

LIFE RAFT GROUP

August 2012

In memory of Gayne Ek, Dereck Juden, Chris Kaczmarek, Ann O'Malley-Luce, Ken Schou and Daryl Wallace

Vol 13, No. 4

A Dutch youth's global search for other patients with Carney's Triad

By Jasper Smit

Since he turned 14, Jasper Smit of the Netherlands has been searching for patients like him. This is very difficult because Carney's Triad is an extremely rare syndrome. Worldwide there are about 30 known patients with a 'complete' Carney's Triad (GISTs, pulmonary chondromas, paragangliomas). Incomplete Carney's Triad affects less than 100 patients in the world. This means that they have two of the three types of tumor (mostly GISTs and pulmonary chondromas). In his own words, here is Jasper's story.

In 2004, when I was nearly 14 years of age, an X-ray of my lungs revealed two lesions in the left lower lobe. The Twenteborg Hospital at Almelo told me that it was nothing serious. We were sent home with the advice to wait for a few months and then come back to have a new X-ray made. My parents thought this was a bad idea, and insisted on a second opinion in an academic hospital. Thus, we went to a pulmonologist at the Wilhelmina Children's Hospital (WKZ) at Utrecht. Pulmonologist Dr. Bert Arets of the WKZ also considered it not a good thing to wait several months to make a new X-ray. In consultation with this doctor, it was decided to do a CT-scan under general anaesthetic, and to perform a biopsy at the same time to examine the lesions. Executing this CT-scan, the radi-



SMIT

Identifying novel treatment options by defining molecular mechanisms

By Dr. Anette Duensing

University of Pittsburgh Cancer Institute
LRG Research Team

GISTs are the most common mesenchymal tumors of the gastrointestinal tract and are caused by activating mutations in the *KIT* or *PDGFRA* receptor tyrosine kinase (RTK) genes¹⁻³. Although they can be effectively treated with the small molecule kinase inhibitor imatinib mesylate (Gleevec®)⁴, approximately 50 percent of the patients develop resistance to the drug during the first two years of treatment⁵. A Food and Drug Administration-approved second-line therapy (Sutent®)

and an array of experimental third-line therapeutic options exist⁶, but most of these compounds also target the activated *KIT* or *PDGFRA* kinases. This "kinase-centric" approach is not unproblematic, however, because the most prominent imatinib-resistance mechanism involves secondary mutations in the *KIT*/*PDGFRA* genes themselves⁷.

Our laboratory therefore uses different approaches to identify novel treatment strategies. One approach focuses on



DUENSING

See MECHANISMS, Page 12

Viva Life Fest! Join us in Las Vegas

By Phil Avila

LRG Program Associate

The Life Raft Group will be marking a milestone at *Life Fest 2012: Celebrating 10 Years of Dedication* on November 9 to 11 at the Red Rock Casino in Las Vegas.

We are at a turning point in our remarkable history as a patient advocacy organization for those who have been diagnosed with Gastrointestinal Stromal Tumor, our 10-year anniversary. It's been a wonderful journey with a com-



munity of patients, medical professionals and scientists who year by year have grown in knowledge and shown amazing courage in their battle with this rare disease. From our humble beginnings as a start-up nonprofit, the LRG has become an essential companion to those

See LIFE FEST, Page 10

See JASPER, Page 11

Ten ways to fundraise for LRG

By Christine Schaumburg
LRG Development Director

As the Life Raft Group celebrates its tenth anniversary and the achievements within the GIST community over the last 10 years, we are busy planning for the future. Our focus remains the same – to cure GIST and support those people affected by this disease until we do. In addition to the services we currently provide, the LRG is working to develop new programs to support our members while also improving our advocacy initiatives to increase GIST awareness and treatment access. The

LRG will also continue to fund our research team who recently completed a two year strategic plan to move forward based on its most recent findings.

Here are 10 fundraising suggestions that have been used by LRG members to support GIST programs and research.

1. Organize a 5K run/walk in your local area. One of our members is organizing a Dam to Dam race in Holland to raise money for GIST research. So far, more than 200 participants have registered!

2. Participation in LRG's annual holiday giving campaign is easy and makes gift buying easy for your friends and family. Once again, we'll send you holiday greeting cards in November for you to send to your loved ones. The message asks them for a contribution in honor of you.

3. It's summertime and everyone loves a barbecue! One of LRG's members just hosted his second annual BBQ for friends, family and colleagues where he set up a table with LRG pamphlets, bracelets and donation envelopes. He's raised almost \$2,000 so far. See article on page 15.

4. If you work for a corporation, a bank or even a smaller company, chances are that your employer has set up a foundation for giving to charities. Take a moment and look on your company website or ask someone in human resources about this. Please forward information to me and I'll be more successful in applying for a grant if the company

knows it has an employee that is an LRG member.

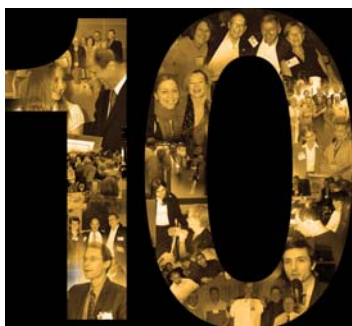
5. Planned giving is a small part of our legacy with great impact on helping sustain a cause that is important to us. If you want outside advice on this difficult subject, I can put you in contact with an experienced financial planner for a free consultation.

6. Dinner parties are social events that we look forward to and are increasingly being held to support social causes. Several of our members have hosted dinners in their homes that featured a brief presentation on GIST and the LRG's research initiative. Careful planning and an invitation that explains the reason for the gathering are key. You will be overwhelmed by the support of your friends and colleagues who have been wanting to help all along!

7. You may have read in a previous newsletter that one of your fellow GISTers ran a marathon last year. As if that wasn't enough, he sought pledges to support LRG research for a cure!

8. Planning a poker tournament or casino night sounds like a lot of work, but after helping LRG's Board President, Jerry Cudzil, host eight successful tournaments (the ninth is coming on September 13), we've become quite efficient at it! Last year, the NYC tournament raised over \$100,000 for GIST programs and research!

9. Dave Safford is one of LRG's Board members from Washington. In 2011, Dave planned a piano concert on Valentine's Day that raised over \$12,000!



Ten Years, Ten Ways

The Life Raft Group

Who are we, what do we do?

The Life Raft Group (LRG) directs research to find a cure for a rare cancer and help those affected through support and advocacy until we do.

The LRG provides support, information and assistance to patients and families with a rare cancer called Gastrointestinal Stromal Tumor (GIST). The LRG achieves this by providing an online community for patients and caregivers, supporting local in-person meetings, patient education through monthly newsletters and webcasts, one-on-one patient consultations, and most importantly, managing a major research project to find the cure for GIST.

How to help

Donations to The Life Raft Group, a 501(c)(3) nonprofit organization, are tax deductible in the United States.

You can donate by **credit card** at www.liferaftgroup.org/donate.html or by sending a **check** to:

The Life Raft Group
155 US Highway 46, Suite 202
Wayne, NJ 07470

Disclaimer

We are patients and caregivers, not doctors. Information shared is not a substitute for discussion with your doctor.

Please advise Erin Kristoff, the Newsletter Editor, at ekristoff@liferaftgroup.org of any errors.

