**Dating with GIST: the who, what, when and just plain how?**

By Erin Kristoff
LRG Newsletter Editor

The perilous world of dating can become even more complicated when you are living with cancer. This article is the second in a two part series on dating with a diagnosis of GIST. Part one, which was published in the February 2011 issue of the LRG newsletter featured experiences from three GIST survivors, Jason DeLorenzo, Eric Tan & Estelle Lecointe on the difficulties approaching the subject of GIST while dating. Part two covers tips on approaching the subject, a success story and new ways to meet people.

**Wildtype GIST & SDH: what to know**

By Dr. Jennifer Wright
University of Utah

What is Wildtype GIST? Wildtype GISTs are tumors that have a protein called “KIT” on their surface but do not have mutations in KIT or PDGFR like regular GIST tumors do. Wildtype GISTs are not treated with imatinib or sunitinib very often because these drugs are most active on tumors with KIT or PDGFR mutations. Most children and younger adults with GIST have the wild-type.

Why was this research done? Carney

**Breaking news update: TDM renews plasma testing**

By Jerry Call
LRG Science Coordinator

On April 21, 2010, the U.S. Food and Drug Administration (FDA) issued a warning letter to Novartis criticizing its promotion of blood level testing on its CML and GIST Alliance websites. As of September 30, 2010, Novartis terminated the CML and GIST Alliance programs which it had contracted with TDM Pharmaceutical Research, LLC. Since then, the Life Raft Group has been working tirelessly behind the scenes to try and resume this critical testing procedure as it has important potential for managing GIST patient care.

At this time, due to perceived potential conflict of interest, Novartis will not review its financial support for blood level testing. Despite the termination of Novartis support, Dr. Linyee Shum, the Executive Director and Chief Scientific Officer of TDM Pharmaceutical Research has graciously offered to continue to provide blood level testing to the GIST patient population. The target date for resumption of testing is May 16, 2011.

**Extra, Extra!**

Check your inboxes in the coming weeks for news on our Pathway to a Cure Research Team! The LRG is incredibly proud of the progress our researchers have made with “Project D Day”, our new initiative which takes a four-pronged approach to fast tracking a cure for GIST, and we can’t wait to share it with you!

Turn to page 7 to find out who’s going to be singing like a canary!
Behind the walls of Brigham & Women’s: Fletcher’s lab

David Josephy is the President of Life Raft Group Canada, a member of the LRG Science Team, and the brother-in-law of GIST patient Elsie Hernandez. David is a biochemistry professor at the University of Guelph, in Ontario. Since September, he has been on sabbatical leave, working as a researcher in the lab of Dr. Jonathan Fletcher, a renowned GIST researcher and leader of the Life Raft Group Research Team. We asked David to tell us about his experiences working at Brigham and Women’s Hospital in Boston.

Life Raft Group: “A sabbatical is like an extended vacation, right? (We asked, cheekily) “
David Josephy: “Hardly! I tell people that I’m now doing three full-time jobs instead of my usual two. I’m still a faculty member in Guelph, with my own lab to run (by e-mail, mainly!) and I’m still helping out with the Canadian Life Raft Group. But now I’m also working every day in Jonathan’s lab in Boston.”

LRG: “So, starting with the science: we’d like to know what you are working on specifically, and we also want to know what’s new and exciting in GIST research?”
David: “Let’s start by giving some context for the Fletcher lab. Jonathan is an M.D. pathologist, and one of the strengths of his work is the close linkage between clinical medicine and basic science. He continues to do clinical diagnostic work, as well as lab research. It’s truly “translational” research - basic research with a close connection to medical practice. One of Fletcher’s special skills is the ability to grow cell lines from GIST tumors; most of the GIST cell lines used around the world started in his lab. The cells are grown under conditions where they continue to behave very much like the cells in the original tumors.”

LRG: “So these cells have been removed from patients at surgery?”
David: “Yes. Several times, while I’ve been in the lab, tumor samples have been brought in from the operating room, and right away, Mark Mayeda or one of the other experienced people in the lab (not me!) puts them into culture medium. Most of the time, nothing useful starts to grow. Often, you just get fibroblasts or other non-GIST cells. But once in a while, GIST cells start growing and a cell line can be developed.”

LRG: “How do you know for sure that they are GIST cells?”
David: “It’s very similar to clinical pathology and diagnosis: you look at the appearance of the cells, and you use antibody stains to see which proteins they are expressing (producing), such as KIT and several others.”

LRG: “So you are growing GIST cells?”
David: “That’s right. I got trained on how to take care of the cells. It’s a bit like having a pet: you have to take care of them and feed them and they don’t know anything about holidays! The cells are grown in plastic flasks, fed three times a week, and “passaged” a few times each month.”

LRG: “Fed? Passaged?”
David: “Feeding means changing the medium in the flasks; passing means using enzymes to detach the cells from the flask, and then transferring them to new flasks. Just doing all the feeding and passing for a large number of GIST cell lines, growing under a lot of different conditions, is a big part of the day-to-day work in the lab. All of the work has to be done in sterile conditions,
April 2011 clinical trials update

By Jim Hughes
LRG Clinical Trials Coordinator

SARC & Novartis halt recruitment of imatinib dose escalation study

The phase III dose escalation study intended to answer questions about Gleevec blood levels has halted recruitment after failing to meet accrual goals, having recruited only five first-line GIST patients in 14 months. Informal discussions with Novartis Pharmaceuticals, the Sarcoma Alliance for Research through Collaboration (SARC) and the trial investigators provided some insight into the reasons for the change in status.

