



The Life Raft's Norman Scherzer speaks at the "New Horizons In Treating Cancer" conference for patient groups representing people with GIST and CML.

The Life Raft travels to Switzerland

Scherzer relates patient concerns at international conference in Europe

Editor's note: The following report was compiled by Norman Scherzer, Life Raft Group executive director

DIESSENHOFEN, Switzerland — This past month the Life Raft Group was part of an international conference, "New Horizons In Treating Cancer," for patient groups representing people with chronic myelogenous leukemia or GIST. Supported by Novartis Oncology, the conference included patient groups and representatives from Australia, Canada, France, Germany, Italy, Israel, the Netherlands, Sweden, Switzerland, the United Kingdom and the United States.

The Life Raft Group was represented by its executive director, Norman Scherzer, and Life Rafter Ulrich and Helga Schnorf from Switzerland and Bertrand de la Comble from France. Dr. George Demetri of Dana-Farber Cancer Institute in Boston and Dr.

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Battling gastrointestinal stromal tumor



LIFE RAFT GROUP

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Finding cancer's cause



At Oregon Health & Sciences University's Cancer Institute, Drs. Michael Heinrich, left, and Christopher Corless show tumor samples during a May 15 tour of their lab given to several GIST patients and caregivers. The tour followed a breakfast that included another GIST researcher, Dr. Charles Blanke, and the presentation of a \$15,000 donation for GIST research by Tania and Robert Stutman, members of the Life Raft Group and GIST Support International. See story, more photos Page 3

New drug outwits Gleevec resistance

Compound plus Gleevec beats resistance in mice with form of leukemia

The drug Gleevec, touted in some circles as a miraculous silver bullet against some forms of leukemia, can still fail in patients who develop mutations that cause the drug to lose

effectiveness.

Now, Howard Hughes Medical Institute researchers, working with mice that are genetically programmed to develop resistance to Gleevec, have shown that this therapeutic hurdle can be overcome by administering a second drug that foils the cancer in a novel way.

The experiments constitute a proof-

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Switzerland: GIST a model cancer for targeted therapy

From Page 1

Sasa Dimitrijevic of Novartis spoke on GIST treatment.

Demetri described Gleevec for GIST as “a paradigm for the development of precision guided therapy.” Scherzer spoke about the experiences of Life Raft Group. Other presenters included the MAX Foundation, Cancer Care and the Leukemia and Lymphoma Society.

There were striking similarities, as well as differences, in the experiences of patients in different countries. Patient groups in the U.S. and Canada are generally more organized and more outspoken, but this difference, given the speed of communications across the Internet, will likely diminish over time. The bond between patients striving to survive rare cancers readily took over the meeting and clearly outweighed any national or cultural distinctions.

The Life Raft Group forged a number of strategic alliances that will enhance the common mission to bring critical information to CML and GIST patients to ensure their survival. Amongst other initiatives, the Life Raft Group will be working on is a collaborative project with a new German organization, the House of Light, for both GIST and CML patients. As German is the major European language this will greatly enhance our common outreach efforts.

The conference also provided the first opportunity for a European Life Raft Group planning session. This was the first time that Scherzer, the Schnorf's and de la Comble had met in person. Discussions ranged over a number of initiatives to increase patient and physician awareness and to expand the reach of the Life Raft Group.

Finally, the conference also provided yet another opportunity for Scherzer to meet with Demetri and Dimitrijevic. The three met for over an hour, on a



European members of the Life Raft Group met April 26 for lunch. From left is Norman Scherzer, executive director of the Life Raft, France representative Bertrand de la Comble, Claire Eldred of the Novartis' public relations firm, Ruder Finn London, Helga and Ulrich Schnorf, the country representative for Switzerland.

Quote:

Gleevec for GIST is “a paradigm for the development of precision guided therapy.”



— Dr. George Demetri,
Dana-Farber
Cancer Institute,
Boston

boat trip down the Rhine, to review the latest Life Raft Group relapse information and to discuss resistance. The willingness of these key researchers to continue to extend themselves to the Life Raft Group should not go unher-

alded.

Before the conference, Scherzer traveled to Basel, Switzerland, to the headquarters of Novartis Pharmaceuticals to meet with its CEO, Dr. Dan Vasella. This meeting provided an opportunity to update Vasella on the progress of the Life Raft Group and, most importantly, to spend more than an hour discussing resistance and relapse.

