Battling gastrointestinal stromal tumor

LIFE RAFT GROUP

September 2008 In memory of Ben Shtang, Linda Martinez, Rose Ellis, & Bonnie Girard Vol. 9, No. 9

Editorial: When is enough, enough?

By Jodi Merry
LRG Volunteer Writer

An August 19 article of *The New York Times* was published about the treatment of cancer and knowing when there are no more options. Doctors and patients alike find themselves asking the question "when is enough, enough?" Doctors have the difficult task of telling a patient that there is nothing else that can be done for them. They don't want to take away the last bit of hope that a patient has, and many patients would do "anything to live just one more day." Many patients will not give up and give in to hospice care because they "fear that they will be left alone," meaning they would lose their priority status with their doctors and caregivers.


MERRY

Doctors talk to their patients early on about their disease management plan, discussing all of their options, including the decision to allow hospice care to take over. A patient could think more clearly about their options in the earlier stages of their disease process rather

See ENOUGH, Page 10

Routine mutational and plasma level testing: The time has come

Norman J. Scherzer
LRG Executive Director

Mutational Testing


SCHERZER

The case for routine mutational testing of GIST patients at diagnosis seems compelling to the patient community and to a select number of GIST specialists who have begun integrating this into their medical practice. The relationships between mutational status and the treatment of GIST with imatinib, sunitinib and other drugs continue to be documented. It seems quite clear, for example, that exon 11 patients respond better to imatinib and that exon 9 patients respond better to sunitinib; furthermore, that exon 9 patients treated with imatinib respond better to higher doses. Despite this growing body of knowledge and despite the availability of mutational testing at a small but increasing number of laboratories, most GIST patients still have not had this test performed and most treatment facilities still do not include mutational testing as a routine part of patient evaluation.

Mutational testing for GIST patients was first

See PLASMA, Page 5

Life Fest 2008: There's still time!

By Nicole Burke
LRG Administrative Assistant

This year's Life Fest is on course to be the best one yet. Not only is it coming at a crucial point in the battle against GIST, but it is full of new workshops as well as some old favorites. Dr. Lee Helman will be our distinguished guest and the recipient of the LRG Humanitarian Award. We have a record number of participants already, especially internationally, and there is still time to be included in the excitement and education that encompass the event.

The room reservation deadline has been extended to September 7 to ensure that anyone who would like to attend has enough time to do so. If you plan on taking one trip this year, make your Chicago travel arrangements now. You certainly do not want to miss our survival strategies, personal survival plan, coping for patients and caregivers, and nutrition workshops, or any of our other informative workshops. In addition, the ceremony on Saturday afternoon celebrates the lives of the GISTers that have passed

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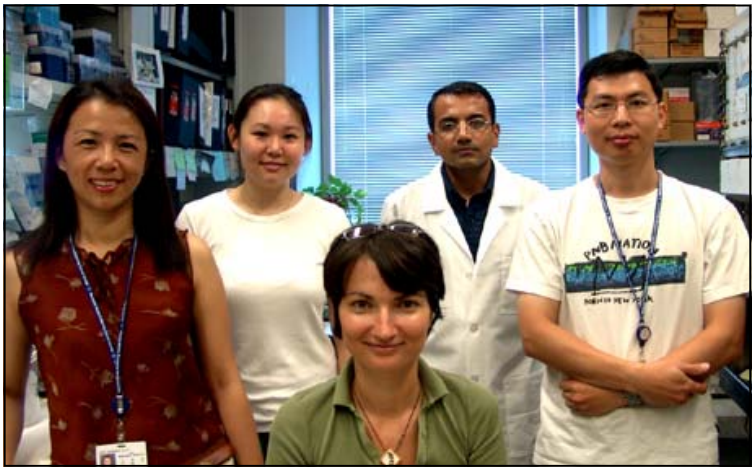
September 7 is the final day to receive the LRG hotel discount!

MSK team finds rare new mutation

By Jerry Call
LRG Science Coordinator

Researchers at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York have found a rare mutation in some GIST tumors. In a series of 61 patients with wild-type GIST, they found that three of them (5%) had mutations in a gene called BRAF. This same mutation, a "V600E" mutation in exon 15 of the BRAF gene, occurs frequently in melanoma. They also found the same mutation in one of 28 GIST patients that were resistant to Gleevec.

The research team was headed by Dr. Cristina Antonescu, one of the members of the Life Raft Group Research team. The results of this study were reported in the July issue of *Genes, Chromosomes & Cancer*. Dr. Narasimhan Agaram was the lead author of the paper.



Dr. Antonescu (seated, center) with members of her laboratory. *Courtesy of Memorial Sloan-Kettering Cancer Center website.*

The most common mutations in GIST occur in the KIT gene and were first reported by Dr. Seiichi Hirota of Hyogo College of Medicine, in 1998. KIT mutations occur in about 80 percent of GISTs; the remaining 20 percent of GISTs were called "wild-type" GISTs, meaning that the KIT gene was "wild-type" (normal/not mutated).

In 2003 researches found the driving force in about one-third of these wild-type GISTs to be mutations in the PDGFRA gene. This discovery was a result of a collaborative effort between Drs. Jonathan Fletcher of Brigham & Women's Hospital, George Demetri of Dana-Farber Cancer Institute and Drs. Michael Heinrich and Christopher Corless of Oregon Heath and Science University. Dr. Hirota also reported PDGFRA mutations at roughly the same time.