Community events such as concerts or comedy shows are terrific fundraisers that also raise awareness.

10. Don't forget to also ask your employer if they participate in a matching gift program. If so, please take advantage of doubling your contribution. It's as easy as sending me your company's matching pledge form when you want to make a donation.

See a great idea? Call or email me at cschaumburg@liferaftgroup.org or (973) 837-9092, ext. 116.

I can help you plan and market an event, provide awareness giveaways and write invitations. I'm here to help you run any fundraiser, large or small!

Research Articles on the Science of GIST

ASCO notes: A closer look at Regorafenib

By Jim Hughes

LRG Clinical Trials Coordinator

Trial investigators for the Global Phase 3 GRID trial reported that the Bayer Pharmaceuticals' drug regorafenib (BAY 73-4506) has the potential to fill the unmet need for advanced GIST patients progressing after imatinib and sunitinib.

Dr. George Demetri of the Dana Farber Cancer Institute was the leading

Principal Investigator and presented the data for the team late in the afternoon on June 4. According to Dr. Demetri, "(regorafenib) potentially represents a new standard of care for this patient population."

From January to July 2011, 236 patients were screened and 199 entered the GRID trial in 17 countries. Dr. Demetri attributed the rapid seven-month accrual to the high degree of international collaboration. We would add that GIST patients are typically knowledgeable

about clinical trials and also willing to participate. In the trial patient profile 40-45 percent of subjects had more than imatinib and sunitinib, and 21-30 percent had received nilotinib.

Progression Free Survival (PFS) was 4.8 Months (95 percent CI 4.1-5.8) and exceeded the trial design estimate targeting a 100 percent improvement. Median OS was not reached and because of cross-over design will probably not be significant. PFS benefit was significantly present for all sub-groups analyzed except for patients exposed to imatinib for less than six months where the benefit was not as clear.

To give some perspective on the reported results, the sunitinib Phase 3 trial reported PFS was 5.6 months.

A "treatment use" trial for regorafenib has just opened up. Treatment use is another term for expanded access. It's a form of compassionate use, but organized like a trial. This treatment use trial "fills the gap" between initial data reporting (ASCO 2012) and the actual drug approval that is anticipated for early 2013. See link on ClinicalTrials.gov: <http://clinicaltrials.gov/ct2/show/NCT01646593>.

Bayer Clinical Trials Contact: clinical-trials-contact@bayerhealthcare.com.

Contact for trial location information (Phone Menu Options '3' or '4') (+)1-888-842-2937.

See REGORAFENIB, Page 8

Several clinical trials updated at ASCO

By Jim Hughes

LRG Clinical Trials Coordinator

Here are updates from the American Society of Clinical Oncology conference on three clinical trials.

Panobinostat (HDAC) Phase 1 in 3rd Line GIST:

LRG research Team member Sebastian Bauer, MD of Essen University in Germany, presented a discussion poster Saturday, June 2, on a Phase 1 trial of imatinib plus panobinostat (LBH589), a Novartis Pharmaceuticals drug that selectively inhibits histone deacetylase (HDAC). HDAC is involved in cell cycle protein expression, cell cycle arrest and apoptosis. HDAC inhibitors may also inhibit transcription of c-KIT and HSP-90 which would also indirectly inhibit mutant c-KIT.

LBH589 in GIST was first discussed by another LRG Research Team member, Maria Debiec-Rychter, at Life Fest 2006 in Dallas. Subsequent data published by Maria, Sebastian and others in two separate studies in 2009 showed panobinostat plus imatinib to be therapeutically active against imatinib resistant human GIST tumor biopsies grafted into mice and in GIST cell lines. HDAC inhibition theoretically works independently from GIST mutation status so this is a potential third line therapy.

The study objective was to establish maximum tolerable dose and safety. Imatinib 400 mg was administered along with escalating doses of panobinostat. At the maximum tolerable dose (MTD) of 20 mg administered orally three times per week with 400 mg imatinib daily there were seven adverse events at grade



3 and higher. Limited activity was seen on PET scans with one partial response and eight stable disease for a 75% benefit

rate based on metabolic response criteria. There were no objective responses (tumor shrinkage on CT scans).

AT13387 (HSP90) Phase 1 in progressing solid tumors:

Daruka Mahadevan, MD at the Arizona Cancer Center in Tucson, Arizona, reported on a Phase 1 trial of HSP90 inhibitor called AT13387 from Astex Pharmaceuticals headquartered in Cambridge, UK, and also in Dublin, California. Many will recall the Phase 3 trial of HSP90 inhibitor IPI-504 that failed in GIST because of toxicity. There were high expectations that HSP90 inhibition would work in GIST based on pre-clinical activity. Unfortunately IPI-504

See ASCO, Page 9

New gene panel takes mutation testing to a new level

By Jerry Call
LRG Science Director

A new panel that tests for mutations in 23 genes at once will help to properly classify wild-type GIST patients.

Working with next generation sequencing and in cooperation with Ion Torrent™ the new GIST panel is being developed by Christopher Corless, M.D., Ph.D., chief medical officer of the Knight Diagnostic Laboratories at Knight Cancer Institute, Oregon Health and Sciences University (OHSU). GIST patients can now be tested for mutations in 23 genes with one test (see Table 1). The Heinrich/Corless labs at OHSU have been leaders in genetic testing (genotyping) in the targeted treatment era (the Gleevec/Sutent/TKI era).



CORLESS

Wild-type GIST has been a diagnosis of exclusion. The current definition is a GIST tumor that does not have a KIT or PDGFRA mutation, the most common mutations in GIST. This definition may not be keeping up with research, howev-

er, as scientists have slowly been uncovering the underlying mutations associated with wild-type GIST. To date, mutations in wildtype GIST have been found in all four subunits of succinate dehydrogenase (SDH); SDHA, SDHB, SDHC and SDHD, as well as in BRAF, KRAS, HRAS and NRAS. Between 6 percent and 25 percent of patients with NF1 (or neurofibromatosis-related protein) may also develop GISTs. BRAF mutations might represent the most compelling reason for testing as BRAF inhibitors, used in melanoma, are clinically available. While the treatment path for those with SDH mutations is not as clear, establishing the correct diagnosis opens the possibility to try alternate therapies that are more directed at SDH-related pathways, such as VEGF receptors and IGF1R.

While the new test won't replace the current testing for KIT or PDGFRA mutations, it should greatly help in identify-



ing a wide range of mutations that might occur in wild-type GIST. In addition to mutations that have already been published, the new panel will examine a number of other genes of interest. The new GIST panel will be available starting in August.

In some cases, a biopsy does not retrieve enough tumor tissue for mutation testing. The GIST panel uses paraffin-based tissue and requires less tissue than previous testing methods. It's possible that some tissue that previously could not be analyzed due to insufficient amounts of tissue might contain enough tissue to be analyzed with the new test.

Immunohistochemistry (IHC), a technique long used to identify which proteins are present in tumor cells, may also have an updated role in identifying pediatric-type GIST as new stains for SDH are developed. However, the ability to stain for SDH may be limited to specialty centers.