The obvious reason was that the 400 patients required to achieve statistical significance could not be recruited in a reasonable time with the current resources. Underlying factors mentioned were:

- Participating SARC member clinics tend to see more resistant GIST patients and fewer newly diagnosed patients who tend to be seen initially by local oncologists.
- The number of SARC centers that signed up for the trial was not enough.
- Gleevec was not provided by the manufacturer.
- Other recruiting front-line trials and the relatively small population of GIST patients (newly diagnosed inoperable GIST) for which they compete.
- The disincentive of patient travel and time for additional testing.
- The awareness of local and community oncologists regarding front-line GIST clinical trials.

Please go to SARC’s website for more information: www.sarctrials.org/

Regorafenib Phase III for resistant GIST now open in Europe, Asia and United States

This phase III trial for GIST patients resistant to both Gleevec and Sutent is now open at 24 sites: two each in Austria, Belgium and Finland; three in France; five in Germany; six in Japan; and one each in Italy, the Netherlands, Singapore and the United States. Check our clinical trial database listing at: www.liferaftgroup.org/treat_trials.html

Phase I trial of HSP-90 inhibitor AT13387 with Gleevec now open in Arizona

Patients who are resistant and who have had three or fewer tyrosine kinase inhibitor (TKI) therapies and who have not had HSP-90 inhibitors are eligible for this phase I safety and efficacy study sponsored by Astex Therapeutics. Initially patients will receive both intravenous AT13387 at one of five dose levels and daily oral Gleevec 400 mg in a 28 day cycle with AT13387 dosing on days one, eight and 15, later patients may receive AT13387 alone. Patients in the United States can contact Astex Pharmaceuticals in the United Kingdom, (Samantha Lewis, +44 1223 435060, s.lewis@astex-therapeutics.com) or the site investigator, (Dr. Daruka Mahadevan, dmahadevan@azcc.arizona.edu) at the Arizona Cancer Center in Tucson, Ariz. Dr. George Demetri, is listed as the Principal Investigator. An earlier phase I trial of AT13387 alone in solid tumors is still ongoing in Boston and in Tucson. Check our clinical trial database listings for details at www.liferaftgroup.org/treat_trials.html

Phase III trial of Tasigna in resistant GIST in Germany now listed

This Phase III trial has been ongoing since 2008 and is now listed in the National Institutes of Health (NIH) clinicaltrials.gov registry. Patients entering must have failed Gleevec 400 mg and/or Sutent or must be unable to tolerate Gleevec and/or Sutent. Patients who have had prior treatment with Tasigna are not allowed. The protocol is open label and is not randomized. All patients who are accepted receive Tasigna. The site listed as open is in Bad Saarow, Germany, near Berlin. The trial contact is Novartis Pharmaceuticals, 800-340-6843.

Phase II Trial of neo-adjuvant Tasigna at MD Anderson Cancer

The goal of this clinical research study is to learn if Tasigna (nilotinib) can cause tumor cells to shrink and/or die in patients with GIST who are scheduled for surgery or who may be eligible for surgery. Newly diagnosed GIST patients who have not yet had Gleevec, Sutent or Tasigna are eligible. A tumor biopsy will be required. Patients eligible for surgery receive Tasigna for seven days (or until their tumors become operable) and then have the surgery. The pre-Tasigna and post-surgery tumor samples will be used to compare the effect of Tasigna. This trial is sponsored by MD Anderson Cancer Center in Houston, Texas. Interested patients/clinicians can contact Dr. Jonathan Trent, at 713-792-3626.

The first steps towards finding a cure for GIST can start with you!

If you or your loved one has had their tumor removed, you are eligible to participate in the GIST Collaborative Tissue Bank (GCTB).

As an added benefit, we also offer free mutational testing with participation.

Contact the LRG at 973-837-9092 to learn about GCTB, and how you can help find a cure for GIST.
Extra Help – Paying for Medicare Prescription Drug Coverage (Part D)

The Extra Help (also called low-income subsidy) provides additional assistance to pay for prescription drugs up to an estimated $4,000 per year. To qualify for the Extra Help, a person must be (1) on Medicare, (2) have limited income and resources, and (3) reside in one of the fifty states or the District of Columbia. Limited income and resources means the following for the recipient per year:

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<th>Income Below</th>
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<tr>
<td>Single</td>
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If you qualify for Extra Help and join a Medicare drug plan, you will get help paying your Medicare drug plan’s monthly premium, any yearly deductible, coinsurance, and copayments; you will not have to pay a coverage gap or late enrollment penalty.

You will automatically qualify for Extra Help if you have Medicare and meet one of these conditions, you: (a) have full Medicaid coverage (b) get help from your state Medicaid program paying Part B premiums, or (c) get Supplemental Security Income (SSI) benefits. If you don’t automatically qualify for Extra Help, you can apply online via www.socialsecurity.gov or call 1-800-772-1213, or visit your state’s Medicaid office.

Medicaid

Medicaid is a state-run program that helps pay medical costs for some people with limited income and resources and meet other eligibility requirements. Medicaid also offers benefits not normally covered by Medicare, like help with personal care and rides to doctor appointments. If you qualify for Medicaid in your state, you automatically qualify to get Extra Help paying for Medicare prescription drug coverage.