This left about 12 to 15 percent of adult GISTs where the mutation/driving force was still unknown. In 2005, Dr. Antonescu and her lab discovered that several genes were overexpressed in pediatric GIST, including the IGF-1R gene. The majority of pediatric GISTs are wild-type GISTs. The finding of overexpression of IGF-1R was verified and extended to adults with wild-type GIST by Dr. Andrew Godwin of Fox Chase Cancer Center in 2008.

In 2007, Drs. P. Aidan Carney, Constantine Stratakis and colleagues from the Carney-Stratakis Dyad Consortium discovered mutations in the SDH gene that caused a rare form of familial GIST, called Carney-Stratakis syndrome.

The three BRAF mutations found in the 61 wild-type patients that had never taken Gleevec had some similar characteristics. All three patients were middle-aged females (49 to 55 years old) with primary tumors located in the small bowel. In contrast, in five young adults (over 18 but less than 30 years old) and 15 pediatric patients (less than 18), no BRAF mutations were found.

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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.).

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.

To donate by credit card, go to www.liferaftgroup.org/donate.htm

Donations by check can be made to The Life Raft Group and 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.

September 2008 international clinical trial update

By Jim Hughes
Clinical Trials Coordinator

United States

IPI-504 Phase III: The first open site for the IPI-504 Phase III trial has been reported at Park Ridge, IL. Please contact the GIST Phase 3 Team at 877-504-INFI or IPI-504inGIST@infi.com.
IPI-493 Phase I: Infinity has announced the opening of a Phase I trial for IPI-493 an oral HSP-90 inhibitor. The goal of the trial is to determine the safety and maximum tolerable dose and to determine a dosing schedule for future trials. The trial is open to patients with advanced malignancies who are progressing. Patients who have had prior HSP-90 therapy appear to be excluded. Concurrent use of tyrosine kinase therapy (Gleevec, Sutent, Tasigna) appears also to not be allowed. There is a long list of specific exclusions that can be reviewed at clinicaltrials.gov by searching for the NCT # 00724425 and/or by calling the site contacts. The trial is reportedly open at two locations in California: Premiere Oncology in Santa Monica, Calif. Contact Marilyn Mulay at 310-633-8400 or mmulay@premiereoncology.com.

The other site is San Diego Pacific Oncology and Hematology Associates in Encinitas, Calif. Contact Karen Brady at 760-752-3340 or kbrady@premiere oncology.com.
PX-866 Phase I: ProIX has initiated a phase I trial of an oral PI3K inhibitor PX-866 for advanced solid tumors. The trial is listed as currently recruiting at two sites: University of Colorado Health Sciences Center in Aurora, Colo. Contact Sharon Hecker at 720-848-0667 or sharon.hecker@ucdenver.edu. Also MD Anderson Cancer Center in Houston, Texas. Contact Rhonda Clement at 713-563-3559 or rclement@mdanderson.org.

International

LBH589 Phase I & Dasatinib Phase I: These two trials, both only in Japan, are now listed as no longer recruiting and have been removed from the list.
Imatinib or Sunitinib Phase III: This trial has added new sites in Italy, Spain and the United Kingdom.
AUY922 Phase I & BGT226 Phase I: These two trials have been recruiting in the US and now have now added sites in Switzerland and Spain respectively.
OSI-930 Phase I: This trial is listed as no longer recruiting in the UK.

Imatinib (Glivec) or Sunitinib (Sutent)

Safety and effectiveness of daily dosing with sunitinib or imatinib in patients with GIST

Phase: III
Conditions: GIST
Strategy: Inhibit KIT and/or impede tumor vascularization
NCT#: NCT00372567
Telephone: 1-877-369-9753
Contact: Pfizercancertrials@emergingmed.com
Sites: Milano, Italy, 20133
Bologna, Italy, 40138
San Giovanni Rotondo, Foggia, Italy, 71013
Barcelona, Spain, 08036
Valencia, Spain, 46009
London, United Kingdom, SW3 6JJ
Lai Chi Kok, Kowloon, Hong Kong
Tuen Mun, New Territories, Hong Kong
Seoul, Republic of Korea, 135-710
Seoul, Republic of Korea, 138-736

Dasatinib (BMS-354825)

Dasatinib as first-line therapy in treating GIST patients

Phase: II
Conditions: GIST
Strategy: Inhibit KIT
NCT#: NCT00568750
Telephone: 41-21-314-0150
Sites: **Hospitalier Universitaire Vaudois,** Lausanne, Switzerland CH-1011
Michael Montemurro, MD

Radiation Therapy as Palliative Treatment of GIST (GIST RT)

Phase: I/II
Conditions: GIST
Strategy: Kill GIST cells (Radiation)
NCT#: NCT00515931
Telephone: 947173208 Ext. 358
Sites: **Helsinki University Central Hospital**, Helsinki, Finland
heikki.joensuu@hus.fi

Imatinib + RAD001 (everolimus)

Treatment with everolimus + imatinib in progressive GIST and imatinib-resistance

Phase: II
Conditions: GIST
Strategy: Inhibit target KIT downstream signaling (mToR)
NCT#: NCT00510354
Telephone: 41-6-1324-1111
Sites: Clinicaltrials.gov lists 9 sites as open in Germany. Use the Novartis number above for specific site information or go to the German Novartis site at www.novartis.de.

