

# Israeli GIST Group brings GIST clinical trial to Israel

By Ben Shtang  
President of the Israeli GIST Support Group

On one sunny Friday morning in the spring of 2001, everything looked as the beginning of an especially happy weekend. I was jogging along the white sandy beach in Tel Aviv. The sea was blue and smooth like glass. Seagulls calmly flew over the water. The morning breeze was about to begin to wrinkle the surface of the water.

What's nicer than this nature scene?

But my head was busy with the masquerade ball I was experiencing that



night. Even stomach pains did not disturb the masks and the dances. Oh, how I love to dance! I was dreaming I was at a party surrounded by people wearing light green costumes, with masks to hide their faces. Music was playing, but nobody was dancing and everybody seemed serious and concerned.

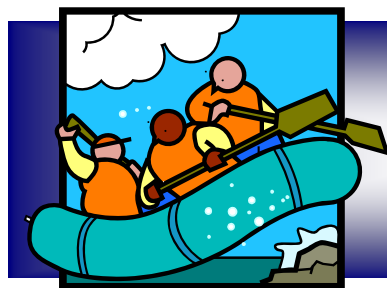
However, this was no dream. The people around me were doctors and nurses in the intensive care unit. The music was in fact the monitors beeping.

"You are hit with GIST," said one of the doctors in army slang. I felt a shock and loss of control.

Now, I am at war with GIST. In war, there are casualties, and the first thing a commander should do is to look for the

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Battling gastrointestinal stromal tumor



## LIFE RAFT GROUP

September 2006

In memory of Henrietta Olsen

Vol. 7, No. 8

# GIST patients and experts head to Dallas for Life Fest

By Norman J. Scherzer  
LRG Executive Director

GIST patients and experts from New York to Hawaii and from points as far away as France, Mexico, Belgium, Poland, Brazil and Switzerland are all heading to Dallas, Texas to attend the Life Fest 2006 meeting from September 15-17.

Fast forward to the afternoon of September 15<sup>th</sup>. Planes are arriving at Dallas International Airport from all over the United States and the world. The reception table at the Adams Mark Hotel is

open to greet early arrivals. The new Life Raft Group tee shirts are stacked up next to the Life Raft Group pins, meeting agendas and educational materials. Staff and volunteers are there to greet and hug each and every person. More and more Life Rafter and invited guests are gathering and checking each other's name tags and connecting internet names with real faces. Internet friends are coming to life.

That morning, the Life Raft Group Research Team just put together its first update report on its search for a cure for GIST. Our Board of Directors met to

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LRG members register at Life Fest 2004 in Orlando. The atmosphere was full of excitement as members introduced themselves to their internet companions.

# Walking the GIST Trail again

By Jim Mills  
Life Raft member

**M**any years ago I learned that all great stories begin with “And there I was!” Any tale that begins this way must be an entertaining account that includes adventure, danger, suspense and finally, a great ending! With those elements in mind, I would like to relate my experience with GIST on a remote hiking trail.

And there I was, in late May 2004 on a 43-mile backpacking trip of the Pictured Rocks National Lakeshore trail along Lake Superior in Michigan’s Upper Peninsula. The trail starts out with 23 miles of easy walking in forests and on sandy bluffs next to the water. Then it climbs steeply for the final 20 miles section along the edge of cliffs that drop 100 to 200 feet straight down into the cold, blue waters of the lake. At the time of this trip I was a fit, forty-six year old with my only significant physical complaint being painful joints from past injuries that I accumulated during past adventures. Although I was hiking alone, the only significant concern on my mind was preventing sore feet.

When I stepped onto the trail late on a Friday morning, everything seemed to be ideal! By Saturday afternoon I had walked 23 miles and the weather was clear enough that night that I slept out in the open amongst the ferns, listening to the waves roll in and looking at more stars than I’d ever seen. On Sunday morning I awoke to find a beautiful rainbow hanging over Lake Superior while two loons fed on placid waters below me. As I sat and enjoyed the view from a high bluff, a bald eagle flew past with the morning sunlight glistening off its pristine, white head plumage. It was less than 30 feet in front of me with the rainbow behind! This was an indescribably perfect moment and I remember thinking to myself that no matter what happened, this brief view had made the trip completely worthwhile. In retrospect,

those moments on the bluff represented a peak in my life as GIST was about to make its introduction.

As I started out that day the trail quickly climbed onto the cliffs. Walking became rougher as there were quite a few trees lying across my path and I had to bypass, or climb over them with a 40 pound pack on my back. Shortly before noon I began to feel a discomfort in my abdomen and as I walked along it slowly grew more noticeable. It felt as if I had taken a blow to my stomach so I decided that I must have injured myself while rolling over a tree trunk. I have a rather high tolerance for pain, but by the time I reached my intended campsite for the day I realized that something was unusually wrong with me.

Thus I decided to keep walking until I reached a place where I could get help if it became necessary. By late afternoon I reached a park visitor center, but after some contemplation, decided that the discomfort was not too severe, and after so much planning and effort I really wanted to finish the entire trail. The final seven miles were a miserable, uncomfortable experience and by the time I walked out of the woods my feet were well blistered and I was holding my right hand over my abdomen. I had walked about 20 miles that day and they were not enjoyable. From start to finish, I had completed the entire 43 mile course in just less than 56 hours.

I did not go to a doctor then, or all summer long as I convinced myself that the pain would go away. But it did not go away, and I was a health & fitness fanatic in serious denial. I said to myself, “This wasn’t anything exercise and diet couldn’t overcome!”

After an especially bad day in late September it finally hit me that I was really ill, and then I told my wife Sabine about it for the first time. The next day our surprised family doctor immediately sent me for my very first CT scan. Thus began a rapid journey through increasingly specialized doctors, and tests to evaluate

## The Life Raft Group

Who are we, what do we do?

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

### How to join

GIST patients and their caregivers may apply for membership free of charge at the Life Raft Group’s Web site, [www.liferaftgroup.org](http://www.liferaftgroup.org) or by contacting our office directly.