Table 1: The new GIST Panel

AKT1	AKT2	AKT3	ATM	BRAF
CDKN2A	HRAS	KIT	KRAS	MAP2K1
NF1	NRAS	PDGFRA	PIK3CA	PTEN
PTPN11	SDHA	SDHAF1	SDHAF2	SDHB
SDHC	SDHD	TP53		

NIH Clinic shares information on 3 trials

By Becky Bensenhaver
Board Member, GIST Support International

The Consortium for Pediatric and Wildtype GIST Research, coordinated by Dr. Lee Helman of the National Institute of Health (NIH) in Bethesda, Maryland, convened in Bethesda, Maryland, on June 13.

The Clinic is a collaboration between clinicians and researchers to collect data,

investigate and develop treatment for Gastrointestinal Stromal Tumor patients who do not have either c-KIT or Platelet-Derived Growth Factor Receptor alpha (PDGFRA) mutations. This includes patients with Carney's Triad, Carney-Stratakis Dyad, and Wildtype GIST. These tumors frequently stain negatively for a protein called Succinate Dehydrogenase, a condition referred to as being Succinate Dehydrogenase-deficient (SDH-deficient). There are currently three clinical trials in development for this population.



The NIH Clinic Research Team

The first treatment study is being conducted by Dr. Margaret von Mehren in

Research Articles on the Science of GIST

MSKCC opens new immunotherapy trial for GIST

By Jerry Call
LRG Science Director

A new clinical trial combining targeted therapy with immunotherapy has just opened at Memorial Sloan-Kettering Cancer Center (MSKCC). This trial is the culmination of extensive pre-clinical investigations by MSKCC researchers.

Although treatment with Gleevec is highly effective, about 50 percent of advanced patients will become resistant to Gleevec within two years. Resistance remains a major problem that is not fully addressed by Sutent or other treatments. Although these drugs help, most advanced GIST patients will eventually become resistant to all current therapies.

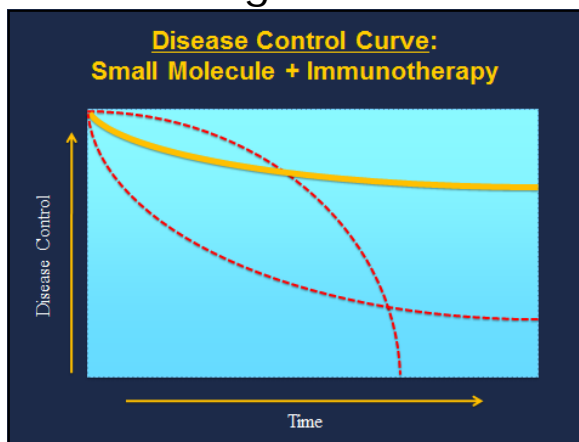
The primary mechanism of action of current GIST therapies, including Gleevec and Sutent, is inhibition of KIT signaling (or PDGFRA in PDGFRA-mutate GIST). Working independently, at least three different groups have also noted a significant anti-tumor response by the immune system when Gleevec is given to GIST patients.

The new trial will try to leverage the existing benefit of KIT inhibition by adding another drug to enhance the anti-tumor immune system response. (See Figure 1.) To inhibit KIT, researchers will start by giving GIST patients dasatinib (brand name SPRYCEL®), a drug that is already approved for leukemia, but not for GIST. After a one week run-in period on dasatinib, patients will be given ipilimumab (brand name YERVOY™). Ipilimumab is a new drug that was recently approved to treat metastatic melanoma. Although both drugs are approved, the combination still needs to be tested for safety and maximum dose, so this is a Phase I trial. Dasatinib and ipilimumab are both made by Bristol-Myers Squibb.

Dr. Vinod Balachandran, Ronald

DeMatteo, MD, FACS, and colleagues recently published some of the results of their work on how Gleevec affects the immune response in GIST patients.

Figure 1



Dr. DeMatteo is the Vice Chair, Department of Surgery and the Head of the Division of Surgical Oncology at MSKCC. Dr. DeMatteo is well known in the GIST community as a surgeon and also as a leader in trials of adjuvant Gleevec. MSKCC has had a long history in immunotherapy that traces its roots back to the end of the 19th century, when another surgeon, Dr. William Coley, noticed that some sarcoma patients that got an infection seemed to have dramatic responses to their cancers.

The recent MSKCC research appeared in *Nature Medicine* and was titled, “Imatinib potentiates antitumor T cell responses in gastrointestinal stromal tumor through inhibition of Ido”. Ido is an enzyme (a type of protein), that increases (catalyzes) the conversion of tryptophan into metabolites. These metabolites promote the development, stabilization and activation of T_{reg} cells. These cells are special immune system cells that regulate the immune response. T_{reg} cells tend to reduce the immune response; too many T_{reg} cells and the immune system cannot mount an effective antitumor response, too few T_{reg} cells and the im-

mune response may be too strong and it could attack normal tissue as well as the tumor.

Some cytotoxic agents, such as cyclophosphamide, can reduce T_{reg} cells throughout the body. While this can increase the antitumor response, it can also increase autoimmune responses. Therefore, a strategy that reduces T_{reg} cells only within the tumor is an attractive alternative. DeMatteo and colleagues found that imatinib was able to achieve this selectivity by reducing Ido within the tumor, resulting in less T_{reg} cells within the tumor but not having an effect throughout the rest of the body. With less CD8+ T cells in the tumor, more tumor destroying immune cells, CD8+ T cells, were able to get to the tumor.

The MSKCC team’s initial research was in a GIST mouse model, developed in the lab of Dr. Peter Besmer. Dr. Besmer has also shown that dasatinib works a bit differently than Gleevec in GIST. Although both inhibit KIT, dasatinib (a KIT/Src inhibitor) also inhibits signaling between cells and their environment, through inhibition of the focal adhesion kinase (FAK)/Src pathway. This survival pathway is actually increased with treatment with imatinib. Conversely, in addition to inhibiting KIT, imatinib inhibits STAT3 and STAT5 in GIST whereas dasatinib does not.

After the mouse experiments, the results were repeated in GIST cell lines (GIST-T1 and GIST-T1R) and finally in samples from 45 matched blood and tumor specimens that were obtained from 36 GIST patients undergoing surgery. The team noted that both regulatory T cells and T cells with antitumor capabilities were able to infiltrate the GIST tu-

Alianza GIST joins forces with Brazilian partner

By Piga Fernandez Kaempffer
Alianza GIST Administrator

Alianza GIST and Oncoguia have formalized a new partnership to work together to benefit GIST patients in Brazil.

The first goal of this partnership is to identify GIST patients in the different regions of Brazil, contact them and give them information about the disease, educate them on their treatment, give them emotional support and guide them on the

best ways to access treatment.

Brazilian GIST patients will greatly benefit from this partnership because through Oncoguia they will have access to updated information that Alianza GIST and the Life Raft Group have on the latest advances in research and GIST



treatments. Also, GIST patients will have access to specific diagnostic tests, such as mutational testing

of their tissue samples.

We hope that this partnership will be successful and lead to regular meetings with patients, formation of a center of excellence for GIST and creation of quality control of procedures for testing of tissue samples.

Agreement in Guatemala to benefit GIST patients

By Silvia Castillo de Armas
President, ASOPALEU

An agreement to secure the entry of Gleevec for Guatemalan GIST and chronic myeloid leukemia patients was reached with the Central American country's government July 10, following advocacy efforts by Novartis Pharmaceuticals, Alianza GIST and the Guatemalan Association of Patients With CML (ASOPALEU). The matter was given urgent priority and passed to the Office of Social Programs of the First Lady (*Secretaría de Obras Sociales de la Esposa del Presidente* – SOSEP), entity responsible for granting the corresponding governmental authorizations.

