's note: Jerry Call, LRG Science Coordinator, attended the 97th annual meeting of the American Association for Cancer Research (AACR) held March 31 – April 5th in Washington, D.C. This is his report on the sessions that he attended.

By Jerry Call

Abstract # 3008-From the lab of Dr. Jonathan Fletcher (Brigham and Women's Hospital and Harvard Medical School), Meijun Zhu presented a poster on "KIT oncoprotein interactions in GISTs: Therapeutic relevance." Zhu et al. used frozen GIST tumors and GIST cell lines to evaluate KIT signaling mechanisms. They found that PDGFRA existed in a complex with KIT and that the activated KIT protein also activated (through crossphosphorylation) the PDGFRA protein. They concluded that the response of GIST patients to Gleevec likely involves inhibition of both KIT and PDGFRA (Gleevec inhibits both of these proteins). The poster also noted the major contributions of PI3-K and PKC θ (protein kinase C theta), both downstream targets of KIT in GISTs. Inhibition of PI3-K (with

LY294002) or PKC θ (by lentiviral shRNA infection) resulted in either inhibition of growth or cell death in four GIST cell lines. The poster concluded that PI3-K and PKC θ are compelling therapeutic targets that might further improve the GIST therapeutic response to KIT/PDGFRA inhibition.

Note: PI3-K has long been avoided as a drug target because it is commonly expressed in normal cells; thus toxicities are expected to be high. It is one of the major proteins involved in tyrosine kinase receptor signaling. One method for targeting PI3-K inhibition to tumor cells (while avoiding inhibiting it in normal cells) is to make a "prodrug" PI3-K inhibitor. This is a drug that is somehow "activated" by the tumor environment (such as by a different pH level in the tumor).

PKC θ represents an attractive target because it is only rarely expressed in normal cells. A type of immune cell known as "T cells" signals through PKC θ .

Abstract #1328-Prenen et al reported on the cellular uptake of both imatinib (Gleevec) and AMN107 in GIST tumor cells. Several studies have reported that P-glycoprotein (PGP) is a transporter of



The 97th annual American Association for Cancer Research (AACR) meeting was held in Washington, D.C. this year.

imatinib and that high expression of the MDR1 gene (the gene that makes P-glycoprotein) could confer resistance to

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SCHERZER

Thoughts from the Executive Director

By Norman Scherzer

It takes a lot of different people to form an organization like the Life Raft Group. One of the best is Richard Palmer who leaves us as Newsletter Editor this issue. His work over the years needs little documentation and will forever be archived on our website and in the homes and offices of thousands of readers. What may be less obvious is the role he has played behind the scenes as observer, peacemaker and friend. Richard has opened his home and his heart to GIST patients all over the world and has provided all with counsel and good cheer.

On a personal note, Richard has rescued me on a number of occasions when I was about to leap in the wrong direction and I shall forever be grateful for that.

What Richard does not yet know (he will find out from reading this Newsletter) is that our Board of Directors voted in Mexico to make him our volunteer of the year and to present him with an award at our membership meeting in Dallas. Knowing Richard, we may have to carry him to the podium to accept, but we have rounded up a large number of Life Raft Group members who have volunteered to do just that.

Largest West Coast gathering of GIST'ers

Patients, caregivers meet together at OHSU grant presentation

By Richard Palmer

A grant presentation by the GIST Cancer Research Fund (GCRF) to Oregon Health & Science University (OHSU) turned into the largest-ever West Coast gathering of GIST patients and caregivers May 3-4.

Tania and Robert Stutman, early Life Raft Group members who launched the GCRF five years ago, traveled from their New City, New York home to Portland, Ore., to present \$40,000 for GIST research. Rachel Hunsinger, director of development for the OHSU Cancer Institute, graciously arranged for presentations by Drs. Brian Druker, Michael Heinrich, Chris Corless and Charles Blanke, and invited any and all GIST patients and caregivers to attend.

The two-day event began with a question-and-answer session featuring Druker, a key developer of Gleevec who first used the drug to treat patients with chronic myelogenous leukemia. Some

40 patients and caregivers attended his May 3 presentation – which also included birthday cake and ice cream in honor of Druker's birthday.

The following morning, a breakfast at OHSU drew 42 patients and caregivers, plus more than a dozen researchers and lab assistants, along with support staff. Blanke led off with an update on the latest developments in GIST treatment, and then he, Heinrich and Corless fielded questions.

Following the Q&A session, Heinrich and Corless led everyone on a tour of their labs. Prior donations by the GCRF had enabled them to purchase equipment to further their research, and they pointed out the instruments, explaining what it enabled them to do.

Many of the GIST patients and caregivers gathered for dinner Wednesday and Thursday nights, sharing their experiences and forging friendships. They came from all across the United States, from Hawaii to the East Coast.