### Privacy

Privacy is of paramount concern, and we try to err on the side of privacy. We do not send information that might be considered private to anyone outside the group, including medical professionals. However, this newsletter serves as an outreach and is widely distributed. Hence, all articles are edited to maintain the anonymity of members unless they have granted publication of more information.

### How to help

Donations to The Life Raft Group, incorporated in New Jersey, U.S.A., as a 501(c)(3) nonprofit organization, are tax deductible in the United States.

Donations, payable to The Life Raft Group, should be mailed to:

The Life Raft Group  
40 Galesi Dr., Suite 19  
Wayne, NJ 07470

### Disclaimer

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

# GIST studies receive substantial interest at ASCO '06 conference

By Jerry Call

The American Society of Clinical Oncology (ASCO) website has a large body of information about GIST. This year over thirty reports were added to their GIST database. For a comprehensive look at all of this information, visit the abstracts section of the ASCO website ([www.asco.org](http://www.asco.org)). All of the presentations, videos and slides from ASCO are available for general viewing as of mid-August.

The following are a few noteworthy studies that were discussed at ASCO.

## AMN107

A report of early results of the phase I trial of AMN107 (nilotinib) in combination with Gleevec (imatinib) was presented in a poster by Dr. Peter Reichardt and colleagues. As of February 1, 2006, 37 patients had enrolled in the trial. Follow-up time is short in this trial so the results should be interpreted with caution; 27 patients (73%), achieved some period of stable disease (14 on AMN107 only and 13 on AMN107 plus Gleevec).

Side effects were similar to Gleevec, but elevated liver enzymes were somewhat more common. At the highest doses of Gleevec and AMN107, skin



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toxicity was the dose-limiting toxicity (side effects during treatment were severe enough to prevent further increase in dosage or strength of treatment). A dose of 800 mg of AMN107 and 800 mg of Gleevec produced excessive skin toxicity; 400 mg of AMN107 and 800 mg of Gleevec was well tolerated according to the poster.

## Measurements of GIST treatment response

1. The inadequacy of RECIST (Response Evaluation Criteria in Solid Tumors), the current standard of response measurement, has been known for several years, especially when measuring GIST responses. RECIST measures the efficacy of a treatment by assessing the change in the longest dimension of a tumor(s) size. A patient with greater than a 30 percent reduction in the sum of all target tumors is said to have a “partial response.”

Studying a different form of measurement criteria, Dr. Robert Benjamin from M.D. Anderson Cancer Center gave a presentation supporting the use of response criteria developed at M.D. Anderson, the Choi criteria (named for Dr. Haesun Choi). The Choi criteria classifies responders as patients that achieve either a 10 percent or greater reduction in tumor volume OR a 15 percent or greater reduction in tumor density. These criteria are highly correlated with response by both PET scans and patient history (follow-up). Dr. Benjamin then went on to make a case that RECIST is not only inadequate for GIST, it is inadequate for all solid tumors.

2. Dr. Alex Le Cesne from the Institute Gustave-Roussy in France gave another presentation on measuring response in GIST. Dr. Le Cesne concluded that RECIST could correctly identify non-responding patients, but not patients likely to respond. The study by Le Cesne and his EORTC (European Organization for Research and Treatment of Cancer)



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colleagues used the change in tumor size to predict response, but unlike the M.D. Anderson study, they did not use changes in tumor density.

The Le Cesne study used change in tumor size at 2 months, 4 months and 6 months to predict response. In agreement with the M.D. Anderson study, they found that a reduction in size of greater than 10 percent at any time point (2, 4, or 6 months) predicted patients that were likely to receive the greatest benefit. They classified these patients as responders.

Patients with less than a 10 percent reduction and no more than a 20 percent increase were defined as patients with an intermediate sensitivity to treatment only at the 2-month and 4-month treatment points. Patients falling into this size reduction category (less than 10 percent reduction and no more than a 20 percent increase) at the 6-month treatment point, did just as well as those in the “responder” category. Patients having

## Corless: mountain climber during ‘off’ and ‘on’ peak time

By Elizabeth Braun

**D**r. Christopher Corless climbs mountains on his spare time as well as at work. When not focusing a microscope, he enjoys spending time with his wife, Linda Musil, Ph.D., on the peaks of local mountains. Dr. Corless and his wife have been together for 25 years and married for 18 years. When not hiking across a glacier, they often spend time rock climbing. Initially a hiker, his need for new challenges led him from being a scrambler to a rock climber to a mountaineer. Most of his trips are weekend trips in the local mountains. He and his wife are planning on visiting Mount Rainier for a second trip later this summer.

His interest in research was sparked in high school. Since the summer of 1979, while he was a student at the University of California, Berkley, he has worked in research labs. In 1981, Dr. Corless moved on to Washington University in St. Louis and enrolled in the Medical Scientist Training Program, a dual M.D./Ph.D. program. His residency training was in anatomic pathology at Brigham and Women’s Hospital in Boston, Massachusetts. He also completed a fellowship in gastrointestinal pathology there. Following a year and a half on staff at Brigham and Women’s, Dr. Corless moved to Oregon Health and Science University (OHSU) in 1994, and has remained there since. Now a full professor of pathology, he serves as medical director for surgical pathology and also as director of the Cancer Pathology Core Laboratory for the OHSU Cancer Institute.

Although Dr. Corless’ primary interest was in research, he decided to go to medical school to broaden his education and skills. He chose pathology because it would allow him both clinical and research opportunities. He felt that concentrating on a small and specific area of expertise would not be as interesting, exciting or challenging.

Even before imatinib, Dr. Corless had a strong interest in GIST. He wanted to know more about what GIST was and how it could be diagnosed. In the early 90’s, once some of the basic research on GIST became public knowledge, it was natural for him to become more deeply involved in GIST research.