Glivec + Interleukin 2 (IL2)

Phase I trial in solid tumor and GIST resistant to imatinib and/or sunitinib (IMAIL-2)

Phase: I
Conditions: Solid tumors and GIST
Strategy: Kill GIST cells (Immunotherapy)
Contact: Dr. Nathalie Chaput
nathalie.chaput@igr.fr
Telephone: +33(0)1 42 11 50 05
Sites: **Institute Gustave Roussy,** Villejuif, France

Multi-Bacteria Vaccine

A Phase 1 study of mixed bacteria vaccine in patients with tumors expressing NY-ESO-1 Antigen

Phase: I
Conditions: GIST
Strategy: Immune response attacks tumor
NCT#: NCT00623831
Contact: Antje Neumann,
069 7601 4161
neumann.antje@khnw.de
Sites: **Krankenhaus Nordwest,** Frankfurt, Germany

AUY922

Phase I-II study to determine the MTD of AUY922 in advanced solid malignancies and efficacy in HER2+ or ER+ locally advanced or metastatic breast cancer.

Phase: I
Conditions: Breast Cancer/Solid Malignancies
Strategy: Destroy KIT (HSP-90)
NCT#: NCT00526045
Contact: **Novartis**
Telephone: 800-340-6843
Sites: Bellinzona, Switzerland

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How long must dying patients wait for justice?

By Erin Kristoff
LRG Newsletter Editor

In a recent edition of the *Wall Street Journal*, Gregory Conko, Director of Food Safety Policy at the Competitive Enterprise Institute, an advocacy group based in Washington DC, wrote an opinion piece entitled, "Sick Patients Need Cutting-Edge Drugs".

The event that inspired this passionate and demanding article was the death of 13-year old Anna Tomalis. Anna battled a rare form of liver cancer called embryonal sarcoma since September 2005. On August 15, 2008, she lost that battle.

At first, surgery and chemotherapy appeared to have worked for Anna. But in March of this year, her cancer recurred. With a little hard work and research, Anna's family discovered an experimental drug developed jointly by Ariad and Merck called Deforolimus.

"If the only alternative is death, then for God's sake let 'em have the drug," — John Rowe, father

KARNES

Anna was too sick and too young to be admitted into the clinical trial, but she fought to gain access to the drug on a "compassionate-use" basis. She and her family fought for months.

Kianna's Story

In 2005, the *Wall Street Journal* wrote a piece about Kianna Karnes. She was also waiting for the FDA to consider her petition to receive an experimental drug. The Journal proposed "Kianna's Law" to reform clinical testing process for drugs to treat life-threatening illnesses.

At a time when numerous "Terri's Law" proposals were being introduced in the wake of the Terry Schiavo case, countless advocates, concerned friends and family and WSJ staff were wondering, "Where is the government intercession for Kianna Karnes?"

In the aftermath of this article, Bayer and Pfizer (developers of two investigational drugs showing much promise for this particularly deadly cancer) both contacted her doctor almost immediately to discuss the appropriateness of providing the compounds. Mrs. Karnes' family was also contacted by the Food and Drug Administration (FDA) and was told that the agency stood ready to approve such treatment on an emergency basis.

It came too late. Karnes died the very day the FDA approved her exemption.

The FDA's Story

According to Conko, new drug approvals by the FDA has fallen dramatically. Last year, just 16 new drugs were approved. This is a shocking number compared to 53 approvals in 1996 and 39 in 1997.

Conko called attention to the heavy fire the FDA has come under after a few "high-profile drug scare", such as the withdrawal of Vioxx from the market.

Last year, the FDA rejected five new cancer drugs, including one that was voted as safe, 13-4, by a panel of cancer experts. The FDA demanded more testing which may delay approval for three more years.

With this information, one wonders, "Is the FDA playing it too safe?"

"Her life was like a stone being dropped in a pond, and the ripples she created continue to affect more and more people, even now that she's gone."— Ron Tomalis, father

TOMALIS

Anna's Story

Anna's struggle for an experimental drug ended this past July when she was finally granted access. Unfortunately, this drug also came too late. Anna's treatment began at the end of July, but she died within weeks.

Despite her declining health, Anna and her family worked closely with two patient-advocate groups, the Abigail Alliance and A Right To Live. The LRG reported on the court case the Abigail

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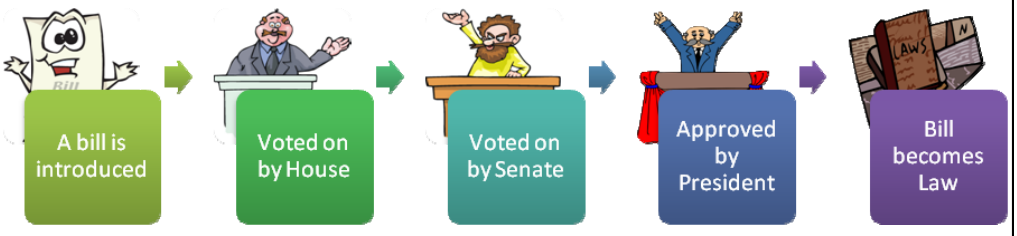
Figure 1: Where is the ACCESS Act?

How a Bill Becomes a Law...



According to Govtrack.us, a civic project to track Congress, the ACCESS Act was read twice and referred to the Committee on Health, Education, Labor, and Pensions in November 2005.

It never became law. The bill was proposed in a previous session of Congress. Congressional sessions last only two years; at the end of each session all proposed bills and resolutions that haven't passed are cleared from the books. Therefore, no more action could occur on the bill.

In May 2008, the bill was reintroduced by Senator Brownback in the new session of Congress; the status has not changed.