Scherzer was able to present the latest Life Raft Group data on relapse and the need to more quickly consider changes in patient dosage levels into any evaluation of treatment effectiveness, including resistance. For example, if a patient starts on 800 mg. of Gleevec but after two weeks changes to 400mg for the next two years, current research protocol treats that patient as if he were still on 800 mg. This so-called “intent to treat” reporting is a standard practice amongst clinical re-

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OHSU rolls out red carpet for GIST'ers

Meeting the researchers, touring their labs among highlight of Oregon trip

By Richard Palmer

Several new drugs for fighting gastrointestinal stromal tumors could be in clinic trials within the next year, according to a researcher at Oregon Health & Science University.

That was just one bit of good news to come out of a two-day visit to the Portland medical center this month by a group of GIST patients and caregivers.

Other highlights included presentation of a \$15,000 donation for GIST research by Tania and Robert Stutman, a breakfast and lab tour with GIST researchers Drs. Michael Heinrick, Christopher Corless and Charles Blanke, and meeting the principal developer of Gleevec, Dr. Brian Druker.

The two-day visit stemmed from regular appointments of GIST patients on the extended phase II trial of Gleevec for GIST. Marina Symcox of Oklahoma and Richard Palmer of Hawaii asked OHSU to schedule their appointments on the same day, which coincided with the appointment of Stephanie Call and her husband, Jerry, of Colorado.

The Stutmans decided to fly from New York to personally deliver the donation from their GIST Cancer Research Fund, timing it so the GIST patients could be present. GIST'ers Beverly Shirts of Oregon and Gerald Snodgrass of Washington state and his wife, Deanne, drove to OHSU to join the party.

Realizing that both donors and GIST patients would be gathered, the OHSU Foundation staff swung into action. Associate Director of Development



LEFT: During a tour of his lab, Dr. Michael Heinrick holds a vial that contains a minute bit of cancer tumor from which the DNA will be analyzed to determine what may have happened to cause the cancer.

BELOW: Presenting \$15,000 for GIST research is Tania Stutman, patient and founder of the GIST Cancer Research Fund. Receiving the donation are, from left, Drs. Michael Heinrick, Charles Blanke, and Christopher Corless.



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In Memoriam

There have been 25 deaths in the Life Raft Group to date:

Debbie Nance, 38, Oct. 2, 2000, wife to Eddie, mother of Chris.

Jim Ackerman, 49, Jan. 16, 2001, husband to Betsy, father of Jill and Tom.

Jim Perham, 63, May 2001, husband to Karen, father of Craig, Kathy, Jennifer.

Amy Barney, 25, June 10, 2001, wife to Reed, mother of Joshua.

Jeff Prichard, 52, July 11, 2001, husband to Joyce, father of Gregory and Scott.

Ron Martinez, 60, July 25, 2001, husband to Jo Ann, father of Ron, Wendy, Natalie.

Ehud Nehemya, Aug. 7, 2001, father to Einat Zelinger, father-in-law of Ophir Zelinger, Hadar Nir.

Bruce Gunn, 43, Nov. 8, 2001, husband to

Roisin, father of Seamus, Liam, Brendan and Aislinn.

Robert Carr, Dec. 30, 2001, father of Robert, Steven, Scott and Melissa.

Jonathan Montague, 23, Jan. 19, 2002, son of Ray and Sheila Montague, brother to Jamie, Adam, Meghan.

Robert Lecca, 49, Jan. 28, 2002, husband to Diane.

Jacob Winfield Waller III, 67, March 31, 2002, husband to Jerry, father to Rita, Richard

Mary Golnik, 50, April 18, 2002, wife to Gary, mother to Timothy

Ana Maria Baldor-Bunn, 30, April 19, 2002, wife to Stan, mother to William.

Stewart "George" Wolf, 51, April 19, 2002, husband to Maggy, father to Thomas.

Michael Cornwell, April 19, 2002, husband to

Cathy.

Jerry Pat Rylant, 61, May 5, 2002, husband to Pamela, father of four, grandfather to 10.

Jill B. Meyer, 53, June 9, 2002, mother of Aliza.

Todd Hendrickson, 44, June 29, 2002, husband to Janet, father to Max, Tyler and T.J.

Chet Duszak, 79, Oct. 5, 2002, husband to Kay, father to Lori.

Nora Shaulis, 42, Nov. 4, 2002, wife to David, mother to Griffin.

Howard Delapenha, 41, Dec. 14, 2002, husband to Sandra, father to Joshua and Hannah.

Kathy Colwell, 45, Jan. 5, 2003, wife to Tom, mother of Katherine, Mary and Tom.

Cynthia G. Whitson, 64, Jan. 19, 2003, wife to Jerry, mother to Steve, Jill, Randy and Donna.

Abdul Hai, 76, Feb. 26, 2003.

Switzerland II

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searchers.