In 1998, Dr. Corless helped OHSU establish a new core facility for handling tissue samples of all types. He was spending much of his time on microscope work when he was approached by Dr. Michael Heinrich about expanding his research on GIST. Since then, Dr. Corless and Dr. Heinrich have worked on GIST as a team. Although both researchers have other separate projects, they share lab space, equipment and personnel.

Dr. Corless has many other interests besides GIST. His work covers a broad spectrum of diseases due to both his interests and the interests of his colleagues. He wants to understand “how all things tick.” In relation to GIST, his current particular interest is mutational testing and how to make the test more widely available, and more cost effective. Mutational testing will allow pa-



Dr. Corless and his wife, Linda Musil, Ph.D., hiked up 14,410 feet to the top of Mount Rainier in Washington in July 2006.

tients to select medications, procedures and trials in a more controlled and educated pattern.

One of the most important lessons that Dr. Corless has learned in 25 years of research is to expect the unexpected. No matter how carefully plans are made, research is inherently chaotic. The results you expect and need are not necessarily the results you get. Instead, researchers must always keep their eyes open for new and unexpected opportunities and take advantage of them as they arise. In other words, research may not always yield the results that we want but it does stimulate new growth and areas to explore. It is more like the stock market than the grocery market.

## ASCO

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greater than a 20 percent increase in tumor size had poor responses to treatment. This is the only category correctly predicted by the current standard, RECIST.

3. When examining PET scans, Dr. Chandrajit P. Raut and colleagues at Dana-Farber Cancer Institute reported on the patterns of PET response after long-term treatment with Sutent. PET “rebound” (which is higher PET activity) has previously been reported to occur in the two week “off-period” of Sutent treatment. Dana-Farber followed 4 patients for over 2 years on Sutent. Initially all 4 had good PET responses with PET rebound during the off treatment cycle. After 6 months of treatment, all 4 patients had complete suppression of PET activity during both the on treatment cycle and the off treatment cycle. After more than 2 years of treatment, some GIST lesions in two of the patients demonstrated PET rebound during the off period but suppression during the on period. The other two patients did not experience PET rebound, even during the off treatment period. None of the four patients had progressive disease.

### Familial GIST

Dr. Eric Kleinbaum and colleagues from M.D. Anderson presented a poster about a family with familial GIST. This family had 15 members with confirmed or suspected GIST. A germ-line mutation, a deletion of codon 579 in exon 11 of the c-kit gene, was found in this family. This makes at least two familial GIST families with this mutation (out of the 10 to 15 known familial GIST families). A deletion of codon 579 is fairly rare in the non-familial GIST population, occurring in about 2 percent of analyzed patients in the phase II and EORTC phase III trials.

### Creatine Kinase Increase

Dr. Paolo Allione gave a presentation about the increase in creatine kinase and its correlation with musculoskeletal complaints in GIST patients taking imatinib. These complaints are common in GIST patients affecting 25 to 50 per-

cent of patients. Calcium and magnesium supplements have occasionally provided some relief. Quinine is an alternative option, but side effects can limit its use according to Allione.

An increase in creatine kinase value occurs during muscle damage. Even a single muscle cramp can cause an increase in creatine kinase (CK) values. Allione and colleagues found that a great majority of patients experiencing musculoskeletal complaints had elevated CK levels. They suggested consideration of testing CK levels into standard clinical chemistry workup; this allows clinicians to add an objective measure of musculoskeletal complaints. The authors note that they had to stop imatinib for one week only in one patient (out of 40 treated) for uncontrolled musculoskeletal complaints.

### GIST reGISTry

Dr. Jonathan Trent and colleagues presented a poster about the GIST reGISTry. This database is designed to provide information on epidemiology, patterns of diagnosis and management of GIST. Since January 2005, 228 patients have been enrolled.

In summary, Trent reported:

- Most of the patients in this study presented localized disease (78.5%).
- Surgery was first-line treatment in 84 percent of these cases and in 55 percent of patients with metastatic disease.
- Almost 80 percent of patients had a surgical biopsy, 14 percent had an endoscopic biopsy and 10 percent had a biopsy done by interventional radiology.
- CT scans were the most popular type of imaging (60%), followed by endoscopy (19%), PET scans (3%) and CT/PET (2%).
- Patients were twice as likely (66% vs. 34%) to be treated by a community-based practice than at a university or academic center.
- While 92.5 percent of patients had testing for c-kit (CD117), only 3.5 percent had genotype testing (mutational analysis).
- Gleevec treatment doses were:
  - 400 mg/day = 71.8%
  - 600 mg/day = 15.5%
  - 800 mg/day = 6.8%
  - Other = 5.8%

## ISRAELI GROUP

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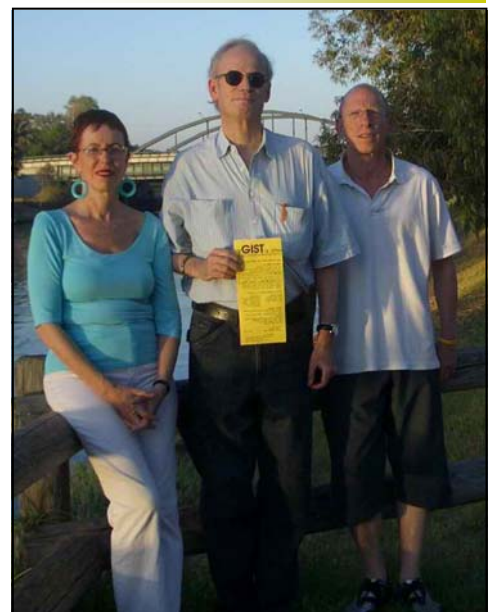
wounded and unify them to help build support and high morale. Most importantly, it is best to use experts and the most efficient weapons (Gleevec), as well as updated intelligence on the enemy and on future weapons (medicines). All of this is important in order to be ready for the next battle.

This framework helped start the Israeli GIST Support Group.