PLASMA

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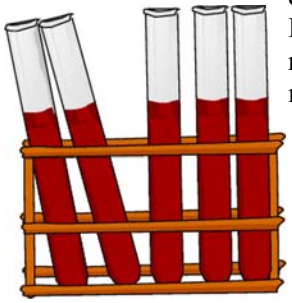
demonstrated on a research basis in 2000 and eight years later it primarily remains there.

For GIST patients with prior surgery (the majority of such patients), the test requires that a tissue sample on file at the hospital where the surgery was performed be shipped to one of the laboratories performing such a test (Please go to www.liferaftgroup.org/mut_testing.html for more information on this process).

Plasma Testing

The case for routine plasma level testing has been somewhat slower in developing a clear rationale, with research in CML leading the way. The past year hasseen a few research papers suggesting that there may be a relationship between the trough levels of imatinib and clinical benefit for GIST, at least with exon 11 patients. There is some suggestion that GIST patients with trough levels above 1100ng/ml may have longer progression-free survival times than those below that level.

In June, 2008 an international gathering of GIST patient advocacy group representatives unanimously adopted the Global GIST Patient Community Declaration calling for routine plasma level testing of GIST patients. In August 2008, a prominent US oncologist wrote to one of his patients that such testing for GIST patients was not necessary and that he would not adjust his patient's dosage based upon the results of such a test. This represents a point of view we feel is not unique in the medical community. Why is there a disconnect between the patient advocates and the medical community? I will let the medical community speak for itself by inviting them to respond in a future LRG Newsletter. For our part, the rationale is based upon two foundations.



Avantix Laboratory has sent free plasma testing kits for Life Fest 2008!

Research: Plasma level data would help research the issue of imatinib dosage levels and resolve the difference between the recent LRG data, which showed a relationship between higher imatinib levels and overall survival, and that of the formal MetaGIST study, which showed that there was no such relationship. Such data would also help explain why some GIST patients with lower imatinib doses continue to do well and why some with higher imatinib doses do not, by addressing whether it is the plasma level of imatinib rather than the dosage level that is the key determinant to overall survival.

Clinical Practice: Although we do not yet know enough about imatinib plasma levels to make clinical decisions based entirely upon such test results, I would submit that knowledge of plasma levels is an important piece of information for patient management and that integrating such a test into routine clinical practice should start immediately. At a minimum, it would be helpful for every patient to have baseline data on where their plasma levels are now. This would be particularly useful for newly diagnosed patients beginning imatinib.

Continuing to perform such a test on a routine basis might well provide the clinician with useful information even though we have not yet established definitive reference test levels related to long term survival. Consider for example a patient on 400mg of imatinib whose trough levels fall over time from an initial 1600ng/ml to 400ng/ml. Might this not be a cause for concern that the dosage level is too low or perhaps that the patient may not be taking all their medication? Consider another example of a patient on a higher dose of imatinib struggling with unacceptable side-effects, whose trough levels remain constant at 2400ng/ml. Might this not provide a supporting rationale for lowering the dosage but continuing to monitor the plasma levels to ensure that they do not drop to alarmingly low levels?

Admittedly, the logistics of ordering a plasma level test are somewhat difficult. They require taking the blood test within a narrow time period (22 to 26 hours after the last time the patient took imatinib) and shipping the blood, after centrifuging it, to a specific laboratory. However, the actual procedure of a blood test requires little imposition upon the patient or the physician. The fact that it can be done free of charge by Avantix Laboratory can only add to the rationale.

The patient community can no longer tolerate the unacceptable time gaps between the development of laboratory tests and their utilization in standard clinical practice. The case for routine mutational testing is compelling. The case for routine plasma level testing is sufficiently developed that it too should become standard clinical practice. Combined with routine mutation status testing this would lay the groundwork for individualizing patient treatment. Imagine the embarrassment of the medical community to have ignored for years basic tools that could have saved lives.

Mark your calendars!

- Don't forget to register for Life Fest! You can still get the special LRG hotel rate until **September 7**.
- This year there are three GCRF "Walks for a Cure". The Oregon walk will be held on **September 27**. The New York event will be held on **October 19** and the California walk is **October 27**. Please go to www.gistinfo.org for more details.
- Kim Trout will be hosting another Pennsylvania GISTers meeting on **October 11**. Please email her at musikwithkim@yahoo.com for more details.

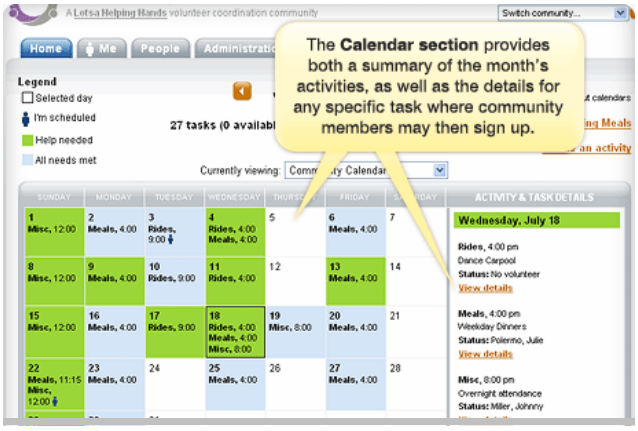
WEBSITE OF WORTH

By Nicole Burke
LRG Administrative Assistant

Keeping track of daily responsibilities can be difficult enough, but add cancer to the mix and it can be nearly impossible. The website Lotsa Helping Hands is a free service, offered through the Lance Armstrong Foundation, that organizes your loved ones that are ready and willing to help with your care. Asking for help is difficult. No one ever wants to "burden" or "bother" their friends and family and admit that they cannot do it alone. However, within minutes a web community can be created by one caregiver and sent to all of the people that would love to help out.