Although the Life Raft Group research information is still too small to draw any firm conclusions, preliminary results do show a strikingly smaller number of relapses amongst patients at higher (600 mg. or more) dosages of Gleevec. This is only apparent, however, when one adjusts the data to show the new (or changed) dosage levels. Vasella agreed that it made little sense not to be looking at the actual dosage that patients are on.

The meeting also afforded an opportunity for Scherzer to make Vasella an honorary member of the Life Raft Group and to present him with the new Life Raft Group lapel pin.

Scherzer left Vasella with a number of recommendations:

1. Immediately factor in actual dosage in all data analysis.
2. Conduct pharmacological studies of GIST patients and correlate the drug level in their bodies with drug effectiveness and resistance.
3. Expand tissue investigation of



Life Raft Group Executive Director Norman Scherzer, left, and Novartis CEO and President Dr. Dan Vasella talk about GIST resistance to Gleevec, and relapse of GIST patients who initially did well on Gleevec — two issues vital to GIST patients.

GIST patients encountering resistance. The Life Raft Group intends to aid this via creation of a tumor bank.

4. Increase coordination of somewhat disparate research studies to more urgently gather data on issues of patient survival, like resistance.

5. Speed the development and application of new drugs and compounds.

Upon his return to New Jersey, Scherzer reviewed the same issues with and made recommendations to Dr. David Epstein, head of Novartis Oncology.

OHSU

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Rachel Stroud Hunsinger set up a Thursday, May 15 breakfast with Blanke, Heinrick and Corless, followed by a tour of the Heinrick and Corless labs.

Since the clinical trial appointments were scheduled the day before, Robert Stutman asked if the two-day window would allow a meeting with Druker. Hunsinger hedged; since developing the first-ever molecularly targeted cancer drug a few years ago, Druker is constantly sought by researchers and pharmaceutical firms worldwide. But after a few phone calls and juggling of schedules, Hunsinger was able to block off a few minutes of Druker's time Wednesday afternoon.

She also made sure the red carpet was unrolled; goodies bags were waiting in the patients' hotel rooms (along with wine in the Stutman's).

After the GIST patients met at the hotel Wednesday morning, the group trooped to OHSU for their appointments. While the Calls remained at the clinic, the rest headed off to Druker's office.

Tall and with the lanky build of a runner, Druker was very gracious, a bit shy, and had "the kindest eyes I've ever seen," in Bev Shirts estimation.

Upon learning that the Druker family had been blessed by the addition of a baby girl just three weeks earlier, Tania Stutman shifted into her grandmother gear and engaged Druker in a parenting discussion that covered, among other things, the fine points of breast feeding.

A framed item hanging on the office wall caught Richard Palmer's eye: It was a U.S. Postal Service Team bicycling jersey, personally autographed by cancer survivor and four-time Tour de France winner Lance Armstrong. The jersey was just one of a host of awards bestowed Druker, the JELD-WEN Chair in Leukemia Research and Howard Hughes Medical Investigator.

The planned 10-minute visit ran more



GIST patients and caregivers pose in the office of Dr. Brian Druker, center. From left, standing, is Robert Stutman, Gerald Snodgrass, Marina Symcox, Druker, Tania Stutman; seated from left, Deanne Snodgrass, Richard Palmer and Beverly Shirts.

than half an hour before the group and the cancer researcher parted company. That evening, the nine GIST patients and caregivers gathered for dinner in downtown Portland.

The Calls had an early flight home Thursday but the rest of the group was treated to a buffet breakfast at OHSU. Present were Drs. Blanke, Heinrich and Corless, along with Hunsinger, Director of Development Carol Koller and Administrative Coordinator Lisa Nolen.

Blanke, who's led OHSU's investigation of Gleevec for GIST, said as many as 10 new cancer drugs that may be effective against GIST could enter clinical trials in the next 12 months. That's good news for patients looking beyond Gleevec, or for whom Gleevec has proven a temporary or ineffective treatment.

Blanke also underscored the importance of gifts like the Stutman's. Not long ago, his research led him to ponder the efficacy of super ASA — so-called "super aspirin" — against colon cancer. He approached both government and pharmaceutical companies

about funding for a pilot study. "I couldn't get a nibble," he said. But then he got a grant about the size of the Stutman's gift, and generated some interesting data. His idea caught on big and today millions of dollars are being spent studying it.

Moral of his story: Gifts don't have to be big to generate big results.

Breakfast was followed by a tour of the OHSU Cancer Institute research labs led by Heinrich and Corless. Surrounded by test tubes and high-tech equipment, microscopes and electronic analyzers, the doctors told of their work finding novel molecular cancer targets, testing of new anti-cancer agents, and how they're developing new ways to identify the mutations that can cause cancer.