The directors of ASOPALEU presented the vice minister of Public Health with a copy of the Cartagena Declaration, which includes the rights and needs of patients with blood diseases. They also reaffirmed their willingness to work together with the Ministry of



Public Health in benefit of ASOPALEU's community attended at Public Hospitals San Juan de Dios and Roosevelt, and to facilitate their access to quality medication.

They expressed their gratitude to Novartis for including Guatemala in the Glivec International Patient Assistance Program (GIPAP), which will improve access for GIST patients.

"This agreement will stop the entry of copies of Gleevec, and assure that GIST patients in Guatemala are receiving effective medication," said Sara Rothschild, LRG Global Relations Director and coordinator of Alianza GIST.



Poker tournament set for Sept. 13 in New York City

By Will Sumas
LRG Program Associate

It's almost time once again to bring your best poker face to the Big Apple! Our 9th annual NYC Poker Tournament, hosted by Life Raft Group Board President, Jerry Cudzil, will be held on Thursday September 13, 2012, at the Midtown Loft and Terrace.

The format of the tournament will be Texas Hold'em with a buy-in of \$500. The winner will receive a \$10,000 seat at the 2013 World Series of Poker. Thanks to generous donations, our second and third prize winners will enjoy Broadway show tickets for two and dinner at the Palm Restaurant.

Patrick Moore, last year's winner, had a great time at the World Series of Poker. He said, "as a pure and true amateur I held my own for 9 hours."

Don't miss this year's event, it is sure to be a full house!



What's up, Doc? Social media and healthcare

By Jim Napier
LRG Program Associate

Social Media, such as Twitter, Facebook and LinkedIn, are an integral part of the daily lives of millions of people all over

the world. People of all ages and backgrounds use social media, and now even healthcare providers are jumping on the bandwagon.

Many physicians and hospitals have created an online presence. Patients can now become more involved in their health, by staying up-to-date with their physician online through tweets, blogs and Facebook fan pages.

Social Media allows for two-way com-

munication between you and your doctor or hospital. Patients can share inspirational stories, photos, and ask questions. It is important to be careful to protect your privacy, and make sure that you do not over share information for everyone to see. Here are some tips to help you

take control of your online health:

—Take Control - Create your own online presence on Facebook/Twitter to stay up-to-the-minute on news that is important to you.

—Get Connected - Build your own online knowledge base of trusted sources. (Doctors, Hospitals, Advocacy Groups), much like you would with an

address book.

—Ask Questions - There is no such thing as a dumb question when it comes to your health, so be sure to ask away. Sending private messages on Facebook, or a direct message (DM) on Twitter is often preferred.

—Share - Becoming an expert is easier than you might think. Any article or information that you think is important to you, may in fact be important to others so do not be afraid to share, and share often.

Be sure to add the Life Raft Group to your social media

knowledge base. Follow us on Twitter at <http://twitter.com/Liferaftgroup> and Like us on Facebook at <http://facebook.com/Liferaftgroup>.



Times series underscores LRG research team's approach

By Phil Avila
LRG Program Associate

The first in a series of *New York Times* articles by science writer Gina Kolata on new approaches to cancer treatment underscored the type of cutting-edge approaches taken by the Life Raft Group's own team of researchers.

The article tells the story of Dr. Lukas Wartman, a cancer researcher who was diagnosed with adult acute lymphoblastic leukemia, a disease he had devoted his life to studying. Through some amazing efforts by his team of researchers and his doctors he has been in remission after be given a drug familiar to patients with GIST: Sutent. But it wasn't an easy path.

Dr. Wartman's team decided to search for the gene mutation that was causing the cancer, and through whole genome sequencing found not only the malfunctioning gene, but matched it to a drug that would shut it down: in this case, it was Sutent, which is primarily used to treat advanced kidney cancer but also

has become a second-line treatment for GIST. So far, the approach seems to have worked. It will now be tested in a clinical trial.

The Life Raft Group's research team uses tissue samples to do gene sequencing in their search for a cure for GIST. Indeed, GIST is considered a model cancer in that some of the genes involved and the mechanisms for shutting them

down have been identified, and targeted treatments like the one that worked for Dr. Wartman are available.

To read the full *Times* story, go to: www.nytimes.com and search for cancer research.

Coming soon, a look at colon cancer research and parallels to the LRG team's approach.

Pfizer Offering Sutent Support Program

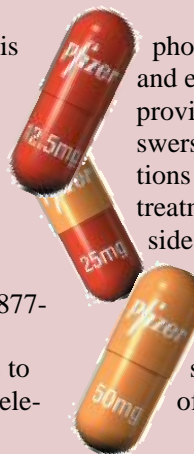
Pfizer Pharmaceuticals is offering Sutent in Touch, a program to support GIST patients on its drug Sutent.

The program is free and patients can sign up at www.sutent.com/in-touch-program.aspx, or by calling (1-877-578-8368).

Sutent in Touch links patients to Oncology Certified Nurses by tele-

phone, mail and e-mail, providing answers to questions about treatment and

side effects. The nurses work together with patients to monitor their well-being while on Sutent. A journal is given to everyone who signs up, so that they can keep track of how they are doing.



REGORAFENIB

From Page 3

PFS appeared to be equal in both Exon 11 and Exon 9 sub-groups. This is similar to the limited data we have for sorafenib and in contrast to imatinib where Exon 11 seems to do better than Exon 9 at 400 mg and in contrast to sunitinib where Exon 9 seems to do better than exon 11.

We don't have comparable data for sorafenib. However, very limited data from the Phase 2 trial (Kindler et. al. ASCO 2011) showed comparable overall beneficial response between exon 11 (n=22) and Exon 9 (n=4).

This data again raise the question of whether there is a better second line choice for Exon 11 than sunitinib...a question that can only be answered by a future head to head clinical trial. Note: this type of trial is rarely accomplished due to the number of subjects required, and the related cost.

Most significant Adverse Events (AEs) (Grade 3 and higher) on regorafenib were very similar to those reported at ASCO 2011 for the Phase 2 sorafenib trial.

Interestingly, Dr. Demetri reported that AE related drug discontinuation was proportionally higher in the Placebo group, where 6.1 percent of patients on regorafenib discontinued because of AE's at median 23 weeks exposure and 7.6 percent of patients on placebo discontinued because of AE's at median seven weeks exposure.

If regorafenib for GIST is approved by the FDA it will be the third drug approved for advanced GIST and the first for third-line use. It has been over six years since the last drug (sunitinib) was approved for advanced GIST for second-line use.

overcome.

*It is important to note that ASCO reports are considered conference reports and they are not the same as peer reviewed published reports. In the pantheon of evidence-based science, conference reports are somewhere below the gold standard--peer reviewed formally published data. They may eventually be published in a peer-reviewed journal, but until then they are not at the higher level of evidence.

New research supports role for crenolanib

By Phil Avila

LRG Program Associate

A new study published by Clinical Cancer Research found that crenolanib is a potent inhibitor of imatinib-resistant PDGFRA kinases associated with Gastrointestinal Stromal Tumor, including the PDGFRA D842V mutation found in about 5 percent of GISTs.