An important weapon in our battle against GIST is high morale. Depression, helplessness and despair are partners with the enemy. For us as patients, high morale can be translated into support, optimism and the strong will to survive. The result is an increasing capability to cope with suffering, pain and side effects, and to improve our quality of life and our life expectancy.

Professor Shulamit Kreitler, head of the Psycho-Oncology Department of Ichilov Hospital in Tel Aviv, conducts workshops that stimulate patients to use their mental strength coupled with personal treatments for healing. I have witnessed depressed patients and their fami-

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From left to right: Varda Chechic, Ben Shtang, and Reuben Chalphi are excited about the formation of the new Israeli GIST Group and new brochure.

# Cancer patient credits experiments for survival

## State worker tests treatment, outlasts doctors' predictions

**By Keri Brenner**

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*The Olympian*

**O**lympia, Wash. (July 31)—In a five-year quest to find the silver bullet drug for his rare cancer, an Olympia man and others like him are becoming test cases for a new way of treating all cancers that targets mutations in the tumor cells' genes, researchers said.

The man, Marcel Szyszkowski, 51, an engineer for the state Department of Ecology, has cancer in the connective tissue of his gastrointestinal tract—a cancer called GIST, or gastrointestinal stromal tumor. Told in 2001 that he had less than a year to live, Szyszkowski—and other GIST patients—are surviving using experimental drugs that target specific sites, known as exons, inside the tumor cells' genes. The targeted approach is seen as less harmful than traditional chemotherapy, which blankets the entire body with strong drugs, killing some healthy cells and causing hair loss and other side effects.

"This is working—it has stabilized my disease," Szyszkowski said of the experimental drug AMN107 he started this year as part of a clinical trial. "This is victory."

In the past few years, researchers at Oregon Health Sciences University in Portland have discovered how to test the GIST tumor cells' genes to see which mutation sites would be receptive to the main GIST drug, Gleevec.

"The approach of analyzing an individual's tumors for mutation testing, and then choosing the drug that matches, may not be a universal approach," said OHSU pathologist Dr. Christopher Cor-

less, who created the testing along with an oncologist there, Dr. Michael Heinrich. "But in some cases, it clearly is the best approach, and I think we'll see more cases down the road."

Gleevec worked for Szyszkowski for a few years, but then his cancer became resistant to it and started growing again.

Corless, who is affiliated with the OHSU Cancer Institute, said he is working on mutational testing for other GIST drugs—such as Szyszkowski's AMN107. Corless said he uses samples of the cancer cells that become resistant to develop new drugs and treatments. He said the future could hold a range of similar testing for other cancers, such as a subset of lung cancer now being studied at Massachusetts General Hospital Cancer Center.

"For some patients, it's a miracle," Corless said. "But it's not a cure-all—we're just managing the disease."

People such as Szyszkowski are leading the way, said Norman Scherzer, executive director of Life Raft Group, a Wayne, N.J.-based worldwide support group for GIST sufferers.

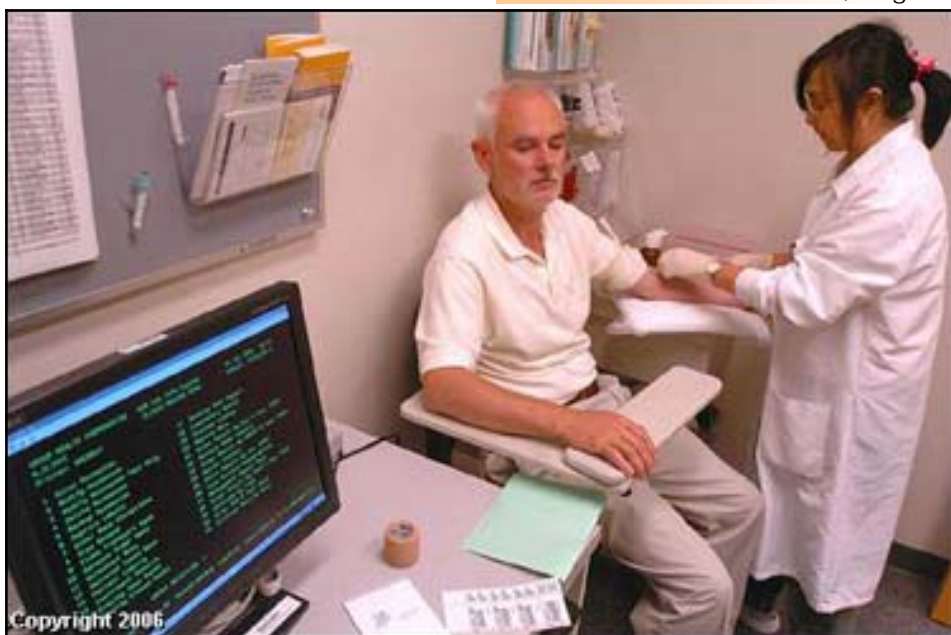
Only five years ago, GIST was thought to be the deadliest cancer, with no known cure or treatment, Scherzer said. Now, it has become a blueprint for mapping cancer gene mutations.

"This is a whole new world in understanding genetic markers and relating them to specific treatments," said Scherzer, whose wife has GIST. "This is the way all diseases will be treated in this century."

Mutational testing for GIST costs between \$700 and \$1,100 and takes up to three weeks. It's not as expensive as cancer drugs, which cost in the tens of thousands of dollars a year, but it's time-consuming and not yet routinely done. Only three research hospitals in the nation—OHSU, M.D. Anderson Cancer Center in Houston and a hospital in Salt Lake City—are doing mutational testing, Corless said.

"Cancer is really a collection of different things that go wrong," Scherzer said of the promise of mutational testing. "If you can find out what's wrong, you can fix it."

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Nenita Apostol, a laboratory assistant at Memorial Clinic, draws blood from Marcel Szyszkowski to test how his body is responding the experimental drug he is taking to treat his rare form of intestinal cancer. "Five years ago they told me I had one year to live. I did not believe them," Szyszkowski said. "And I was right."

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He likens traditional chemotherapy to “having a fly on your chest and smacking it blindly with a 2-by-4.”