Whether it is a hot meal, transportation, or good conversation, it can all be arranged on your Lotsa Helping Hands site. It is a private site that can only be viewed by members that have been invited. Many people in your circle may not know each other. Friends, family, neighbors, colleagues or community organization members can all gather in this one place online to sign up for things that you need assistance with. You can also use your site to post up your GIST medical updates, photographs, and even receive encouragement and love on your "Well Wishes" message board. Lotsa Helping Hands makes it very easy to develop your community. You will be supplied with many templates and instructions on how to make it work best for your situation. Once your site has been developed, volunteers can immediately begin signing up. What's more is that all volunteers that sign up for an activity will receive an email reminder one month, one week and one day before their scheduled time. That way, forgetting will be virtually impossible.

Scheduling is never a fun task. Let Lotsa Helping Hands free up your time so that you can spend more of it with the people you love, doing the things you love. Getting help has never been as effortless as it is now. Visit www.lotsahelpinghands.com for more information and to start coordinating your schedule today.



LIFE FEST

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away. Candles will be lit in memoriam during a very moving gathering of GISTers and their caregivers.

We will be holding a Pediatric GIST breakfast on Saturday morning for those interested.

However, the most beneficial part of the weekend is not scheduled into a time slot. The camaraderie developed is incomparable to any other experience. The opportunity to meet other GISTers from around the world is one that should not be taken for granted.

Life Fest 2008 is being held at the Hyatt Regency O'Hare in Rosemont, IL. It is located at 9300 Bryn Mawr Avenue, and reservations can be made by calling 847-696-1234. Be sure to tell them you are with the Life Raft Group to ensure receiving our special rate of $109+tax per night. Visit www.liferaftgroup.org/members_lifefest.html to register with us for Life Fest. If you do not use the internet, call our office at 973-837-9092 and we would be happy to take care of it for you. Won't you join us?

Gleevec receives FDA priority review as first therapy to reduce recurrence of GI stromal tumors after surgery

East Hanover, August 27, 2008 — Novartis announced today that Gleevec® (imatinib mesylate) tablets has been granted priority review status by the US Food and Drug Administration (FDA) as the first therapy to be reviewed for use after surgery in kit-positive gastrointestinal stromal tumors (GIST). FDA priority review status is granted to therapies that could potentially fill a currently unmet medical need and accelerates the standard review timing from ten to six months[1]. Similar regulatory submissions have been filed in the European Union and Switzerland and will be filed in other countries shortly.

The Gleevec submissions are based on data from a Phase III, double-blind, randomized, multicenter, international study of more than 700 GIST patients who had surgery to remove their tumors. The results showed a dramatic 89 percent reduction in risk of kit-positive GIST returning after surgery (adjuvant setting) in patients treated with Gleevec versus placebo[2].

In early 2007, the study met its primary efficacy endpoint, showing an advantage for Gleevec in recurrence-free survival. At that time, following the recommendation of the independent study data monitoring committee to stop the trial accrual early, the study investigators made public the interim results and offered Gleevec to patients receiving placebo[3].

Approximately half of all patients with newly diagnosed GIST are considered candidates for surgical resection, or removal of their tumors. Of those who have the surgery, about half will suffer a recurrence[4]. If approved for this indication, Gleevec will be the first treatment option available to GIST patients after surgery to reduce the risk of disease recurrence or to possibly prevent the disease from returning.

"The dramatic clinical results from this study of Gleevec in the adjuvant GIST setting are especially encouraging when we consider the incremental benefit we typically see with other adjuvant therapies for solid tumors," said Rainer Boehm, MD, Executive Vice President, North American Region Head, Novartis Oncology. "The adjuvant use of Gleevec, if approved, would represent an important advance in the ongoing post-surgery management of GIST."

Gleevec is currently indicated in both the US and EU for the first-line treatment of metastatic or unresectable (inoperable) kit-positive GIST. If approved, the use of Gleevec for the treatment of GIST in the adjuvant setting would add to its eight current indications, which include Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML) and five other rare diseases. Novartis also has a therapy for the treatment of carcinoid tumors and acromegaly and multiple treatments in the pipeline targeting rare diseases.

Filing data

The study on which the regulatory filing is based compared the recurrence-free survival of GIST patients taking Gleevec 400 mg/day versus placebo for one year immediately following surgery. The results showed that 98 percent of patients receiving Gleevec remained recurrence free at one year following surgery compared to approximately 82 percent of those receiving placebo[3]. This shows that as a result of adjuvant therapy with Gleevec, there was an 89 percent reduction in risk of GIST returning[2].

The study, known as ACOSOG Z90001, was conducted at multiple cancer centers throughout the US and Canada, under a Cooperative Research and Development Agreement between Novartis and the National Cancer Institute (NCI). The study was led by the American College of Surgeons Oncology Group (ACOSOG).

The investigators reported that Gleevec therapy was well tolerated by most patients, with side effects similar to those observed in previous clinical trials with Gleevec. These include nausea, diarrhea and swelling (edema)[3].

More information can be found at www.novartis.com or www.gleevec.com.

References

1. Fast Track, Priority Review and Accelerated Approval. US Food and Drug Administration • Center for Drug Evaluation and Research. http://www.accessdata.fda.gov/scripts/cder/onctools/Accel.cfm. Accessed 31 July 2008.