The group got to meet and thank several of the interns, assistants and students who do much of the basic lab and analysis work.

Before they parted company, the GIST patients and caregivers agreed that OHSU had treated them royally, and that the research being done there should give cancer patients hope.

Resistance

From Page 1

of-principle that resistance to Gleevec can be defeated by using a second drug to shut down the activity of the drug's main target, the tyrosine kinase enzyme.

"Patients with a broad range of cancers that can be blocked by these inhibitors might in the future be treated with 'customized cocktails' of drugs tailored to their specific cancers," said the study's senior author, Dr. D. Gary Gilliland, a Howard Hughes Medical Institute investigator at Brigham and Women's Hospital and Harvard Medical School.

In an article published in the May 20, 2003, issue of the journal *Cancer Cell*, Gilliland and his colleagues showed that administering the drug PKC412 effectively thwarts a Gleevec-resistant form of leukemia, called hypereosinophilic syndrome (HES).

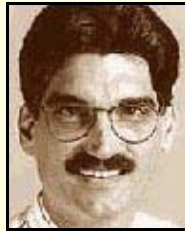
Gilliland's collaborators included researchers from the Center for Human Genetics and Flanders Inter-university Institute for Biotechnology in Belgium, Stanford University School of Medicine, Brown University School of Medicine, Emory University, Dana-Farber Cancer Institute and Novartis Pharma. Lead authors on the paper are Jan Cools, a postdoctoral fellow, Elizabeth Stover, a Harvard Medical School M.D., Ph.D. student, and Christina Boulton, a student at Harvard Medical School and an HHMI predoctoral fellow, in Gilliland's laboratory.

Gleevec works by inhibiting enzymes called tyrosine kinases. When the activity of tyrosine kinases is unregulated — which can occur when chromosomes improperly exchange chunks of genetic material, creating chromosomal arrangements — cancer may develop.

Quote:

"So we infer from these findings that we can either treat Gleevec-resistant patients with PKC412 to treat the resistance mutation, or we could combine the two drugs up front ..."

— Dr. Gary Gilliland, Howard Hughes Medical Institute researcher at Brigham and Women's Hospital and Harvard Medical School



Gleevec has proven highly effective in treating chronic myeloid leukemia (CML). And in a recent research article, Gilliland and his colleagues showed that the drug was also effective against HES. Those studied also demonstrated that HES is a form of leukemia.

The current study with PKC412 was prompted when Gilliland and his colleagues identified a patient in their HES study who acquired resistance to Gleevec.

"While this patient did respond to Gleevec," said Gilliland, "after about three months on the drug, his leukemia began to recur. We were concerned that he had developed a resistance mutation to Gleevec because resistance had been reported in CML patients who had been treated with the drug."

Gilliland and his colleagues confirmed their suspicions when tests showed that the patient had acquired a mutation in the activated

kinase PDGFR-alpha that causes HES. That mutation, they found, was analogous to a mutation that causes Gleevec resistance in CML patients.

"We had preliminary data that PKC412, an alternative tyrosine kinase inhibitor that also inhibits PDGFR-alpha, might overcome resistance to Gleevec," said Gilliland. He and his colleagues tested their hypothesis both in cell culture and mouse models of leukemia, and showed that the leukemia that was resistant to Gleevec could be cured with PKC412.

"So we infer from these findings that we can either treat Gleevec-resistant patients with PKC412 to treat the resistance mutation; or we could combine the two drugs up front — if they don't have overlapping toxicities — and preclude the development of the resistance mutations," said Gilliland. Overlapping toxicities might occur if the drugs also inhibited other kinases that when blocked in combination might damage or kill cells. However, initial indications are that toxicity from the combination of two drugs with minimal side effects would probably be modest in comparison to conventional chemotherapy, said Gilliland.

Over the long term, the latest findings that Gleevec and PKC412 show complementary action against kinases bode well for the future development of kinase inhibitors as drugs. "It's a very important point that these two drugs block tyrosine kinase action in different ways," he said. Furthermore, studies by other researchers have found different resistance mutations in the kinase that causes CML, suggesting that there are many other targets of opportunity for kinase inhibiting drugs.

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Life is a beach for the Salas family



Life Rafter Cordelia and Rodrigo Salas of Monterrey, Mexico, took their family to the resort of Cancun during Easter vacation. In back from left is José Miguel, 15, Paulina, 9; Rodrigo Jr., 17; bottom row from left, mom Cordelia, Emilio, 8, Corde, 11, and dad Rodrigo.