Low income is not the sole criteria for getting Medicaid benefits. For the Medicaid application, the eligibility is as follows:

- Individuals receiving Supplemental Security Income
- People facing disability, blindness and/or are over 65
- Pregnant women and children under six with family income at or below 13 percent of the federal poverty level
- Children between the age 6 and 19 who have family income below federal poverty level
- Teenagers who are living on their own and are up to the age of 21
- Adults who take care of children below 18

Medicaid does not pay money to you; instead, it sends payments directly to your health care providers. Depending on your state’s rules, you may also be asked to pay a small part of the cost (co-payment) for some medical services. Each state’s program and rules are different. If you are not sure whether you qualify, if you or someone in your family needs health care, you should apply for Medicaid and have a qualified case-worker in your state evaluate your situation. Based on our Patient Registry Database, we have selected the locations where we have the highest number of GISTers in order to provide brief state information on Medicaid.

⇒ California – www.dhcs.ca.gov/services/medi-cal/Pages/default.aspx
Medi-Cal is California’s Medicaid program which provides needed health care services for low-income individuals who are under 21 years of age, seniors, persons’ with disabilities, foster care persons, pregnant women, and low-income people with specific diseases such as tuberculosis, breast cancer or HIV/AIDS.

⇒ Illinois - www.health.illinois.gov/
The Department of Healthcare and Family Services (HFS) of Illinois medical benefits may be available for individuals who are age 65 or older, blind or have a permanent disability. To qualify for HFS Medical, persons must live in Illinois and meet income and asset limits. Per-
State of the GIST Community Part 2: What do we know about your diagnosis?

By Magda Sarnas
LRG Patient Registry Supervisor

One of the most common questions GIST patients ask of the Life Raft Group is how many cases of GIST are there like mine? With a total of 1,279 GIST cases reported to us as of December 31, 2010, in the LRG’s Patient Registry, one would think all GIST patients would be in the same boat. However, it is not as easy an answer as you may think. There are a few variables that need to be taken into consideration to see if a GIST diagnosis is truly the same. Two areas that should be looked at are location of the tumor and how advanced the disease is when it is discovered (i.e. single tumor or metastases at diagnosis).

When we looked at location of tumor, 533 or 41 percent of cases of GIST were reported to us in the stomach at diagnosis, while 414 (32%) cases were located in the small intestines. While the majority of GIST cases do appear in the stomach and small intestines, we do have cases reported in which tumors appear in other areas such as the rectum, colon, and junction points like the small intestine and large intestine. Each of these areas comprise of less than 5 percent of the patient registry.

When we also looked at the type of tumor at diagnosis, we see that 63 percent had a single tumor while 24 percent had metastatic GIST.

These numbers may make you feel like a rare part of a rare disease, but they are not meant to make patients feel isolated. On the contrary, the intent is to provide you details about your individual diagnosis so that you can identify groups of patients who have gone through similar experiences and are willing to share and connect with you. The Life Raft Group can help to facilitate this if you are looking to connect with patients who have similar diagnostic characteristics. Please feel free to contact us by email at liferaft@liferaftgroup.org, or call our office at 973-837-9092, and let us know who you are looking to connect with.
Safford’s Valentine’s concert brings in over 15K

By David Safford
LRG Director

The Valentine’s Day Piano Concert with Anthony Padilla, cosponsored by the Life Raft Group and Columbia Basin College was a tremendous success with 140 guests enjoying a romantic evening of music.

The concert, featuring the works and transcriptions of Franz Liszt, mesmerized the audience. Each piece was introduced by Mr. Padilla reading a brief narrative describing the background of the music. One was about a boat on the water and you could actually hear the boat fighting the storm in the action of the music, a nice touch considering it was a Life Raft event. It was truly fantastic.

The concert was held in the Performing Arts Theater of Columbia Basin College (CBC), the local community college in Pasco, Wash. A pre-concert reception of champagne, strawberries and chocolates in the neighboring art gallery got everyone loosened up for the concert. Guests were welcomed by the President of CBC and the CBC Foundation as they explained the mission of the college and that this was the first ever collaborative fundraising event between CBC and an outside non-profit organization. I then introduced my friend, world renowned concert pianist, Anthony Padilla to the stage.

The event also marked my one-year survival of my diagnosis of unresectable metastatic GIST. What a difference a year makes, as many friends and family at the concert clearly recall the dire news of my advanced cancer before the type was determined. Ironically, it was the best news I ever received that it was GIST because if it was any other type of cancer, based on where and how widespread it was, I would not be here today.

The fact that so many people in the community know my story really helped raise awareness for the event. I am very thankful for the sponsors and guests who donated money and bought tickets benefitting the LRG’s Pathway to a Cure.

Anthony Padilla donated his time, talent, and travel expenses. CBC donated all their expenses including the cost of facilities and staff, invitations, postage, ticket sales and accounting, programs, and the pre-concert reception of champagne, strawberries and chocolates. The fundraising effort brought in over 15,000 dollars with 12,075 dollars for the LRG, 3,000 dollars for the CBC foundation (for needy student scholarships) and 500 dollars as the only advertising expense.

A word from the President of the Board, Jerry Cudzil:

“Dave has not only proven to be a wonderful addition to the LRG Board of Directors, his efforts and dedication to this cause in such a short amount of time has been an inspiration. We’re very grateful to have him on board.”