The OHSU presentation was the fourth by the GCRF this spring. The first grant presentation was held March 29 at Memorial Sloan-Kettering Cancer Center in New York. It was the largest grant, \$45,000, with a sizable portion dedicated

to pediatric GIST research. Among the researchers attending the presentation were Drs. Cristina Antonescu, Peter Besmer, Murray Brennan, David D'Adamo, Ronald DeMatteo and Robert Maki.

On April 5, GCRF presented \$25,000 to doctors at Fox Chase Cancer Center in Philadelphia. Dr. Margaret von Mehren and Andrew Godwin, Ph.D., gave a presentation to the patients and caregivers in attendance.

Next stop was Dana-Farber Cancer Institute in Boston. There, Dr. George Demetri accepted a \$30,000 check from the Stutmans on April 19. In addition, a \$5,000 grant was made to Dr. Anette Duensing at the University of Pittsburgh Cancer Institute for her promising research.

All told, the GIST Cancer Research Fund raised \$147,000 and gave out \$145,000 to GIST researchers this year, the bulk of it raised at the annual Walk for a Cure. This year's walk will be held Sunday, Oct. 15, at Rockland State Park in Congers, New York. For details, see www.gistinfo.org.

Richard Palmer is a GIST patient and former editor of the Life Raft newsletter.

GIST Cancer Research Fund presents check to OHSU



GCRF check to OHSU: Fueling the fight against GIST was \$40,000 given May 4 to the Oregon Health & Science University Cancer Institute. From left are Dr. Michael Heinrich of OHSU's Heinrich & Corless Labs; Dorothy and Brian McBride, coordinators of the pediatric division of the GIST Cancer Research Fund; Robert and Tania Stutman, founders of the GCRF and GIST researcher Dr. Charles Blanke. The check presentation was made at a breakfast attended by the largest-ever West Coast gathering of GIST patients and caregivers.

AACR

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imatinib.

The Belgium scientists reported that imatinib uptake into two GIST cell lines, GIST882 and GIST GDG1, was significantly reduced compared to AMN107. Levels of AMN107 were 3 times higher than imatinib in GIST882 cells and 10 times higher in GIST GDG1 cells. Their findings suggest that AMN107 might be less susceptible to resistance caused by multi-drug resistance proteins.

Editor's note: In a separate paper, White et al. found that AMN107 was also less affected by the influx pump, OCT1. They concluded that OCT-1 influx may be a key determinant of response to imatinib (low expression of OCT-1 may confer resistance), but it is unlikely to affect patient responses to AMN107. The unanswered question is whether it would be more effective to give AMN107 as front-line therapy before resistance developed, or to give it to patients once they become resistant to imatinib.

Abstract #1158-Salto-Tellez et al. from the National University of Singapore, reported that VEGF-A protein is a main biomarker that is able to differentiate low-risk GISTs from high-risk GISTs ($p=0.0003$). The authors concluded that their study showed VEGF-A status is important in the biological understanding (of GISTs), as well as clinical characterization of GISTs, and may point to an alternative and/or complementary treatment strategy to GIST.

Editor's note: VEGF-A is one of at least five different growth factors that are able to activate one or more of the three different VEGF receptors (VEGFR-1, VEGFR-2 and VEGFR-3). VEGF-A is known to activate both VEGFR-1 and VEGFR-2. Many of the newer multi-targeted tyrosine kinase inhibitors, such as Sutent, AMG706, and BAY 43-9006, inhibit two or three of the known VEGF receptors. Thus, drugs that inhibit VEGFR-1 and VEGFR-2 would be expected to inhibit signaling caused by the VEGF-A growth factor. Avastin (Bevacizumab) is another drug that blocks the signaling of VEGFR1 and VEGFR2. Avastin is a monoclonal antibody that is given intravenously and has been shown to improve survival in colon cancer when given together with chemotherapy. A new trial is being planned for GIST patients that will test whether the combination of Gleevec and Avastin will be more effective than Gleevec alone. This trial is expected to start this summer.

Abstract #4038-Yamamoto et al. reported on a multi-targeted kinase inhibitor, E7080. E7080 is made by Eisai CO. LTD, Japan. It was tested in a mouse model that had human GIST tumor cells (GIST882). E7080 inhibits VEGFR-1, VEGFR-2, FGFR1, and PDGFRbeta. All of these targets have been implicated in angiogenesis (the growth of new blood vessels that feed tumors). In addition, it also inhibits KIT

at slightly higher concentrations. E7080 was able to stabilize the GIST tumors in the mice at doses of 30 mg/kg. Doses of 100 mg/kg caused tumor shrinkage of about 40 percent in this mouse model.