Resistance II: Heart of beast is proliferative signaling

From Page 6

“It is wonderful that we have a spectrum of inhibitors with different chemical structures — it should be possible to design a custom cocktail of inhibitors to attack tumors caused by any particular tyrosine kinase,” said Gilliland.

Beyond CML, HES and a third major blood disease, acute myelogenous leukemia, other similar malignancies are proving treatable by Gleevec and/or PKC412 — including gastrointestinal stromal cell tumors, which are solid tumors,

said Gilliland.

“We’re very excited about that finding,” said Gilliland. “Our experience in studying hematologic malignancies indicates that the heart of the beast is the proliferative signal, and that not only leukemias but all cancers require such proliferative and survival signals to thrive as tumors. And, if you can target that one genetic lesion, you have a very good chance of having an impact on that tumor.”

Gilliland and his colleagues are

conducting genetic screening of the cancers they study to discover activating mutations in kinases. HHMI investigators Bert Vogelstein at The Johns Hopkins School of Medicine and Sanford Markowitz at Case Western Reserve University recently undertook a similar approach and identified new kinase mutations involved in colon cancers.

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In back, from left: Jim Hughes, John Gorsky, Mary Lou Gorsky, Ken Lundell, Corrine Lundell, Darlene Rigg, Steven Rigg, Dick Kinzig. Seated, from left, Frank Lenkszus, Nancy Welsh, Paula Vettel, Carolyn Lenkszus.

Chicago area group gears up for ASCO

The Chicago chapter of the Life Raft Group held its second meeting of the year Saturday, May 3, at the Wellness Place in Inverness, Illinois, U.S.A.

Attending were Frank and Carol Lenkszus, Paula Vettel, Nancy Welsh, Ken and Corrine Lundell, Darlene and Steve Rigg, Mary Lou and John Gorsky, Jim Hughes and Dick Kinzig. While there were seven GIST survivors present, the total area membership has grown to 18 GIST'ers in the last eight months.

The group welcomed new members Mary Lou and John Gorsky and provided them with brief bios on the GIST history of those present.

Paula Vettel provided the group with some insight on mutation testing being

done at Oregon Health Sciences University in Portland. Although early in the research stage, it looks promising for patients who want to know the exon readings of their GIST. Patients should consider obtaining this information whenever tissue from new surgery is available.

John Gorsky provided a handout "Ask the Doctor Checklist" to help patients remember all the questions they need to ask when seeing the doctor.

A good deal of the meeting was spent discussing the American Society of Clinical Oncology meeting that will take place May 31-June 2 at McCormick Place in Chicago. The Chicago chapter has been asked by the Life Raft Group's executive director, Norman Scherzer, to staff a Life Raft Group booth during those three days.

Jim Hughes, with the help of Nancy Welsh, has graciously agreed to spearhead this project. Jim has had experience with trade shows and conventions, and he presented a comprehensive array of data, timetables, and brochures that are a part of making this program a success.

Area coordinator Dick Kinzig thanked Jim and Nancy for accepting this challenge and promised area members would support them in every way possible.

Those present agreed that Saturday meetings are best because of work schedules and the distance many area members have to travel. Therefore, the next meeting will be Saturday, Aug. 23 from 10:30 a.m. to 2:30 p.m. at Wellness Place. A luncheon is planned.

Mark your calendars: Life Raft dates to remember

The first Dutch Life Raft Group meeting will be Saturday, June 28, starting at 3 p.m. in the home of Ton and Ineke de Keijser in Ridderkerk, the Netherlands.

So far 13 people — seven patients and six caregivers, have said they'll attend. Those who'd like to attend can e-mail akeijser1@chello.nl for details

In the U.S.A., the Detroit area Life Raft Group is planning a gathering June 7. Contact Alan Tobes for details at atobes@comcast.net

Ten-year GIST survivor Michael Byrne will be competing in an Olympic length triathlon June 28 to raise money for the Life Raft Group.

"I would not be able to compete in

this race without the information that I received from The Life Raft Group and other groups like it," says Michael, who with wife, Mia, and son, Matthew, live in Plymouth, Michigan.

Tax-deductible contributions can be made payable to: The Life Raft Group, 555 Preakness Ave., Level Two East, Suite 2, Totowa, NJ 07512.

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Who are we and what do we do?

The Life Raft Group is an international, Internet-based, non-profit organization providing 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. Most members are being successfully treated with an oral cancer drug Gleevec (Glivec outside the U.S.A.). This molecularly targeted therapy inhibits the growth of cancer cells in a majority of patients. It 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.

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 newsletter items are edited to maintain the anonymity of members unless they have granted publication of more information.

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