Crenolanib is an investigational new drug being developed by AROG



Pharmaceuticals. Crenolanib is a tyrosine kinase inhibitor that acts by inhibiting PDGFRA and PDGFRB.

The study was done by Michael C. Heinrich and colleagues and was titled "Crenolanib Inhibits the Drug-Resistant PDGFRA D842V Mutation Associated with Imatinib-Resistant Gastrointestinal Stromal Tumors."

Based in part on these results, a phase II clinical study has been initiated.

Table 1

Grade 3 or Higher AE's		
AE	Sorafenib	Regorafenib
Hand Foot Syndrome	45%	20%
Hypertension	21%	24%
Diarrhea	8%	5%

The two Bayer drugs, regorafenib and sorafenib, are very similar in design (regorafenib differs by the addition of one fluorine atom) but behave differently as drugs. Regorafenib is taken in 160 mg per day doses for three weeks of a four week cycle versus sorafenib which is taken in twice daily in doses of 400mg each with no break. Regorafenib is also a relatively stronger inhibitor of c-KIT (~10X). Both drugs inhibit BRAF, c-KIT, PDGFRb, Raf, and VEGFR 2/3. Regorafenib differentially inhibits RET and VEGFR1, and to a lesser extent TIE2. Sorafenib differentially inhibits Flt3. Dr. Demetri reported that regorafenib has active metabolites that carry the drug's effect into a one-week off period.

These differences may not have carried into the side effect profile. (See Table 1). Investigators reported "no new or unexpected safety findings with regorafenib".

Two Other Drugs

Clinical trial designs, and particularly controls, have figured into trials of two other drugs for GIST that have attempted to fill the third-line slot. IPI-504 Phase 3 in advanced GIST was terminated in April 2009, when the trial was stopped by the safety committee due to toxicity. The IPI-504 trial had a placebo control which arguably limited accrual and therefore patient exposure. At the June 2010 ASCO investigators reported that nilotinib Phase 3 in advanced GIST did not achieve its efficacy goals when other TKI's were used as controls. The trial accrual process resulted in some non-progressing patients entering the trial and affecting the outcome. But the residual efficacy of imatinib and/or sunitinib in the third line control group was a significant design hurdle for nilotinib to

ASCO

From Page 3

shared the toxicity profile of the first generation of HSP90 inhibitors that were based on geldanamycin, an antibiotic derived from soil bacteria.

AT13387 is a second generation small molecule HSP90 inhibitor discovered by Astex Pharmaceuticals via a screening process. AT13387 is being developed under a five-year agreement with the National Cancer Institute

The primary objective of the trial was establishment of a MTD dose. Patients were dosed once or twice weekly in four-week cycles with three weeks on and one week off the drug. AT13387 is given as an IV infusion over one hour. Fifty-three patients with different solid tumor types have entered the trial. Six patients experienced adverse events that were generally reversible. The MTD will be 260 mg/m² administered once weekly. Seven GIST patients entered the trial. One GIST patient with both a primary Exon 11 mutation (Del 558-572) and secondary Exon 17 mutations (D816H & D820H) had an objective Partial Response for eight months. Two other GIST patients had stable disease lasting seven months and eleven months. The Phase 1 trial continues to accrue at the MTD. A Phase 2 study of imatinib plus AT13387 is ongoing at eight sites in the US.

Masitinib (c-KIT) Phase 2 in Second Line GIST

Antoine Adenis, MD, Principal Investigator from Centre Oscar Lambret, Lille, France, presented results from the Phase 2 trial for advanced GIST comparing 23 patients receiving masitinib to 21 receiving sunitinib for imatinib resistant GIST. Dr. Adenis reported that Median Progression Free Survival (PFS)

was virtually the same, 3.7 months for masitinib and 3.8 months for sunitinib based on investigator measurements using RECIST criteria. Median Overall Survival (OS) for masitinib had not been reached. For sunitinib it was reported at 16 months.

Patients taking masitinib experienced significantly fewer serious side effects and fewer stopped treatments for adverse events.

Side Effects

Most side effects on masitinib were reported as Grade 2 or less and followed a pattern typical of tyrosine kinase inhibitors.

The most serious side effects reported on masitinib were skin rash and low neutrophils (white blood cells). See Table 1. In a separate report Dr. Axel LeCesne updated the five year results of the first line masitinib phase 2 trial in 30 newly diagnosed advanced GIST pa-

gressing on sunitinib did not have an option to receive masitinib. In his response Dr. Adenis acknowledged that Dr. Benjamin was right, this was an issue.

It was also noted by another questioner that progression free survival was relatively short for both masitinib and sunitinib patients.

In his conclusion, Dr. Adenis indicated that a Phase 3 trial of masitinib versus sunitinib sponsored by the manufacturer had recently started and that the primary endpoint would be Overall Survival.

In sum, the report of the trial of masitinib versus sunitinib seemed promising but raised several issues about reported results and trial design. In light of the results of the Phase 2 trial presented in June, it will be important for the phase 3 trial comparing these same two drugs to address the PFS and overall survival questions.

Masitinib also seems to have a relatively better side effect profile. Hopefully a Phase 3 comparison trial can establish an improvement in side effects and quality of life. Given the harshness of many tyrosine kinase inhibitors, a TKI that can demonstrate equivalent clinical benefit and at the same time definitively reduce side effects and improve quality of life would be a major benefit for GIST patients.

Table 1: Side Effects for patients on Masitinib (n=23)

	Grade 1-2	Grade 3
Nausea/Vomiting	57%	
Rash/Puritis (itch)	48%	4%
Diarrhea	48%	
Edema	43%	
Neutropenia (low neutrophils - WBCs)	9%	
All patients	96%	17%

tients. Dr. LeCesne reported that for patients taking masitinib in that trial adverse events occurred mainly during the first year, particularly over the initial three months, with good long term tolerance experienced thereafter.

During the discussion after the presentation Bob Benjamin from MD Anderson asked if masitinib had an Overall Survival advantage because patients in the sunitinib arm were not able to cross-over to masitinib. Seventeen of 23 of patients receiving masitinib were given sunitinib on progression. Patients pro-

Mark your calendars!

• The Life Raft Group's 9th Annual NYC Poker Tournament will be held in New York City on **September 13** at the Midtown Loft and Terrace.

• **November 9-11** the LRG will hold Life Fest 2012: Celebrating 10 Years of Dedication at the Red Rock Casino in Las Vegas.

• The Connective Tissue Oncology Society will host its annual conference in Prague, **November 14-17**.

• Faster Cures will hold its Partnering for Cures conference **November 28-30** in New York City.



LIFE FEST

From Page 1

with GIST, and a leader among cancer patient organizations.

So we'll be celebrating those 10 years and those who have walked side by side with us at Life Fest.

Registration, hotel and sponsorship information is available on our website, along with a draft agenda, at www.liferaftgroup.org/members_lifest.html.

On Friday November 9, we will take time to recognize those who have contributed to the fight against GIST, honoring at a gala dinner a select group from the patient, medical, scientific and pharmaceutical communities who have furthered the understanding and treatment of GIST and made a difference to the survival of patients.