2. Internal data.

3. Z9001: A Phase III Randomized Double-blind Study of Adjuvant STI571 (Gleevec®) Versus Placebo in Patients Following the Resection of Primary Gastrointestinal Stromal Tumor (GIST). http://www.cancer.gov/clinical trials/ACOSOG-Z9001. Accessed June 2008.

4. Van den Abbeele A., Benjamin R., Blanke C, et al. Clinical Management of GIST. Recurrence patterns and prognostic factors for survival. 2003;1-24.

What's in a name?

Would a rose by any other name smell as sweet?

Navigating the internet for information when you are first diagnosed can be difficult. Your first instinct may be to type "Cancer" in the search engine and hope for the best. **Here's a hint, those three letters at the end of your url make a big difference.**

CANCER.COM	CANCER.NET	CANCER.GOV	CANCER.ORG
Stop. This site requires a password to enter. Nothin' here.	This is run by the American Society of Clinical Oncology for cancer survivors.	This is the National Cancer Institute and is very helpful with clinical trials.	The American Cancer Society. It covers a broad range of cancers and issues.

Keeley Bihr: Remembering a mountain man

By Scott Snyder

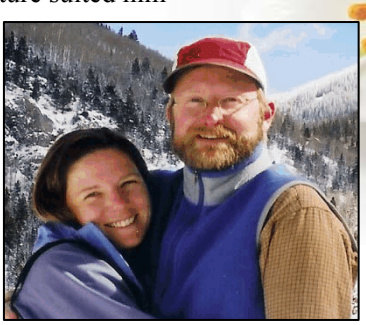
Keeley Bihr of Albuquerque, New Mexico died on July 26, 2008 after a courageous two-year battle against GIST. He was thirty-six years old. The following text is from a talk given by his close friend, Scott Snyder, of Boise, ID at a Life Celebration on July 31. It is a memorable description of who Keeley was and how he lived his life.

A tale of two best friends: *Scott and Keeley met each other in junior high school and formed a bond that carried their friendship through high school and college. When Scott left Nebraska for Albuquerque, New Mexico, to do his residency and fellowship, Keeley soon followed suit and landed a job there. When Keeley and his wife bought a fixer-upper home, they stayed with Scott while doing the work. Two years ago, Scott, a neonatologist, moved to Boise for work. However, like a true best friend, he could not stay away and came back to care for his friend through two surgeries. Scott also visited Albuquerque twice in the last month of Keeley's life to be by his best friend's side.*

"Today is a celebration. A celebration of all of the wonderful memories that were compressed into 36 brilliant years. I would say that Keeley is here with us in spirit, but as most of you are probably aware, his spirit was up at the crack of dawn, had eggs and green chile for breakfast, and is now hiking the La Luz trail in the Sandias wondering if the rest of us have gotten up yet. As beautiful as it is here, I still think he's got the right idea.

I had the good fortune to meet Keeley in Jr. High School nearly twenty-five years ago in Waverly, NE. Since then he has grown from a friend to a brother, and his wonderful wife, Stephanie, a sister. Despite his Midwestern upbringing, he needed elevation. Keeley was a mountaineer and outdoorsman. He climbed mountains, he studied them, he skied down them, he fell off them. He traversed summits on three continents.... this is where he found his religion.

Keeley trained with the National Outdoor Leadership School and earned a Masters in Ecology, training that drew him to New Mexico. The topography, ecology, cuisine and culture suited him quite well. He loved the beauty of mountain islands within the desert. He was a dedicated steward of the environment and believed that our natural resources are a gift not to be squandered. He rafted the Colorado River through the Grand Canyon, not as a tourist but as a scientist. And I can't help but grin when I think of him putting field mice in a shake-n-bake bag full of fluorescent powder and then chasing them through the nighttime wilderness with a black light.



Keeley with his wife, Stephanie

Family and friends meant so much to him. He adored his nieces and spoke proudly of their accomplishments. He loved his cars and loved to make them go fast. Fortunately, he had a wife who not only allowed it, but outright encouraged it. His dogs, Luna and Rojo, were his children and Luna's shiny, freshly brushed coat consistently made my dog jealous. His love of cooking meshed nicely with his friends' love of eating. The fact that he was quite good at it was an added bonus. As an interesting side note I might add that Keeley is the only person I have ever known who possessed a one gallon jug of Tabasco sauce. And the man wondered why he had reflux...

He was a craftsman. He and Stephanie labored many hours to renovate their beautiful home. Keeley and I learned construction lessons together - not just that any given project will take three times longer than you think it should, but also that it is inadvisable to believe that you can rip a hole into the exterior of your house at 11 pm and expect to have it sealed up in time for bed. That experience also taught us the value of a 24hr Home Depot.

I cherish the multitude of fond memories I hold of Keeley and could share hundreds more. I look forward to hearing others' tales of adventure with the mountain man. Perhaps his spirit will come down from the mountain long enough to join us, and maybe even make us lunch.

I'd like to leave you with a quote from John Muir:

Let the children walk with Nature, let them see the beautiful blending and communions of death and life, their joyous inseparable unity, as taught in woods and meadows, plains and mountains and streams of our blessed star, and they will learn that death is stingless indeed, and as beautiful as life."

Fight ends with family by her side

Linda Regar Martinez, 54, passed away peacefully with her family at her side after a long, courageous battle with cancer on Aug. 4, 2008.

She was born on Oct. 31, 1953, in Phoenix, Arizona. She was a devoted and loving mother, grandmother, daughter, sister & friend. She is survived by her sons, Carlos (Renee) Martinez, Christopher (Holly) Martinez, former husband & friend, Carlos F. Martinez, mother, Rosie J. Ramos, sister, Deborah Hardy, grandchildren, Alec, Jake & Chloe (Carlos & Renee), Madison & Mia Linda (Christopher & Holly).