Welcome!

The Life Raft Group is pleased to announce that long time member Janeen Ryan, caregiver to Larry Ryan, has accepted a program associate position with us. Janeen will help us expand and strengthen our patient registry, which is critical to being able to monitor cutting edge treatment management being utilized in real time to keep Gleevec and Sutent resistant GIST patients alive. We’re very excited to have her on board and helping us with this crucial project.

-Norman Scherzer
Italian GISTers hold 4th national meeting

By Gabriella Tedone
A.I.G. Associazione Italiana GIST

A.I.G.’s (Associazione Italiana GIST) fourth national meeting was held at Fondazione IRCCS Istituto Nazionale dei Tumori (INT) in Milan on February 26, 2011. The focus of the meeting was, “What is GIST and How to Treat It.”

Dr. Paolo Casali, head of the Sarcoma Department at INT, Milan, discussed the changes in the past ten years of care and treatment for patients with GIST and what is medically possible in the years ahead. Dr. Casali noted, as we look to the future, there are things that no one thought possible years ago with regard to medicine and GIST treatment. Collaborative efforts and initiatives between various groups are important aspects for oncology research including cooperative relationships with tissue banks. Patient associations play a vital role in the management of these tissue banks and the studies performed on the tissues.

The meeting proceeded with a discussion from Dr. Alessandro Gronchi, surgeon at INT, on the stages of GIST from diagnosis to treatment from the viewpoint of a surgeon. Dr. Elena Fumagalli, oncologist at INT, then explained the current issues of drug therapies and side-effects management of target therapy. During the second session, the group decided to expand A.I.G. meetings to include some GIST research centers in Italy via live conference call. This will enable A.I.G. to not only partner with these centers but also have the most up to date information on GIST research.

Meeting participants also included:
- Dr. Guido Biasco, and Dr. Maria Pantaleo - University of Bologna, Policlinic Suor Orsola Malpighi
- Dr. Silvia Gasperoni, AOU Careggi, Florence
- Dr. Giuseppe Badalamenti, Policlinic P. Giaccone, Palermo
- Dr. Raffaella Bracci, AOU Umberto I Torrette, Ancona

When we asked everyone in our March GIST Link email to help push us to our goal of raising 50,000 dollars by mid-March, we were holding our breath and crossing our fingers. But you did it! You helped us raise an impressive $53,206.41!

For those of you who don’t remember our GIST Link plea, let us refresh your memory:

Perhaps many of you are aware of Norman’s uncanny ability to rally those around him. In keeping with true form, he has sparked a challenge of sorts here for the LRG regarding our annual fundraising campaign.

Perhaps it was the formidable spring in his step left over from our successful Life Fest meeting in June 2010, but when September arrived, and the thousands of envelopes were being stuffed, Norm playfully queried “How about we take this fundraiser a step further and try to break $50,000, and as a matter of fact, if we meet this goal, I will dress up like a sailor and sing ‘Thank You For Being a Friend’, and I’ll even let you videotape it for all the Life Rafters who helped us out this year.”

After waiting a few minutes to see if he was joking or serious, we burst out laughing and agreed to push for this goal to experience this thrill of a lifetime. (And we have just the backdrop!)

Norman will be performing from our Life Raft, which some of you remember from Life Fest 2010)

At our next NJ local group meeting on May 7, Norman will “sing for his supper” if you will and regale us all with our favorite of TV theme songs.

Look out for the video to be online shortly after!
Ensuring That No One Has To Face GIST Alone — Newsletter of the Life Raft Group — April 2011 — PAGE 8

Stratakis syndrome is the combination of paragangliomas and GIST in the same patient. Paragangliomas are masses of tissue that make nervous system hormones and can be either benign or cancerous. They are often found in the neck or near the spine. Research has shown that Carney-Stratakis patients have a germline mutation in the succinate dehydrogenase complex (SDH). The SDH complex is made up of several different proteins named SDHA, SDHB, SDHC, etc. These proteins are responsible for controlling metabolism and oxygen in the cells of the body. When mutations cause an abnormality in the SDH complex, it makes the body think cells are low in oxygen. In turn, the body increases blood flow, oxygen, and glucose to the cells, which may promote tumor growth. Because of what we already know about SDH mutations, researchers wanted to see if they could find SDH mutations in wildtype GIST patients and their tumors.

What research tests were done? The NIH Pediatric and Wildtype GIST Clinic has collected tumor and blood samples from patients with wildtype GIST for the purpose of research (with patient permission). None of these patients had paragangliomas, only GISTs. First, Dr. Jane-way and the other researchers looked to see if there is a problem with the amount of SDH in the tumors. In tumor samples from patients age 18 or under, all of the samples were missing the SDHB protein. In the samples from adult patients, the SDHB protein was absent 67 percent of the time and present in very low levels the other 33 percent of the time. If the same test is done in KIT mutated GIST, SDHB is missing only 6 percent of the time. Next, they looked to see if the SDH complex was working normally in spite of the missing SDHB protein. In the samples from adult patients, the SDHB protein was absent 67 percent of the time and present in very low levels the other 33 percent of the time. If the same test is done in KIT mutated GIST, SDHB is missing only 6 percent of the time. Next, they looked to see if the SDH complex was working normally in spite of the missing SDHB protein. In the wildtype tumor samples, there was almost no activity of the SDH complex. In KIT mutated GIST, the SDH complex activity was decreased a little, but was pretty close to normal. Finally, the researchers looked at the blood samples of the wildtype GIST patients for germline SDH mutations. Four of the 34 patients tested were found to have a mutation of one of the SDH proteins throughout their bodies.