Soluble KIT (s-KIT) was also evaluated as a potential biomarker in the mouse model. Normal mice (no GIST) did not have detectable levels of s-KIT. Mice with implanted GIST tumors did have detectable levels of s-KIT which was correlated with tumor weight. Treatment with E7080 clearly reduced levels of s-KIT. The author's conclusions were that E7080 has therapeutic potential via inhibition of KIT in GISTs and s-KIT might be useful as a biomarker in GIST patients.

Editor's note: Three phase I clinical trials for E7080 were listed in the clinicaltrials.gov database. These trials included solid tumors and were located in Amsterdam, Netherlands; Glasgow, United Kingdom; Dallas, Texas (USA) and Tokyo, Japan.

Abstract #1634-Jahn et al. reported that the KIT protein is recruited to lipid rafts at the cell membrane. Inhibition of lipid raft formation prevented KIT-mediated activation of AKT and blocked KIT mediated cellular proliferation, including KIT mutants that were resistant to Gleevec. They hypothesize that inhibition of receptor tyrosine kinase (RTK) recruitment to lipid rafts may be a useful strategy for control of tumors dependent on RTK activity.

Chicago Life Raft chapter focuses on 'positive thinking'

By Dick Kinzig

Area Coordinator for Chicago Chapter

The Chicago Chapter of LRG met for the second time this year on May 21st at The Wellness Place facility. Sixteen GIST'ers and spouses attended: Pam Lewkovich, Jim and Margi Hughes, Stan and Carmen Drab, Ron and Paula Newburger, Paula and

Phil Vettel, Elaine Rys, Lucy Madsen, Nestor and Beth Sanchez, and our newest member, Leigh Borland.

The guest speaker was Dr. Harvey Wolf, Psy.D., CSC, P.C. who previously spoke to our group at our second meeting back in January 2003. He is a health psychologist known for his insight and humor. His topics covered the tyranny of positive thinking, listening & communicating skills when dealing with doctors,

insurance companies, and other cancer patients. Other issues included stress, anger management, and the role of the caregiver, which is often overlooked.

The social hour was thoroughly enjoyed by all and it provided ample opportunity to get to further discuss issues with the members.

The group voted to hold the next meeting in September following the 2006 Life Fest meeting.

Life Raft Board of Directors meet in Monterrey, Mexico



Board Members meet for dinner (pictured from left to right): Rodrigo Salas, Robert Book, Stan Bunn, & Jerry Cudzil.

TRIAL UPDATE

From Page 11

- University of Pittsburgh Cancer Institute- Pittsburgh, Pennsylvania
- Medical College of Wisconsin- Milwaukee, Wisconsin

Genasense + Gleevec

A phase II trial testing the combination of Genasense plus Gleevec in patients with Gleevec-resistant GIST recently opened. Genasense (Genta Inc.) is an antisense drug that inhibits bcl-2. Bcl-2 is a protein involved in cellular survival. This drug is administered intravenously. It is hoped that Genasense may help Gleevec kill tumor cells by making them more sensitive to Gleevec.

This trial is currently open only at M.D. Anderson. Several other trial sites are planned including: Dana-Farber Cancer Institute, Boston, Mass.; University of Michigan Comprehensive Cancer

Center, Ann Arbor, Michigan; Mayo Clinic Cancer Center, Rochester, Minnesota; and Memorial Sloan-Kettering Cancer Center, New York, New York.

Perifosine + Gleevec

Perifosine is an oral drug that inhibits the AKT protein. AKT is an antiapoptosis protein. It is speculated that inhibition of AKT might enhance therapy. Apoptosis is a form of controlled cell death, a type of cellular suicide where the cell issues its own death warrant. The phase II trial, which combines Perifosine with Gleevec is open at M.D. Anderson Cancer Center and accruing Gleevec-resistant GIST patients.

BMS-354825 (Desatinib)

BMS-354825 is a tyrosine kinase inhibitor of Src, abl, KIT, and PDGFR. We understand that this trial may expand to phase II soon. We will update trial sites and the scope of the trial as this information becomes available.

PTK787/ZK222584

This is a phase II study being conducted at the University of Helsinki in

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

Glivec

Also recently added to the ClinicalTrials.gov database is a trial called "Open-Label Trial of Glivec With Unresectable or Metastatic Malignant Gastrointestinal Stromal Tumors." This study has been designed to gain more experience with the treatment of GIST in several Central and Eastern European Countries. The rationale is to assess the clinical and biological activity of Imatinib and to compare the data with historic data. This trial includes sites within the following countries:

Austria, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Lithuania, Romania, Serbia and Montenegro, Slovakia and Slovenia.

Further information can be found at the ClinicalTrials.gov website.

THE LIFE RAFT GROUP

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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:

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