“You keep smacking and trying to hit it, and in the process, you may hit it, but you also do a lot of damage to your body,” he said.

Scherzer points to Szyszkowski as an example of how the Internet and expanding communications are helping cancer patients find new treatment methods even before those drugs are released.

“If you’re waiting for the gurus of the world to come to a consensus and finish their research, it takes too long,” Scherzer said. “It’s the difference between life and death - finding the right drug can save a person’s life.”

For Szyszkowski, the necessity of doing his own research hit him early on. His first test for cancer came up negative, and doctors told him to go home and rest. He insisted right away on a

second test, and they found GIST, which is not detectable with a simple blood test.

“For the first time, I realized, ‘You’ve got to take it in your own hands—they’re too busy,’” Szyszkowski said.

Thus began an odyssey that has led to two surgeries, three experimental drugs, cross-country hospital visits, Internet research and, finally, connecting with the Life Raft Group, which publishes a newsletter listing all of the cutting-edge research developments with GIST.

The online connection was important to Szyszkowski, because just 5,000 to 10,000 people nationwide develop GIST annually, compared with an estimated 1.3 million people who contract all forms of cancer.

He doesn’t know of anyone else in Olympia with GIST, but there might be some fellow sufferers in the Seattle area, he said.

Szyszkowski, who is married and who, with his wife, has a blended family of four children, said the journey has made him fearless, including not fearing death.

“I’m willing to put everything, including my life, on the table,” he said. “I’m willing to risk a lot to try to achieve something.”

### What is GIST?

GIST is a rare type of cancer in the connective tissues, bones or muscles of the gastrointestinal tract. GIST stands for gastrointestinal stromal tumor.

What is an exon?

Exons are sites in genes of cancer tumor cells where mutations occur. Certain drugs, such as Gleevec, are used to target specific exons that are receptive to those drugs.

### On the Web

Life Raft Group (for GIST sufferers):  
[www.liferaftgroup.org](http://www.liferaftgroup.org)

OHSU gene mutation research:  
[www.heinrich-corless.net](http://www.heinrich-corless.net)

Reports on genetic discoveries in medicine:  
[www.personalizedmedicinecoalition.org](http://www.personalizedmedicinecoalition.org)

*Keri Brenner covers Thurston County and Tumwater for The Olympian. She can be reached at 360-754-5435 or [kbrenner@theolympian.com](mailto:kbrenner@theolympian.com).*

## LIFE FEST

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review all of the details of the meeting to make sure that everything is in its place.

Six o’clock in the evening arrives as everyone gathers for the opening reception. Richard Palmer, our volunteer of the year honoree, is there in his Hawaiian shirt. Dr. Jonathan Fletcher, our scientist of the year honoree, is standing next to him in his Dana-Farber best. Kerry Hammett and her Texas volunteer team have their western hospitality handshakes ready. A cluster of pediatric GIST families are in one corner of the room meeting David Epstein, the President of Novartis Oncology. In another corner are the clinicians, oncology nurses, nutritionists, surgeons, pathologists and researchers from M.D. Anderson, Stanford University, Oregon Health and Science University, Dana-Farber Cancer Institute, Fox Chase Cancer Center, Memorial Sloan-Kettering Cancer Center, the University of Washington,

the Cleveland Clinic, the Texas Children’s Cancer Center and the Catholic University of Leuven, Belgium. Clusters of patients and caregivers are scattered throughout the room.

A little buzz goes through the room. Dr. Daniel Vasella, the Chief Executive Officer of Novartis, has just arrived. He heads over to a group of GIST patients and caregivers and recognizes Anita Scherzer. “Anita, how are you,” he exclaims in his polished Swiss accent. Dinner is served. Awards are presented. Vasella gives his keynote address. Some of the Life Raft Group pediatric kids make a special presentation. Desert. Time to leave but most just mingle. A few folks head to the bar. It is Friday evening and we have just begun.

Saturday morning: breakfast is served. The LRG Research Team is in another room with David Epstein getting ready for their presentation. The program is

about to begin. Stan Bunn, our LRG Board President, formally welcomes everyone. The LRG Executive Director reports on what the Life Raft Group is doing to help patients survive. The Research Team reports on its efforts. There is a medical update on GIST treatment and management. A seminar is given on GIST survival issues. Another is presented on pediatric GIST. Another one is given on treatment compliance. A second major address is presented at lunch by David Epstein.

There will be more than enough workshops to attend.

Saturday’s program ends with a special candle ceremony. Folks head to dinner around Dallas, many guided by members of the Texas Life Raft Group.

Sunday arrives: breakfast is served. Sessions and workshops continue. The pediatric GIST kids are back with a presentation.

And we adjourn. It’s time to say goodbye. Warm embraces. Hugs. Time to hit Dallas again before we all leave for home.

## ISRAELI GROUP

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lies reach out to Professor Kreitler and become optimistic and full of energy.

The Israeli GIST Support Group is small but united. This allows a personal touch to the group, allowing for members to develop close relationships. I try to work with each new patient that joins the group, building up their morale and identifying the quality of family support he or she is receiving. My first priority is to provide encouragement and then I direct them to expert medical professionals.

My main objective is to increase membership in our group to at least 100 out of the 250 reported cases of GIST in Israel. Our goal is to bring new clinical trials to Israel. Even though medical science in Israel is as developed and advanced as top western countries, most GIST clinical trials have not reached Israel. We would like to see equal opportunities for clinical trials in Israel just as it is presented in the United States and Europe.

One of our group's top achievements was bringing the Sutent clinical trial to Israel in 2005. I identified several patients that needed a second-line weapon due to Glivec resistance. The continuous follow-up with new medicines that were in trials showed that Sutent was nearing the finished line with significant results. Being the Israeli patient representative, I addressed the pharmaceutical companies and expert GIST doctors in order to bring Sutent to Israel. It was a tough course with lots of bureaucratic difficulties (especially since it was involving a rare form of cancer like GIST).