Family, history and cars made it a colorful life for Jan-Einar

By Håvard Moe

Everything has it's time. Also a life. Jan-Einar Moe passed away peacefully at hospital on July 8, surrounded by his loved ones. Jan-Einar was born on February 18, 1945 in Oslo, where he lived his whole life.

Jan-Einar's life was closely connected to three things: family, cars and history. Jan-Einar married Solveig in 1967 and they had two children and four grandchildren. He lived his life for the family and couldn't get enough time with his grandchildren. His entire working career was connected to Peugeot cars. He was employed in Peugeot Norway in 1972 and stayed there until he passed away. He worked on all levels from mechanics to top chief and he loved it all. He learned to speak French and had close connection with France throughout his career. Every year he had at least five to six trips to France and he knew every part of the country, but it was specially Paris and St. Tropez that made him happy. He kept coming back again and again and they said in France when they heard the news, "Now we've lost monsieur Peugeot Norvegé." In his spare time he loved reading and researching about history, especially about the history of his family and about cars and transportation. He also had two old cars; one 1937 model and one 1964 model (Peugeot of course!), which took a lot of his time.

Jan-Einar loved cars, especially Peugeot.

MOE

Jan-Einar lived a colorful life with trips all around the world. The only thing he never got to do was to take a trip to Minnesota, to try and find some family who emigrated in the late 1880s.

After he got sick five years ago, he spent a lot of time and found great hope, fun and comfort being in the Gist-Network/LRG and it meant a lot to him all the love, support and understanding he found among his friends in this network.

He will be deeply missed but also warmly remembered as a loving husband, great father, funny grandfather, warm friend and colleague.

Devoted wife, mother and volunteer passes

Rose Ellis, 82, of Crystal River FL, formerly of Sudbury for 30 yrs, died July 25 in No. Andover. Recently widowed in March by the death of McGhee "Mac", husband of almost 66 years, Rose leaves daughters Rosemary Ellis (Lowell) and Beth Poulo and husband Louis (Andover). Her beloved grandchildren are Rebecca Poulo (Andover) and David and wife Loren (Wilmington). Rose was a devoted wife and mother, involved in scouting, church and school activities. A two-time cancer survivor, her strength and humor give her family lasting memories.

ELLIS

WAITING

From Page 4

Alliance was involved in since 2003 in our April 2008 issue. The Alliance cited "Due process" and argued that terminal ill patients who have run out of options have a constitutional right to try experimental drugs without FDA approval.

The case gained some ground in 2006 when a court of appeals voted in favor of the Alliance, but in January 2008, the case ended unfavorably in the Supreme Court.

Anna worked closely with these organizations to try and improve the compassionate-use process. The Access, Compassion, Care and Ethics for Seriously Ill Patients Act (ACCESS), which was originally introduced in 2005 and was reintroduced in May 2008 (Figure 1, page 4), is the fruit of these labors.

Mark's Story

The GIST community is not untouched by this kind of tragedy. In late 2006, photographer and GIST patient, Mark Thomas struggled for and won the right to receive an experimental drug on a compassionate-use basis. Mark waited for the drug for months. On Christmas Day 2006, the drug arrived at Mark's house. Unbeknownst to Mark, who passed away that day, still waiting.

Waiting

Anna knew that the ACCESS Act would arrive too late to help her, but she continued to fight for it until she could fight no longer.

While countless others sit and wait for times to change, Conko asks the supreme question, "Why do terminally ill patients have to wait so long to get access to the only treatments that hold any promise of saving their lives? And why is it not their right to decide?"

TRIALS

From Page 3

BGT226

A phase I/II study of BGT226 in patients with advanced solid malignancies including those with advanced breast cancer.

Phase: I
Conditions: Solid Tumors, Breast Cancer, Cowden Syndrome
Strategy: Target KIT dowstream signal (PI3K)
NCT#: NCT00600275
Contact: Novartis
Telephone: 800-340-6843
Sites: **Hospital Vall d'Hebron**, Barcelona, Spain

OSI-930

Dose escalation study of daily oral OSI-930 in patients with advanced solid tumors

Phase: I
Conditions: Solid Tumors/Sarcoma
Strategy: Multiple Targets
NCT#: NCT00513851
Contact: **This study is ongoing, but not recruiting participants**

XL147

Study of safety and pharmacokinetics of XL147 in adults with solid tumors

Phase: I
Conditions: Cancer
Strategy: Target KIT downstream signaling (PI3-K)
NCT#: NCT00486135
Contact: Gemma Sala, gsala@vhebron.net
Telephone: +34 93 489 4158
Sites: **Hospital Universitario Vall d'Hebron**, Barcelona, Spain, 08035
Jose Baselga, MD, PhD

XL765

Study of safety and pharmacokinetics of XL765 in adults with solid tumors

Phase: I
Conditions: Cancer
Strategy: Target KIT downstream signaling (PI3-K)
NCT#: NCT00485719
Contact: Gemma Sala, gsala@vhebron.net
Telephone: +34 93 489 4158
Sites: **Hospital Universitario Vall d'Hebron**, Barcelona, Spain, 08035
Jose Baselga, MD, PhD

Don't miss Jim Hughes hosting a new GIST treatment update workshop at Life Fest 2008!