The following awards will be given: Dr. Jonathan Trent will be named *Humanitarian of the Year*; Dr. Michael Heinrich will be named *Clinician of the Year*; Alianza GIST will receive the *Global Award of Excellence*; Kim Tallau will be named *Allan Tobes Volunteer of the Year*; Emilie Van Karnabeek Pit will be named *Arnie Kwart Philanthropist of the Year*; Brian Rubin will receive the *Jeroen Pit Science Award*; and Sanofi Pharmaceuticals will receive the *Patient Outreach Award*.

Those to be inducted into the *GIST Hall of Fame* include The Baldor Family, Dr. Jerzy Lasota & Dr. Markku Meitinnen, LRG Executive Director Norman J. Scherzer and The Max Foun-

dation.

Saturday and Sunday, November 10 and 11, will be full of workshops and seminars on the latest GIST developments. There will be plenty of opportunity to get answers to your questions from the many GIST experts who will be attending Life Fest.

As a part of the event, the LRG is publishing a commemorative book highlighting our achievements and pulling together memories from the past decade. You can help us mark this milestone by

contributing to the book. It's a perfect place to share a story, memory or photograph from your GIST journey or to let us know how the Life Raft Group has helped you. If you would like to contribute to this book, please

go to sponsorship tab on Life Fest web page.

Our journey has been marked by innovations and achievements, including a comprehensive Patient Registry and GIST Collaborative Tissue Bank that provide valuable data for research, the formation of our own team of scientists working collaboratively on a cure for GIST, and the emergence of scores of local chapters. We will highlight these accomplishments at Life Fest and glimpse into the future.

More than anything else, Life Fest offers an opportunity for the GIST community to come together to celebrate our progress and move toward finding a cure. It promises to be informative, insightful and inspirational.



The Red Rock Casino



NIH

From Page 4

partnership with the Sarcoma Alliance through Research and Collaboration (SARC). This trial will utilize OSI-906, an insulin-like growth factor inhibitor (IGF-1R). IGF-1R is highly expressed in Pediatric and many adult Wildtype GISTs. Initial trial recruitment will be at Fox Chase Cancer Center in Philadelphia, Pennsylvania, with hopes of expansion to multiple clinical institutions in the future.

Second Study

The second treatment study will utilize a drug called Vandetanib, an inhibitor of vascular-endothelial growth factor (VEGF) and endothelial growth factor receptor (EGFR). The efficacy rationale is based on the response of a type of kidney cancer bearing a genetic mutation similar to SDH-mutant GIST. This study will open initially at the NIH in Bethesda. If results are promising, additional trial accrual sites will be added.

The third treatment study is designed specifically to help understand how to administer Sutent to younger people who have GIST and to better understand how well it works. Dr. Katherine Jane-way from the Dana-Farber Cancer Institute will supervise this trial.

Although Sutent has previously been used to treat Pediatric and Wildtype GISTs, neither OSI-906 nor Vandetanib have. As it is not yet known which of the treatments will prove most efficacious, the trial designs allow patients to participate without sequence restriction.

As treatments are becoming available, the NIH Pediatric and Wildtype GIST Clinic is transitioning from being held every six months to once a year. The hope is that patients will be receiving treatments through trial participation and will be seen at the various institutions for ongoing follow up.

To read more about the 9th Pediatric and Wildtype GIST Clinic go to: <http://www.gistsupport.org/pediatric-gist-carney-triad/nih-clinic-for-pediatric-gist-news-from-the-9th-nih-clinic.php>

JASPER

From Page 1

ologist suggested that it would be wise to do not only the lung scan, but my whole body, and so they did. During this whole body scan, they saw a tumor of approximately 10 cm in my stomach.

In September 2004, a biopsy was taken of the tumor in my stomach. A few days later, on September 23, 2004, the day that the famous Dutch tear-jerking singer, André Hazes, deceased, we received the results of the biopsies. It proved indisputable that the tumor in my stomach was a Gastrointestinal Stromal Tumor. They explained briefly what GIST cancer is, and that it was never discovered in a child in The Netherlands till then. At the Academic Medical Centre (UMC) at Utrecht, of which the WKZ is part of, they had no experience with GIST in children. The advice was to go for treatment to the Emma Children's Hospital (part of Academic Medical Centre, AMC, at Amsterdam).

A week later, I was admitted to the Emma Children's Hospital. There they first performed a keyhole surgery (an endoscopy), to inspect what the tumor in my stomach looked like. They also had taken a piece of tissue from the tumor, and sent it to the laboratory.

My doctors, Dr. Arnauld Verschuur (pediatric oncologist), and Dr. Daniël Aronson (pediatric surgeon), explained the treatment plan to us. Initially, a stomach operation would be performed in order to remove the primary tumor. After rehabilitation, part of my left lung, in which the lesions were situated, would be removed. At first, the doctors were assuming that the whole stomach had to be taken out. During the operation (on October 28, 2004) it appeared that about 70 percent of my stomach had to be removed. This piece was the lower part of my stomach, and they also took away a piece of intestine. The tumor indeed had a diameter of 10 cm.

A fortnight later, being well-recovered from the stomach surgery, the lung surgery was performed. During this operation the lower lobe of my left lung was

removed. At a MIBG-scan and a PET-scan it appeared that GIST cells had spread (metastasized) to my liver, about 20 spots. Also there was a paraganglioma behind the breastbone (stable disease, with one hotspot in the aortic arch with non-elevated catecholamine).

In order to treat the GIST metastases in my liver, I have taken imatinib, from 2004 to 2006. Because of imatinib my situation is stable since 2004. Dr. Verschuur characterized my situation as a Carney's Triad, an extremely rare syndrome.

When I reached the age of 18, I could

no longer be examined at the department of Pediatric Oncology at the Emma Children's Hospital at Amsterdam. It also happened that Dr. Arnauld Verschuur moved to France, to start working in a children's hospital at Marseille. I then decided to consult Dr. Winette van der Graaf in the future, at the University Medical Centre St. Radboud (UMC St. Radboud) at Nijmegen. At first, I had to go for a MRI-scan every four months, but now, this is every six months! The results are very positive each time till now, and I am, despite many side effects, confident about my future.

How Jasper and I worked together

By Ellen van Arem de Haas

The creation of www.carneytriad.com

In 2011, I came in contact with Jasper Smit. At his request in 2012, my son Maarten and I made this special website for him. Are you a GIST Carney's Triad patient, or are you a parent of a child with Carney's Triad, contact us at <http://www.carneytriad.com>.

One patient already contacted us when www.carneytriad.com was just being launched. We were greatly astonished when a young woman with a complete Carney's Triad contacted us via our website, as she happens to live only a 25 minute drive from Jasper's city. What a joy and recognition!! Henriëtte and Jasper met immediately and she went for a second opinion to his own expert oncologist Dr. Winette van der Graaf at Nijmegen.

Dutch representation since 2012 for UK-based PAWS-GIST

In 2011, I brought Jasper in contact with Jayne Bressington of PAWS-GIST in the United Kingdom. This organization is founded by mothers of teenage daughters with GIST, and is a member of GIST Support UK. They are working in partnership with experts in America and Europe, aiming to improve treatment and care of these patients in the United Kingdom, and beyond. And, of course, to search for a cure for young GIST patients. At the request of Jayne, Jasper and I are now the Dutch representation of PAWS-GIST, something we of course love to do!

HAPPY CANCER-VERSARY TO JIM!



July 7th marked my 11-year Cancer-versary. Last year for #10, we had a great celebration with some friends and family with hopes built on #11 and here it is. Now let's go for #12!