After a year and a half of intensive actions, we were able to launch the first

Sutent clinical trial in Israel. The final push for opening the trial in Israel was given by Professor Gabi Barabasch, director of Ichilov Hospital in Tel Aviv.

However, there was a feeling that there were patients that did not know anything about the trial. I emotionally addressed the directors of all oncology departments in hospitals across Israel, both verbally and in writing. Within two weeks, the



Professor Ofer Merimsky consults GIST patients at Ichilov Hospital in Tel Aviv.

number of participants in the trial doubled in size.

Among the patients who joined was a man by the name of Dima. He was a 30 year old new immigrant to Israel without family or relatives. During 2005 his condition was very serious. When I first met him he was desperate to get any kind of treatment. His bilirubin was high and the doctors said that he did not "fit" the clinical trial criteria.

I decided to coach and guide him with long hours of persistent conversations. Together with the new hope that the trial brought, his morale gradually improved. I took him to GIST specialists and, with his last strength, and lots of hope and willpower, he reached the Sutent trial.

The trial began with great excitement

in February 2006. As weeks went by, Dima's condition improved. Many other patients benefited from the trial as well.

Special thanks goes to Professor Barabasch, Professor Ofer Merimsky, a GIST specialist in Israel, and Dr. Arie Figer, head of the Sutent trial in Israel, all from Ichilov Hospital in Tel Aviv; Professor Aderka from Sheba Hospital; Dr. Peter Reichardt from Berlin, Germany; and

Dr. George Demetri from Dana-Farber Cancer Institute. A very special thank you to Norman Scherzer, executive director of the Life Raft Group. Professor Karen Nalbandyan, assistant researcher, Professor Figer, and Professor Merimsky worked vigorously with patients. The cooperation among them all was truly exceptional.

On behalf of all the Israeli GIST

patients, we are deeply grateful from the bottom of our hearts for the collaboration among all the doctors to get the Sutent clinical trial to Israel. We hope that the thousands of scientists and researchers that work frantically to find and design new weapons for us will soon encounter success. We especially hope to hear of successful results from the Life Raft Research Team.

*While writing these lines we already experience a new battle. Patients expelled from the Sutent trial (including myself) are urgently seeking the next weapon to fight our enemy. In order to improve my morale, my life companion and I go out to dance. As the LRG director Norman Scherzer says, "No more Last Dances."*



# Tap helps start sarcoma program at UCLA

By Erin Kristoff

**D**r. William Tap feels that oncology patients are the “most rewarding group of patients” that he has found, especially GIST patients and he’s not afraid to say it, “GIST patients are wonderful in that they are extremely active and extremely educated.” Dr. Tap first discovered these wonderful patients through Dr. Peter Rosen, who saw a large amount of GIST patients at the University of California-Los Angeles (UCLA). At a CTOS (Connective Tissue Oncology Society) meeting he talked to other GIST experts from around the country and furthered his knowledge about the rare cancer. He came to believe that it is because of GIST that we are making great strides in the drug development and research area of cancer.

Tap received his undergraduate degree from Bucknell University in 1992, from there he went on to do doctoral work at Columbia University. He spent two years at the New York University Medical Center, one year at Rockefeller University, and then at Jefferson Medical College where he received his medical doctorate. Dr. Tap went on to Vanderbilt University where he completed his internship and residency in internal medicine before he finally went to UCLA to do his fellowship in hematology/oncology.

Tap wanted to become a doctor even when he was young, “I really enjoyed being with people; it’s something that drew me to the field, the relationships.” While Tap was heavily interested in science, no other field seemed to suit him, “I just didn’t find the excitement in the business or engineering world. I went back to the people.”

While oncology is Dr. Tap’s great love, he is also interested in third world medicine, “Wherever you find an opportunity in another area of tremendous need a little involvement goes a long way.” While doing his residency at Vanderbilt he flew down to the jungles of

Guyana in South America to immunize locals and educate them on the dangers of HIV/AIDS. While there, he was thrown into a harrowing predicament when a local pilot tried to fly a woman in labor to the closest hospital, Dr. Tap was forced to deliver the baby from 10,000 feet in the air.

However, when he went to do his fellowship, it was sarcoma patients that he wanted to help. Currently, he is trying to build up the sarcoma program at UCLA and designate it as a translational program. “We have some of the best surgeons when it comes to sarcoma.”

Because of this, UCLA became a referral center which prompted Tap to sit down with Dr. Rosen, Dr. John Gaspy and Dr. Frederick Eilber to discuss the sarcoma program, “It’s been one of the most amazing learning processes of my career.”

“I want to let people in Southern California know that we are working hard on this program for them.” Patients with GIST will be a large focus of the translational sarcoma program. Besides the clinic, Tap and his colleagues have also developed an active laboratory that will be researching GIST/sarcoma. “This is in conjunction with Dr. Dennis Slamon, a physician and scientist who has helped revolutionize how we treat patients with cancer. Dennis has committed a significant amount of his resources



Dr. William Tap is a GIST specialist that works at UCLA.

to help build up the laboratory aspect of the sarcoma program.”

Tap also hopes to offer comprehensive care in the next few years, “It stems down to providing them with best care possible. It includes the biopsychosocial complete care of patients, concentrating on what the disease is doing to patients from all these standpoints, the biological, psychological and the social.”

Dr. Tap also looks forward to developing the type of relationships that patient groups have with their members, “The Life Raft Group is like ‘big brother’ in their corner.” He believes that patient groups aid in the communication between the patients and their doctors. “It’s really helpful for us; the goal here is to make the process of being a patient as easy as can be, we don’t want barriers.”

If any GIST patients are interested in contacting Dr. Tap as a specialist, he can be reached at 310-794-4955.