Why are these results important? First, knowing about the SDH mutations may help us understand how wildtype GISTS are formed. Second, this information may help pharmaceutical companies make drugs tailored to treat wildtype GIST. Finally, it means that wildtype GIST patients with SDH germline mutations have the chance of developing paragangliomas. This is important because there are tests available right now for these patients that screen for paragangliomas and can lead to earlier treatment and hopefully better outcomes.

What does this mean for you? The bottom line is that the NIH Pediatric and Wildtype GIST Clinic recommends anyone with wildtype GIST to undergo testing for this mutation. If you have wildtype GIST but have not had this testing, your doctor, The Life Raft Group, or other support groups can help you find somewhere to have this test done. The testing is done with a genetic counselor who will explain in more detail what a positive or negative test means, how much the test costs (this depends on insurance), if other family members need testing, and more. This testing is not recommended for most patients with KIT mutated GIST, since positive results are uncommon.

SDH
From Page 1

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This obituary has been reprinted from The Greenville News.

Rachel J. Tate, 64, went to be with her Lord and Savior Jesus Christ on March 19, 2011.

Born in Marion, NC, she was a daughter of the late Weldon and Pearl Bowman. She was a devoted mother and grandmother, and a member of St. Andrews Presbyterian Church.

Surviving are three sons, Ty Tate and his wife Samantha, Paige Tate, and Matt Tate and his wife Sara; eight grandchildren; one sister and two brothers, Bettz Whitehead and her husband Ray, Weldon Bowman and his wife Snow, and Billy Bowman and his wife Susan.

Any donations in Rachel’s honor may be made to St. Andrews Presbyterian Church, 1860 Reid School Rd., Taylors, SC 29687; The Life Raft Group, 155 Rt. 46 W., Suite 202, Wayne, NJ 07470; or to Hope Lodge Center, 125 S. Huntington Ave., Boston, MA 02130.
Why do plasma testing?

The amount of Gleevec absorbed by patients can vary widely between patients. For patients taking 400 mg of Gleevec, some will have a high concentration of Gleevec in the blood and some will have a low concentration. Plasma testing measures the actual concentration of Gleevec in the plasma (a part of blood) of a patient. Emerging evidence suggests that some GIST and CML patients may not have concentrations that are adequate to ensure a long-term response to Gleevec.

There are several reasons for doing plasma testing. Measuring imatinib plasma levels may identify patients that are not taking their imatinib on a regular basis. This is a significant problem (affecting 25% or more of patients) and several reports have identified poor adherence as a predictor of imatinib failure in CML. Monitoring imatinib plasma levels may also help evaluate cases of apparent imatinib toxicity. For example, in a patient taking 400 mg of imatinib with intolerable side-effects, plasma testing might confirm high imatinib levels as the reason for the toxicity. In the case of a dose reduction, a second plasma test might give some reassurance of adequate imatinib levels even though the dose may be below 400 mg.

In addition to studying patient compliance, plasma level testing may help prevent resistance. In 2009, Dr. George Demetri and colleagues reported in The Journal of Clinical Oncology that imatinib plasma levels are linked to clinical benefit in patients with unresectable metastatic GISTs. Demetri and colleagues evaluated plasma data from GIST patients in the original imatinib phase II trial, in which the authors concluded that “preliminary analysis suggests that a low (steady state) plasma level of imatinib (i.e. 1,100 ng/mL) might contribute to drug failure in patients with advanced GIST...we found that patients with a low plasma exposure (Cmin less than 1,100 ng/mL) showed a trend of low rate of objective response and rapid evolution of resistance (short time to progression). These results suggest that a minimal plasma threshold may be necessary to achieve and maintain clinical response. This hypothesis is best supported in patients with KIT exon 11 mutations, which exhibited improved clinical outcomes with imatinib trough levels more than 1,110 ng/mL.” Furthermore, Demetri and colleagues state “in patients with advanced GIST, imatinib trough levels at steady state were associated with clinical benefit. Patients with imatinib Cmin (trough level) below 1,100 ng/mL showed a shorter time to progression and lower rate of clinical benefit (OOBR). Further studies are justified to test whether monitoring IM plasma levels might optimize clinical outcomes for patients with GIST”.

If you have questions about this procedure, please contact The Life Raft Group (1-973-837-9092).

Samples should be sent to the following address:

TDM Pharmaceutical Research, LLC
100 Biddle Ave Suite 202
Newark, DE 19702
1-866-990-0007
support@tdmrxresearch.com

The Life Raft Group would like to extend special thanks to Dr. Shum for his efforts and generosity. To learn more about the man behind the testing, a profile on Dr. Shum will be published in our next newsletter.
in a flow hood, and you have to be careful all the time. Just brushing a pipette tip against your arm by mistake could contaminate a flask and ruin an experiment.”

**LRG:** “You sound like you are speaking from experience?”

**David:** “Actually not! So far, I haven’t managed to contaminate anything!”

**LRG:** “OK. Now let’s get back to our question: what you are working on, and what’s new and exciting in GIST research?”