—Jim Carmichael

MECHANISMS

From Page 1

dissecting the mechanisms of action of imatinib to identify the molecular players that are involved in imatinib-induced apoptosis and quiescence⁸ (LRG's October 2009 Newsletter issue). In a second step we are using our knowledge to target these molecules for therapeutic purposes.

We have previously shown that imatinib treatment of GIST cells leads to increased amounts of a certain cellular protein, histone H2AX^{9,10} (also see LRG Newsletter December 2007). In our study, we could show that this process is causatively involved in killing GIST cells. A second finding in our study involved the notion that the amount of H2AX contained in a cell is regulated by a pathway that controls protein degradation, the so-called ubiquitin-proteasome machinery.

This discovery was the first step at asking whether it would be possible to increase H2AX levels in GIST cells by a different means than by treatment with imatinib. Based on our findings above, one way of increasing the amounts of H2AX would be by inhibiting its degradation. This could be done through inhibition of the ubiquitin-proteasome machinery. In fact, the concept of proteasome inhibition has been of interest for the pharmaceutical industry for a while, and a number of compounds already exist.

Bortezomib (Velcade®) is such a drug and so far the only FDA-approved compound of its kind. Bortezomib is currently used for the treatment of multiple myeloma and mantle cell lymphoma¹¹. We therefore wanted to test the hypothesis that increasing the amounts of H2AX by inhibiting its degradation with the proteasome inhibitor bortezomib would have a therapeutic effect in GIST cells¹².

We started out testing an array of different concentrations of bortezomib asking whether the compound can induce

cell death in GIST cells. Employing various methods for experimental readout, we could confirm that bortezomib is active in GIST. In fact, it was able to kill cells at the same concentrations that are reportedly used to kill multiple myeloma cells – indicating that our results comprised a specific effect of bortezomib in GIST.

However, we were not satisfied with

is known that GIST cells are critically dependent on the expression of oncogenic KIT¹³, its downregulation most likely plays a substantial role in bortezomib-induced apoptosis in GIST.

It was surprising, however, that treatment with a drug that inhibits degradation of proteins (hence leading to their accumulation) should result in decreased levels of KIT. How could we explain this curious finding?

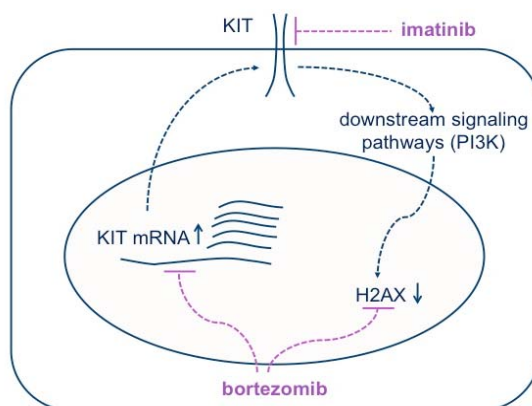
One way through which cells control protein levels is regulating the rate at which they are produced.

This process starts with the transcription of the protein's DNA sequence. When transcription from DNA is reduced, less messenger molecules (RNA) are being made and hence less protein is produced. We therefore tested the possibility that bortezomib could affect the transcription of the *KIT* gene. Indeed, we found that bortezomib affected the levels of KIT messenger molecules (RNA). However, further tests pointed to the fact that bortezomib affects transcription on a more general level by reducing the transcription of many genes across the cell's DNA. (It has previously been shown by other researchers that protein degradation is essential for transcription to function properly¹⁴.) In addition, our group has previously found that GIST cells are exceptionally sensitive to transcriptional inhibition⁹. Therefore, our results explain very well, why GIST cells are affected by transcriptional inhibition through bortezomib.

Taken together, the above results point to a dual mechanism of action of bortezomib in GIST: increasing the amounts of H2AX within the cell, but also decreasing the amounts of active KIT through transcriptional inhibition

Because our initial experiments were carried out in an imatinib-sensitive cell line model (GIST882), we next tested whether bortezomib is active in imatinib-resistant GIST cell lines (in collaboration with LRG Research Team member Sebastian Bauer, University of Essen, Germany). After all, the main goal of

Figure 1



knowing that bortezomib is able to kill GIST cells. We wanted to know more about its mechanism of action and whether our hypothesis was correct – that bortezomib acts through increasing the levels of histone H2AX by inhibiting its degradation (See Figure 1).

So, in a next step we tested whether H2AX levels increased after bortezomib treatment. Using a technique called immunoblotting, we were indeed able to show that the amounts of H2AX were higher in cells that received bortezomib, seeming to prove our hypothesis. By carrying out a number of other experiments, however, we found out that H2AX upregulation is most likely not the only mechanism of action of bortezomib.

While searching for the possibility of an additional mechanism of action of bortezomib, we detected to our surprise that it led to a dramatic reduction of KIT protein levels accompanied by loss of KIT tyrosine phosphorylation. Since it

MECHANISMS

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our study was to find new therapeutic options for imatinib-resistant GIST patients. To our surprise, these cells were even more sensitive to bortezomib than GIST882 cells. Moreover, cells that were directly derived from an imatinib-resistant tumor of a GIST patient also responded to bortezomib treatment, just as we had hoped.

We then went one step further and treated mice engineered to get GIST with bortezomib (in collaboration with LRG Research Team member Brian Rubin, Cleveland Clinic). Although the results from these studies were not as clear-cut as the studies in the tissue culture dish, some mice clearly responded to the treatment. These promising results indicate that bortezomib indeed has an effect *in vivo* further corroborating our approach.

Taken together, our results provide a compelling rationale for clinical trials testing the efficacy of bortezomib in GIST patients¹⁵. However, bortezomib has known disadvantages with respect to adverse effects and its efficacy in solid tumors – potentially because of problems concerning its bioavailability. Because of these issues, there is an increased interest in the development of second-generation proteasome inhibitors with improved pharmacologic characteristics. Some of these compounds have already entered advanced clinical trials for multiple myeloma. Our laboratory has recently started testing several of these novel compounds in GIST with very promising preliminary results.

In summary, our approach to dissect the molecular pathways that are involved in imatinib-induced cell death were successful in identifying a novel therapeutic target (histone H2AX) and have led to the discovery of a new therapeutic strategy for the treatment of GIST, namely, the use of inhibitors of the ubiquitin-proteasome machinery.

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GIST friends meet in Oregon

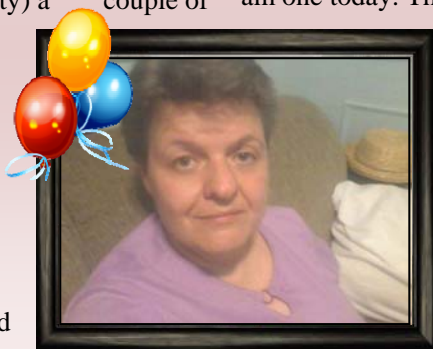


Left to Right: Dirk and Lori Niebaum from Montana, Vicki Dotson and Richard Becker, who have just moved to Oregon from Wisconsin, Sandie Ross from Portland, and Tim and Gail Mansfield from Portland.

HAPPY CANCER-VERSARY TO PATTI!