## GIST TRAIL

From Page 2

a “tumor of unknown origin.” In mid-October a 17x18 cm GIST was removed from the back side of my stomach along with my gall bladder and appendix. I was given a picture that was taken as the tumor was being removed and it actually made me feel better to see that I hadn’t complained about something “wimpy.” It was amazing that I never noticed anything except a slight bulge in my upper abdomen that I was unsuccessfully fighting for years with sit-ups and abdominal crunches. Due to my otherwise healthy physical condition I was able to be discharged from the hospital five and a half days after surgery.

As I approached the first anniversary date of my surgery in October 2005 I found myself getting rather distracted as my mind began to dwell on a backpacking trip. Thus I made a sudden decision to go back to the Pictured Rocks trail. I just knew that I needed to be there on the exact day of my surgery. I walked a leisurely 30 miles over three days and marked the hour of surgery by contemplating the sun setting into the mists over Lake Superior as I sat on the same bluff where I admired the rainbow in 2004. I had come full circle. As I walked back to my car the next morning I felt much more confident about my physical well being than I had in over a year. In



Mills rests after a three-day backpacking trip to Pictured Rocks National Lakeshore in Michigan’s Upper Peninsula in May 2004. This trip was the first time he started experiencing abdomen pains which he later discovered was GIST.

retrospect I can see that I found something on that trail that I did not even know I lost there.

However, I still felt that something was missing and that I needed another round of “trail therapy.” In May of this year I returned to Pictured Rocks with the goal of hiking the entire trail again on the same weekend as the original trip. From start to finish it took me 71 hours with no abdominal pain to mar my memories. The therapeutic benefit of walking amongst a carpet of wildflowers and listening to waves for three days can not be understated as somewhere on the

trail I left behind a lot of anxiety that I had been containing.

So there I was! This temporarily concludes the story of my unique GIST journey. My walks along the Pictured Rocks Trail represent the beginning, middle, and end of a tale and memories that I do not want to tarnish. Therefore I need to find a new trail for my next adventure; I am considering the 30-mile Fox River Pathway for a September trip as this was where Ernest Hemingway fished for trout and was inspired to write a wonderful book!

## Correction on AMG706 GIST trial article

By Norman J. Scherzer

In our August 2006 newsletter, the headline, *AMG 706 will not get FDA approval for GIST*, was misleading in that it

implied that the Food and Drug Administration (FDA) had turned down an application for approval. The FDA did not disapprove an application nor has AMGEN submitted one; instead, AMGEN concluded at the end of the phase II



clinical trial to not pursue a filing with the FDA because the non-randomized design of the phase II study was unlikely to support a filing in GIST. This is because Pfizer has already been granted a full approval for Sutent® in the same

indication. We apologize for the misunderstanding we may have created.

*Note: The Life Raft Group welcomes comments about it’s articles and is always interested in presenting different points of view.*

**New website  
launched for Global  
GIST  
Network!**



**Go visit  
[www.globalgist.org](http://www.globalgist.org)**

# September 2006 clinical trial update

**By Jerry Call**  
LRG Science Coordinator

## Sutent

In the United States, Canada and the United Kingdom, Sutent is now approved for patients failing Gleevec or those who cannot tolerate Gleevec. In addition, Sutent continues to be available to patients via the "Treatment Use Protocol," which is "four weeks on/two weeks off" (50 mg). There are many sites open throughout the world. Site information changes frequently; for the most current information, contact EmergingMed at 1-877-416-6248 (outside the United States) or at 1-800-620-6104 (inside the United States). If international patients have problems with the listed number, use email at: [sutant@emergingmed.com](mailto:sutant@emergingmed.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 but undergoes fairly frequent start/stop periods as cohorts accrue. Contact the trial centers for current information.

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 is projected to start this fall.

The combination of AMN107 and Gleevec may have a broad spectrum of

activity against primary and secondary mutations in GIST. The generic name for AMN107 is nilotinib and our understanding is that the brand name will be Tasigna.

## 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 for two weeks followed by a one week off period.

## Genasense + Gleevec

A phase II trial testing the combination of Genasense plus Gleevec in patients with Gleevec-resistant GIST recently opened. Genasense (Genta Inc.) is an antisense drug that inhibits bcl-2. Bcl-2 is a protein involved in cellular survival.

This drug is administered intravenously. It is hoped that Genasense may help Gleevec kill tumor cells by making them more sensitive to Gleevec. This trial is currently open only at M.D. Anderson.

Several other trial sites are planned including: Dana-Farber Cancer Institute, Boston, Massachusetts; University of Michigan Comprehensive Cancer Center, Ann Arbor, Michigan; Mayo Clinic Cancer Center, Rochester, Minnesota; and Memorial Sloan-Kettering Cancer Center, New York, New York.

## Perifosine + Gleevec

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

## RAD001 + Gleevec

Both RAD001 and Gleevec are manufactured by Novartis. RAD001 is an

mTOR inhibitor that may improve the effectiveness of Gleevec. The phase 2 portion of the trial is completing its stage I enrollment; the decision to expand the trial will be made in the coming months. Additional sites are being opened in anticipation of the future work.

Current sites are: Dana-Farber (Boston); Berlin, Germany; and the University of California (Los Angeles). Fox Chase Cancer Center in Philadelphia is expected to open soon.

## PTK787/ZK222584

This is a phase II study being conducted at the University of Helsinki in Finland and in Milan, Italy. 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. See the July 2006 Life Raft Group newsletter for an article about this trial.

## BMS-354825 (Dasatinib)

BMS-354825 is a tyrosine kinase inhibitor of Src, abl, KIT, and PDGFR. Dasatinib is available in a phase I trial at Dana-Farber and Glasgow, Scotland. Future plans include a SARC phase II trial. We will update trial sites and the scope of the trial as this information becomes available.

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

This drug was approved in December 2005 for kidney cancer. BAY 43-9006 inhibits several kinases including KIT, VEGFR-2, VEGFR-3, PDGFR-β, RAF, FLT3, and RET. The phase II trial for BAY 43-9006 is open and recruiting patients.