**David:** “I’d highlight a couple of things: new technology and new targets - maybe leading to new drugs. Jonathan asked me to help with a large study called an “RNA pooled screen”. The idea is to make a “library” of GIST cells, where each library carries an extra little piece of DNA, a slightly different piece in each cell. The DNA causes the cell to make a little piece of RNA, and that in turn suppresses (that is, turns down without completely shutting off) the cell’s ability to make a specific protein. Each cell is a different “book” in the library, so it shuts down a different gene. Next, the cells are grown for a few months in the presence of a drug, such as Gleevec. Some of the cells - cells that are shutting down certain specific genes - grow faster under those conditions, and some grow more slowly. At the end of the experiment, we sequence DNA from the cells - it’s like making a catalogue of the library - and we identify the genes that have helped or hurt the cells. That way, we can identify possible new targets. Proteins that are helping the cells to grow, to overcome the effect of the drug, are probably proteins we want to attack, perhaps by using a second drug in combination with the first. So, I’m using this system to study one particular compound.”

**LRG:** “A GIST drug like Gleevec?”

**David:** “Well, it’s a compound that is being tested clinically in several cancers, but not yet in GIST.”

**LRG:** “And this is new technology?”

**David:** “Yes. The RNA interference screening technique has only been developed in the last five years or so. A lot of scientists are rushing to apply it to basic problems in cell biology and to improve therapies for HIV and for lots of different cancers. To make it work you have to be able to grow the cancer cells, and that’s where the Fletcher lab expertise is so critical. The DNA technology side of the study is done with the help of scientists at the Broad Institute, across the Charles River in Cambridge. We’ve been going over there a lot.

Related to this RNA interference technology, there’s also been an amazing improvement in the ability to catalog which genes are turned off or turned on in particular cells. Back in the 1990s, we studied gene expression by testing one gene at a time, now we can look at the entire human genome in one experiment. It’s like you’ve been working with a little pocket calculator for a few years and then suddenly you have a supercomputer sitting on your desk. A few months ago, this type of research turned up a previously unsuspected gene that is really important in GIST, a gene called ETV1, and a lot of people are now looking at ways to build on that discovery and devise new therapies for GIST.”

**LRG:** “How is your typical day in the Fletcher lab different from your typical day in your own lab in Guelph?”

**David:** “For me, it’s very different! Back in Guelph, I just sit in my office all day, doing paperwork and writing grants and talking to students… and teaching classes, of course. Here, I come to the Thorn building, put my backpack in a locker and my lunch in the fridge and then I spend the whole day in the lab, doing experiments and analyzing data - no phone calls, no committee meetings, no distractions. It’s great.

It’s also very different to be working in a hospital lab rather than a university campus. When you go to the cafeteria, the people you meet in the hallways are doctors, nurses and patients, not students. If you ever wonder what it’s all about, you can just walk along the “Pike”, the long corridor that connects all the buildings at Brigham and Women’s Hospital. You see the patients and you remember the reason why you’re doing the work.”

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**Mark your calendars!**

- The much-anticipated Alianza GIST gathering in Brazil will take place the week of April 11.
- NJ GISTers will be meeting on May 7, at the LRG office in Wayne, NJ. Email us at liferaft@liferaftgroup.org for details.
- The American Society of Clinical Oncologists (ASCO) meeting will be held once again in Chicago, June 4-8. If you’re there, watch out for the joint Max Foundation-LRG-Monterrey Tech-Alianza GIST project!
- Also that weekend… National Cancer Survivor’s Day is June 5 this year!

The 2010 Annual Report will be a coming out soon. Can you guess this year’s cover?
DATING
From Page 1

fore you share something that you feel is very personal.
• You tell them right away to get it over with and see how they react.
• You take things on a case-by-case basis and tell people you are dating when the moment feels right.

There is no right or wrong answer here; each individual must gauge their own situation.

Pediatric GISTer, Jason DeLorenzo offers one approach “When breaching the subject, I do it casually and pay attention to reactions. Since most of my symptoms are food based, I’ll turn down a dessert and casually say ‘I’ll get sick if I eat that’”, either on the first and second date. They will invariably ask why, and the door is opened. I explain the sickness and answer questions honestly and openly.”

“If I wait for several dates to speak about my GIST story, then I feel like I am not very honest towards myself and the one I’m dating with,” says Estelle Leconte, Pediatric GISTer and founder of Ensemble contre le GIST, “Furthermore, I now consider I do not really know who the people really are until they know who I am and what I am doing. When I keep my story secret, I know I also expose myself to an abrupt reaction. Of course, first reaction will be: “It does not matter. The most important thing is who you are.” But unfortunately, most of the time these people will silently disappear without giving you any explanation.”

It’s difficult to open yourself up when facing this issue with a new partner, especially if this situation has gone in a bad direction before. Livestrong.org offers some suggestions that may help if you are having difficulty starting new relationships or are anxious about dating:
• Make a list of positive qualities about yourself that make you a good partner.
• If you are anxious about rejection, try to imagine being rejected and practice what you might say and how you will handle the situation.
• Don’t give up if someone doesn’t share your feelings. Everyone is entitled to their feelings when faced with cancer.

American Cancer Society suggests having “the cancer talk” when you and your partner are relaxed and feeling close. “Ask your partner a question that leaves room for many answers. The question gives them a chance to think about the new information and respond, and helps you see how your partner takes this news.”