I am one today

Hello, LRG family:
Since joining (the email community) a couple of months ago I haven't really posted much. I have, however, been reading your posts and following all that's been going on with everyone.
I am awed by all of you. Your passion and



determination humbles me. Your experiences and knowledge with life and GIST guide me.

Today is my one year cancer-versary. I am one today. This event eclipses my own birthday, Christmas, New Years and every other holiday combined. No one else would understand how that is but you. My family doesn't understand. I didn't get one single message of congratu-

lation today from them and that's OK. It's the kind of thing you have to live through to value. They didn't really live it. I did.

So, I raise a glass to all of you. I thank you for your support and all the information you've shared with me about your lives, your status, the condition of GIST and the disease itself.

The only difference between us and most others is that we KNOW what it is we have. This disease makes living all the more important, love all the more special. We aren't here to play. We're here for keeps.

God bless you all. Here's one for you and I. May God offer us many more.
Cheers

—Patti Williams

TRIAL

From Page 5

mors. Compared with resistant tumors, Gleevec-sensitive tumors contained greater numbers of CD8+ T cells (as well as CD3+ T cells). In two of three patients that had both Gleevec-sensitive and Gleevec-resistant tumors removed at the same time, they observed a higher ratio of CD8+ T cells to T_{reg} cells in the sensitive tumors. In addition, in 13 patients they tested, the ratio of CD8+ T cells to T_{reg} correlated with IDO protein expression, suggesting that inhibiting IDO was primarily responsible for the positive effect on immune cells.

After noting the positive effect of CD8+ T cells in the mouse model and responding GIST patients, Dr. DeMatteo and colleagues sought another method to influence T cell response. They added an inhibitor of CTLA-4 to Gleevec. CTLA-4 (cytotoxic T lymphocyte-associated antigen) is a known modulator of effector T cells, T_{reg} cells and Ido. In their mouse model, this combination significantly decreased tumor size.

As stated previously, ipilimumab was recently approved for treatment of metastatic melanoma. Ipilimumab is a drug that blocks CTLA-4. It is the first drug that has been shown to improve survival in advanced melanoma patients, increasing median overall survival from six

months (in patients that received a different drug) to 10 months. While this is good by cancer standards, the really interesting thing about this drug is that some of those patients had a very long response to the drug, the kind of response that cancer patients hope for. In one trial testing ipilimumab with interleukin-2, 17 percent of melanoma patients had a complete response. With longer follow-up, the results of three trials (alone or in combination with interleukin-2 or gp100 peptides) suggest that some patients have a very long response; with 14 of 15 patients that had a complete response, still in complete response with a median follow-up of 54+ to 99+ months.



CARVAJAL

The principal investigator for the new clinical trial will be Richard D. Carvajal, MD. Dr. Carvajal is a medical oncologist with a special interest in melanoma and sarcoma. Dr. Carvajal has extensive experience working with ipilimumab.

The trial will have two stages; the first stage will be open to all GIST patients, both sensitive (no previous Gleevec and/or Sutent) and resistant. Once the highest safe dose of the combination is

determined, the second stage will open. In the second stage, only third-line patients (resistant to Gleevec and Sutent) will be eligible. This is a really interesting and potentially important approach. One possibility is that the sensitive patients could have a really good response to this combination, since they would potentially have KIT inhibition (dasatinib) as well as Ido inhibition (which is KIT/ETV4 dependent) due to the dasatinib and CTLA-4 inhibition from ipilimumab. Thus the inclusion of Gleevec-naïve as well as Gleevec/Sutent resistant patients will allow researchers to explore the relationship between KIT/Ido inhibition to response in this combination.

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Dereck loved writing and movies

Dereck A. Juden, 38, a former resident of the Forest Grove community late of Beaverton, died Friday morning, June 29, 2012, at his home in Beaverton, Oregon.

Dereck was born May 9, 1974, in Hillsboro, Oregon, the son of Danny and Linda (VanLoo) Juden. He was raised and received his early education in the Newberg community, until moving to the Forest Grove community, where he completed his schooling, having been a graduate with the Forest Grove High School class of 1992. Following his graduation, he attended Pacific University where he majored in Creative Writing. While attending college he worked at the Forest Grove Theater and at Piccadilly's.

He was united in marriage to Wendy M. Peterson on October 7, 2006, in Las Vegas, Nevada. Following their marriage they have made their home in the Beaverton community. Dereck and Wendy celebrated their five-year wedding anniversary this past October.

Dereck worked at The Kroger Company Regional Headquarter Office in Portland for the past eight years as a Help Desk Manager.

Among his special interests he enjoyed

watching movies, as he was a movie buff, painting miniatures and role playing with his group that met weekly.

Survivors include his wife, Wendy M. Juden, of Beaverton, Oregon; his father and his wife, Dan and Barb Juden, of

Hillsboro, Oregon; his mother, Linda VanLoo, of Sheridan, Oregon; his grandparents, Clifford and Janice VanLoo, of Forest Grove, Oregon; his sister and brother-in-law, Angela and Cliff Fowler, of McMinnville, Oregon; his stepbrother, Troy Sandberg, of Forest Grove, Oregon and his-in-laws, Eric and

Kay Peterson, of Beaverton, Oregon. Also surviving are his nephew, Devin Fowler and niece, Roselin Fowler and numerous aunts, uncles and cousins.

The family suggests that contributions be sent in remembrance to The Life Raft Group, 155 Rt. 46W, Suite 202, Wayne, New Jersey 07470, in his memory.



Dereck wrote a blog for the Life Raft Group. He recently commented: 'While it's true that there are quite a few things that upset me, being angry at god for having cancer just isn't one of them.'

Gayne was active volunteer in Texas

Gayne Ek, 78, of Allen, Texas, passed away June 18. He was born September 5, 1933, in Flint, Michigan, to Henry and Ruth Ek. On January 29, 1971, Gayne married Joleta Haney in Plano, Texas. He is survived by his children, Gil Ek (Sheryl) of McKinney, Texas, Cindy Ek, Cheri Ek Rizer (Ken) of Cedar Rapids, grandchildren, Ryan Leach, Carly Ek, Andrew, Nicole, Anna and Will Rizer, great-grandchildren, Spencer and Bryson Leach, and a sister, Janine (Richard) Merrick of Minnesota. Gayne graduated from Franklin High

School in Cedar Rapids and received a Bachelor of Science degree in Electrical Engineering from Iowa State.

He worked for Collins Radio, Pan Am, then moved to Dallas and partnered with a co-worker to start Forum Communications,

where he was president until his semi-retirement in 2003. Gayne and Jo enjoyed traveling the world and visiting family and friends. He was an active volunteer and did a variety of charity work including Crew Chief for a Dallas chapter of Habitat for Humanity and various work for child advocacy centers. Gayne is preceded in death by his wife, Joleta, and his parents, Henry and Ruth.



Member's BBQ raises funds and awareness in Virginia

Life Raft Group member Jason DeLorenzo held his annual "DeLoBQ" fundraiser last month in Alexandria, Virginia. The BBQ has raised almost \$2,000 thus far, and donations are still coming!

Jason explains the growing success of his event, "People look forward to this

event every year. Despite a massive storm that closed roads and knocked power out of almost a million area residents the night before, attendance was very good. This year's events included a bluegrass band, swimming, karaoke, great food, and a rock, paper, scissors competition."



Jason with his girlfriend, Jill.

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