Three trial sites are open in Illinois and one in New York:

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

# THE LIFE RAFT GROUP

## Life Raft staff

Executive Director	<b>Norman Scherzer</b>	nscherzer@liferaftgroup.org
Executive Assistant	<b>Tricia McAleer</b>	tmcaleer@liferaftgroup.org
Administrative Assistant	<b>Erin Kristoff</b>	ekristoff@liferaftgroup.org
Program Coordinator	<b>Sara Rubinoff</b>	srubinoff@liferaftgroup.org
Research Coordinator	<b>Elizabeth Braun</b>	ebraun@liferaftgroup.org
Research Assistant	<b>Pamela Barckett</b>	pbarckett@liferaftgroup.org
Science Coordinator	<b>Jerry Call</b>	Jerry.Call@comcast.net

## Contact the Life Raft Group

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

## Life Raft volunteers

General Counsel	<b>Thomas Overley</b>	guitarman335@msn.com
Accountant	<b>Kristi Rosenberg</b>	kristi@mackeyctas.com
Database Consultant	<b>Steven Rigg</b>	StevenRigg@aol.com
List Manager	<b>Mia Byrne</b>	mebmcb@wowway.com
Newsletter Editor	<b>Sara Rubinoff</b>	srubinoff@liferaftgroup.org
Newsletter Editor Emeritus	<b>Richard Palmer</b>	richardpalmer@hawaii.rr.com
Web Designer	<b>Tami Margolis</b>	tami@comcast.net
Fund-raising co-chairs	<b>John Poss</b>	John@PossHaus.com
	<b>&amp; Gerald Knapp</b>	gsknapp@winfirst.com
Science Team	<b>David Josephy</b>	djosephy@uoguelph.ca
	<b>Michael Josephy</b>	mjosephy@gmail.com
	<b>Richard Singleton</b>	dick@garlic.com
	<b>Antonio Ramos</b>	ramos.antonio@inbox.com

## Life Raft regional chapters

Arizona	<b>Linda Martinez</b>	linda.martinez1@cox.net
Illinois	<b>Richard Kinzig</b>	rjkinz@aol.com
Colorado	<b>Jerry Call</b>	Jerry.Call@comcast.net
Connecticut	<b>Anita Getler</b>	aquarius2550@comcast.net
California	<b>Floyd Pothoven</b>	floyd@keralum.com
	<b>Martha Zielinski</b>	3zielinski.ca@att.net
Massachusetts	<b>Janice Leary</b>	jleary@orr.mec.edu
Michigan	<b>Ellen Rosenthal</b>	ebrosenthal@comcast.net
New Jersey	<b>Amy Spires</b>	amy_spires@ml.com
New York	<b>Dan Cunningham</b>	Daniel.Cunningham2@pseg.com
Ohio	<b>Kaye Thompson</b>	tnt.1@sbcglobal.net
Texas	<b>Kerry Hammett</b>	yaloo@gvtc.com
	<b>&amp; John Poss</b>	John@PossHaus.com
Washington	<b>Deanne Snodgrass</b>	g-d-snodgrass@comcast.NET

## Board of Directors

### Executive Committee

<b>Stan Bunn</b> , President	SBunn@BSTGlobal.com
<b>Jerry Cudzil</b> , Secretary-Treasurer	Jerry.Cudzil@DACFunds.com
<b>John Poss</b> , Fund-raising	John@PossHaus.com

### Directors

<b>Robert Book</b>	RMBook2@aol.com
<b>Mia Byrne</b>	mebmcb@wowway.com
<b>Chris Carley</b>	ccarley@fordhamco.com
<b>Jim Hughes</b>	tjhughes43@comcast.net
<b>Gerry Knapp</b>	gsknapp@winfirst.com
<b>Dr. Arnold Kwart</b>	amkbmp@aol.com
<b>Rodrigo Salas</b>	rsalas@maprex.com.mx
<b>Silvia Steinhilber</b>	nswplas@mb.sympatico.ca

## Life Raft country liaisons

Australia	<b>Katharine Kimball</b>	katharine_kimball@hotmail.com	Kenya	<b>Francis Kariuki</b>	bridgestone@coopkenya.com
Bolivia	<b>Virginia Ossio</b>	vossiop@accelerate.com	Malaysia	<b>Yong Choo Sian</b>	ycspj2005@yahoo.com
Brazil	<b>Vanessa Passos</b>	vanessa@endo.med.br	Mexico	<b>Rodrigo Salas</b>	rsalas@maprex.com.mx
Canada	<b>David Josephy</b>	djosephy@uoguelph.ca	Netherlands	<b>Ton de Keijser</b>	tdk@liferaftgroup.nl
China	<b>Ruijia Mu</b>	mu_ruijia@yahoo.com	Norway	<b>Jan Einar Moe</b>	jeinmoe@online.no
Columbia	<b>Jaime Peralta</b>	peraltas@cable.net.co	Poland	<b>Stan Kulisz</b>	listy@gist.pl
Costa Rica	<b>Michael Josephy</b>	mjosephy@gmail.com	Romania	<b>Simona Ene</b>	si_mi_ene@yahoo.com
France	<b>Estelle LeCointe</b>	gist.estelle@laposte.net	Russia	<b>Tanya Soldak</b>	tsoldak@citihope.org
Germany	<b>Markus Wartenberg</b>	wartenberg@lebenshauspost.org	Singapore	<b>Yong Choo Sian</b>	ycspj2005@yahoo.com
Iran	<b>Negar Amirfarhad</b>	negaraf@sympatico.ca	Switzerland	<b>Ulrich Schnorf</b>	ulrich.schnorf@bluewin.ch
Ireland	<b>Carol Jones</b>	roycal-re-gist@hotmail.com	Turkey	<b>Haver Tanbay</b>	tanbay@tanbay.net
Israel	<b>Ben Shtang</b>	ehuds@merkavim.co.il	U.K.	<b>David Cook</b>	D.Cook@sheffield.ac.uk
Italy	<b>Anna Costato</b>	anna.costato@virgilio.it			