When you are ready to talk to your partner, some of the issues you may want to discuss are:
• The possibility of recurrence
• Your ability to have children
• Whether your life expectancy is shortened

Before talking about these topics, some people may find it easier to write down what you are going to say or practice with a friend. Learn more about talking with a partner.

“More than the disease in itself, this children thing has quickly become a big issue for me as I realized it could bring a lot of complexity in the setting of a new relationship,” says Estelle.

When faced with such heavy obstacles, Livestrong.org suggests keeping a diary or journal to help you understand and find meaning in what is happening in your life. “Writing down your thoughts and feelings about your experiences can help you feel more in control. It can also help you release emotions like fear and anxiety that you might be holding in-side.”

In a recent New York Times article, “Difference Is the Norm on These Dating Sites” by Karen Barrow, this very issue was approached.

One of the article subjects, Sherry Nevius, was a single 52 year old woman living with cerebral palsy, “It’s hard enough to find someone with similar interests,” she said. “Finding someone O.K. with your disability just makes it harder.”

Another subject, Dr. Michael T. Maurer, 57 and living with HIV said that the worst part of dating was the anxiety over disclosing his H.I.V. status.”

Maurer joined an online community of people with H.I.V., “[It] allows relationships to form without the burden of the big reveal hovering overhead.”

“Here everyone knows you have H.I.V.,” he said, “so it gets that barrier out of the way.”

“Awkward issues that come with an illness can be discussed frankly and openly,” Bower posits, “in an online space in which everyone is dealing with something out of the ordinary.”

Some cancer patients have followed this same route. Cancermatch, an online group which offers many support features seeks to tackle this issue. Listed on its website, www.cancermatch.com, is the bullet, “Meet new friends and, maybe, even fall in love”

It’s a tall order to fill for someone facing years and maybe even a lifetime of awkward conversations over drinks.

Whether you choose to meet others facing the same obstacles as you, or people you encounter in everyday life, your manner should remain the same, respect your partner while always respecting yourself.

Hope is one of our most fulfilling and fortifying strengths. It’s best to keep it going. As Jason so poignantly points out, “You’ll be sure that when you finally do enter a long term relationship that your partner is truly loving and authentic, thanks to GIST.”
FDA too rigid in review of drugs for critically ill

Reprinted article by George Miller on Fiercebiotech IT

Scott Gottlieb has fired a shot across the FDA's statistical-confidence bow. The former FDA Deputy Commissioner, using the Wall Street Journal as his command post, charges the regulator with "steadily disregarding" the provisions of the FDA Modernization Act that give it "broad discretion" to reduce the quantity and rigor of clinical data needed to approve drugs targeting grave illnesses.

The U.S. Congress, says Gottlieb, now a fellow at the American Enterprise Institute, should force the regulator into speeding the availability of such drugs. It should reaffirm the provisions of the Modernization Act and mandate that the agency approve drugs for severe conditions on the basis of one study or, at least, a "more lenient statistical orthodoxy" than the current norm of two randomized placebo-controlled trials.

The Act has given the FDA the power to do so since 1997, but the agency more often chooses to reserve that power. "While Congress may not want to get into the business of establishing the FDA's analytical methods, it can call on the agency to convene an advisory panel to cultivate principles that are more permissive when it comes to very bad diseases," Gottlieb writes. And Congress also needs to improve FDA's review process to make it more inclusive. "The science embedded in the most novel drugs is increasingly complex, requiring collaboration across many disciplines, including clinical medicine, pharmacology and statistical modeling."

Go to http://online.wsj.com and search "The FDA Is Evading the Law" to read Scott Gottlieb's article for the Wall Street Journal.
Every year, the US News & World Report releases their “Best Rankings” list, featuring the best in education, hospitals, business and others. The list of top cancer hospitals is one such list. The institutions are judged on a number of criteria including reputation with specialists, survival, patient safety, patient volume, nurse staffing (the balance of nurses and patients) and whether it is a “Nurse magnet Hospital” (the hospital was recognized by American Nurses Credentialing Center as meeting high standards for nursing excellence).