Search and shop for a cause

By Matthew Mattioli
LRG Administrative Assistant

Did you ever wish that shopping could help out a cause like the Life Raft Group? Well now it can with the help of iGive and Goodshop. These are 2 sites that donate money to non-profits for shopping. The main idea behind both of them is the same but they both have special features that one might want to note.

Here are some features of iGive (www.iGive.com) and Goodshop (www.goodshop.com):

- iGive has you set up a Username, which allows you to choose if you would like a tax deduction or if you would like to remain anonymous..
- The iGive homepage shows you special offers that are going on.
- With Goodshop, enter the cause you are supporting, there is no need to enter personal information.

Also, remember that searching through www.goodsearch.com and www.isearch.igive.com, which are both powered by Yahoo, donate money to the Life Raft Group for each search you do.

ENOUGH

From Page 1

than when they're grasping for each and every extra day of life. Patients need to be made aware that they shouldn't feel "abandoned" by starting hospice, and that hospice could provide comfort and support to both them and their family in the end of life stages. Studies have shown that aggressive therapy at the end stages of disease only "hastens the process" of death. Whereas without treatment, a patient could be comfortable and have greater quantity and quality of time to spend with family and friends. However, some patients are afraid to die and will continue treatment even when it isn't doing any good.

Again, doctors find it difficult to tell a patient "enough is enough", for fear that they are robbing that patient of hope. The article even goes so far as to say that doctors may even be looking at their own livelihood, in that the cost of treatment is what keeps them in business. One would certainly hope this is not the case, and I, as a cancer patient myself, don't believe it is. From personal experience, I have found doctors in this field of medicine to be very compassionate and they have always kept my best interests in mind.

So, when is enough, enough? Should treatment cease even when a patient is willing to continue? A patient's autonomy must be respected by the doctor, and defended under all circumstances. Ultimately, the patient is always in the driver's seat when it comes to disease management.

MSK

From Page 2

In addition to the BRAF mutations found in wild-type GIST patients, the MSK team found an identical BRAF mutation in a patient with secondary resistance to Gleevec. The team looked at 28 tumors from 26 Gleevec-resistant patients that lacked an identifiable mechanism of resistance. The patient with the BRAF secondary mutation was a 66 year old male whose primary tumor was in the stomach and had a PDGFRA exon 18 mutation (4 amino acid deletion 842-845).

BRAF is a "downstream" protein that is activated by many receptors including KIT. In melanoma, it is mutated about 50 percent of the time. A clinically available drug, Nexavar (sorafenib), has undergone clinical trials in melanoma. Nexavar inhibits several different targets including BRAF, KIT, VEGFRs, CRAF and PDGRFB. Even though Nexavar has in-vitro activity against the common V600E BRAF mutation, it has shown little activity against melanoma in clinical trials. The reason for this is still unclear. Is it because Nexavar is unable to inhibit BRAF sufficiently or because there is another important melanoma target that is not inhibited by Nexavar?

Even though the clinical activity of Nexavar against BRAF mutations remains somewhat unclear, it has shown potent activity against other relevant targets including mutant KIT (especially the exon 14 T670I "gatekeeper" secondary mutation) and wild-type KIT. Nexavar is in phase II trials for GISTs that are resistant to Gleevec and Sutent. Other more potent BRAF inhibitors are in development.

In the GIST patients with BRAF mutations, several questions remain to be answered. Is KIT still activated and/or important? Which is more important, the BRAF mutation or KIT activation? Will inhibition of BRAF be sufficient for a response or will inhibition of BRAF and KIT be needed? Given the rarity of this mutation, these answers may be hard to come by. Another question that remains is when or if mutational testing will be recommended for select GIST patients.

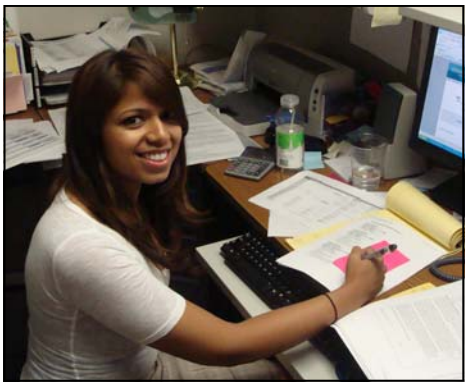
Did you see the LRG on PEREZHILTON.com

Celebrity gossip blogger, "Perez Hilton" has begun a new practice on his site, perezhilton.com. Besides scribbling inventive but mean nicknames on celebrity photos and posting video interviews with his favorite artists, Perez has begun posting organizations and charities that he deems worthwhile causes and asks the millions of gossip-starved teens and fans that watch his every move, to donate. A week ago, the LRG was added to those ranks. **Thanks Perez!**

Hilton, right, with Elton John

With Melanie C. of the Spice Girls

LRG says goodbye to summer intern



KASABWALA

This summer, the Life Raft Group took on its first summer intern. Many of you probably spoke to her on the phone.

Thursday, the LRG bid a fond farewell to Khushabu Kasabwala, who returns for her senior year as a physiology major at Boston University.

This summer, Khushabu did more than make coffee and run errands, she started a plasma testing initiative, redid the LRG side-effects survey, created a compliance survey and did a remarkable presentation on placebo-use in clinical testing. We'll miss you Khushabu!

GISTers gather in Northern California

Six GIST patients and their spouses met in Sunnyvale, California for an interesting afternoon of story exchanges on Saturday August 16, 2008. From left to right: Gerald and Susannah Liu; Martha Zielinski (Northern California Chapter Coordinator); Vicki and Leo Zuber; Irene and Ron Wing.

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