Here is the most current list of the top ten hospitals for cancer in the United States. While some of these centers are known to have GIST specialists, not all of them do. Please check out the LRG GIST Specialist Database at www.liferaftgroup.org/gist_directory.php if you would like to find a specialist in your area.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Hospital</th>
<th>U.S. News Score</th>
<th>Reputation with Specialists</th>
<th>Patient Safety</th>
<th>Patient Volume</th>
<th>Nurse Staffing</th>
<th>Nurse Magnet Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>University of Texas M.D. Anderson Cancer Center Houston, TX</td>
<td>100.0/100</td>
<td>Very strong</td>
<td>Much better than expected</td>
<td>Low</td>
<td>Highest</td>
<td>Highest</td>
</tr>
<tr>
<td>#2</td>
<td>Memorial Sloan-Kettering Cancer Center New York, NY</td>
<td>93.9/100</td>
<td>Very strong</td>
<td>Much better than expected</td>
<td>Medium</td>
<td>Highest</td>
<td>High</td>
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<tr>
<td>#3</td>
<td>Mayo Clinic Rochester, MN</td>
<td>79.1/100</td>
<td>Strong</td>
<td>Much better than expected</td>
<td>Lowest</td>
<td>Highest</td>
<td>Highest</td>
</tr>
<tr>
<td>#4</td>
<td>Johns Hopkins Hospital Baltimore, MD</td>
<td>75.1/100</td>
<td>Strong</td>
<td>Much better than expected</td>
<td>Lowest</td>
<td>Highest</td>
<td>Highest</td>
</tr>
<tr>
<td>#5</td>
<td>University of Washington Medical Center Seattle, WA</td>
<td>60.6/100</td>
<td>Strong</td>
<td>Much better than expected</td>
<td>Lowest</td>
<td>Highest</td>
<td>Lowest</td>
</tr>
<tr>
<td>#6</td>
<td>Dana-Farber Cancer Institute Boston, MA</td>
<td>58.5/100</td>
<td>Strong</td>
<td>As expected</td>
<td>Highest</td>
<td>Lowest</td>
<td>Low</td>
</tr>
<tr>
<td>#7</td>
<td>Massachusetts General Hospital Boston, MA</td>
<td>57.1/100</td>
<td>Strong</td>
<td>Better than expected</td>
<td>Lowest</td>
<td>Highest</td>
<td>Highest</td>
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<tr>
<td>#8</td>
<td>University of California, San Francisco Medical Center San Francisco, CA</td>
<td>56.2/100</td>
<td>Significant</td>
<td>Much better than expected</td>
<td>Medium</td>
<td>Highest</td>
<td>Highest</td>
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<tr>
<td>#9</td>
<td>Cleveland Clinic Cleveland, OH</td>
<td>52.6/100</td>
<td>Significant</td>
<td>Much better than expected</td>
<td>Medium</td>
<td>Highest</td>
<td>Highest</td>
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<tr>
<td>#10</td>
<td>Ronald Reagan UCLA Medical Center Los Angeles, CA</td>
<td>51.8/100</td>
<td>Significant</td>
<td>Much better than expected</td>
<td>Medium</td>
<td>Highest</td>
<td>Highest</td>
</tr>
</tbody>
</table>
The Life Raft Group is always on the lookout for anything that may be helpful for people dealing with cancer. When we see that other organizations are providing services that may help the GIST community, we like to share that information for everyone's benefit.

AUSTIN, TX--(March 25, 2011) - Today, LIVESTRONG celebrated the opening of the LIVESTRONG Cancer Navigation Center at an open house for the entire Austin community. The Navigation Center is pioneering a unique new service that will help cancer survivors from Central Texas with all the questions and challenges that accompany cancer. The grand opening event included a program featuring U.S. Rep. Lloyd Doggett; Texas Rep. Eddie Rodriguez; cancer survivor, champion cyclist and LIVESTRONG founder and chairman Lance Armstrong; and three-time cancer survivor and LIVESTRONG president and CEO Doug Ulman.

"The effects of cancer are felt throughout the Central Texas community, but they hit underserved families especially hard," said Armstrong. "We created the LIVESTRONG Cancer Navigation Center in East Austin to help anyone affected by cancer overcome the tough challenges that arise after a diagnosis, like insurance problems, treatment concerns and dealing with the emotional impact of the disease."

"LIVESTRONG is incredibly proud of the milestone we're celebrating today," said Ulman. "Opening the LIVESTRONG Cancer Navigation Center allows us to serve people who need help in their fight against cancer and connect them with the support they need to face the disease on their terms. This free bilingual service has the potential to transform cancer care and improve the health of the most vulnerable members of our community."

"At a time when state and federal funding for cancer may become more scarce, LIVESTRONG is helping to close the gap for Austin-area cancer survivors in a very real and meaningful way," said U.S. Rep. Lloyd Doggett. "Cancer affects not only the patient but their family and their community. The LIVESTRONG Cancer Navigation Center will be a great asset to the community as it supports people fighting this disease."

"People in East Austin struggle with the often overwhelming challenges of cancer," said Texas Rep. Eddie Rodriguez. "The services provided by the LIVESTRONG Cancer Navigation Center are much needed in our community and I’m very glad to see LIVESTRONG has found a way to provide direct support to the families and medical professionals here."

The opening of the LIVESTRONG Cancer Navigation Center, co-located at the LIVESTRONG Headquarters in Austin, marks an expansion of the direct services the foundation offers to people affected by cancer, which have been available online and by phone and now for the first time are available in-person. This community-based center, one of just two facilities of its kind in the U.S., provides free, confidential, one-on-one support to anyone affected by cancer including cancer survivors, their friends and family, health care professionals and caregivers of those diagnosed with the disease. Trained, bilingual navigators are onsite to help individuals address a wide-range of needs including the following:

- **Emotional Support** - assistance coping with a cancer diagnosis, help accessing support groups, as well as peer-to-peer connections

- **Fertility Risks and Preservation Options** - information on fertility risks and help accessing discounted rates for fertility preservation options

- **Insurance, Employment and Financial Concerns** - information on employment rights and benefits, financial assistance and debt management, including insurance and billing issues as well as medication co-pay assistance

- **Treatment Concerns** - general cancer and treatment information, and matching to clinical trials

To schedule an appointment, email cancer.navigation@livestrong.org or call (512) 220-7777.

For more information, visit www.LIVESTRONG.org/GetHelp/Austin

If you know of local resources that may benefit other Life Rafters in your area please let us know. You can contact us at liferaft@liferaftgroup.org.
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