

GIST TALKING

Volume 1, Issue 1
Summer 2008

www.gistsupport.org

INSIDE THIS ISSUE:

| | |
|---------------------------------|----------|
| <i>Pediatric GIST/ NIH</i> | 2 |
| <i>ESMO with Anna</i> | 3 |
| <i>Nutrition and Dr.D'Amato</i> | 4 |
| <i>Why Music ?</i> | 5 |
| <i>Marina Sez !!</i> | 6 |
| <i>Living to be 90!!</i> | 7 |
| <i>History of GSI</i> | 8 |

Special points of interest:

Marina just returned from Milan, Italy representing GSI at a "New Horizons" meeting for GIST and CML- with prominent Researchers and Mds..

For more NIH/ Pediatric GIST info, see below—

<http://www.gistsupport.org/ped-carney-gist/nih-clinic-for-pediatric-gist.php>

GSI Visits ASCO

Carolyn Grobe, Marina Symcox and Sherri Janousky attended ASCO May 30 -June 2 in Chicago at McCormack Place on Lake Michigan. On the massive exhibit floor, Big Pharma was pushing pens and coffee drinks; one company even provided a compass, undoubtedly to help us find our way back and forth to the educational sessions in the East or West buildings of this vast complex.



Carolyn Grobe, Marina Symcox, and Sherri Janousky attend ASCO for GSI

It seems just as challenging to present the huge amount of information presented at ASCO. To assist in this process, here is the list of GIST-related abstracts:

http://gistsupport.medshelf.org/Main_Page#Member_Reports_from_GIST_Conferences

National Institutes of Health Hosts First ever Pediatric GIST Clinic

Becky Bensenhaver- GSI Science Comm., Phyllis Gay- GSI Pediatric List Director, Dr.Janeway-DFCI, Constantine Stratakis, MD- NIH; Su Young Kim, MD- NIH ; with his back to the camera is Michael LaQuaglia, MD- MSKCC



On June 19, 2008 14 pediatric GIST patients traveled from all over the US as well as Europe to meet in Bethesda Maryland at the National Institutes of Health for the groundbreaking initial Pediatric GIST Clinic.

The NIH sponsored clinic has been in the works for months with the original announcement of the clinic being made in November, 2007. Extensive planning and the bringing together of the top GIST professionals was coordinated in order to initiate this initial and hopefully ongoing clinic for pediatric GIST.

Moms meet and connect faces with internet friendships.

It is a situation that most Mothers would not wish on their worst enemy. Mothers just wish that they could trade places with their child; though, this is not possible in reality. However, some Moms who have found themselves in this unfortunate situation, have found support through the GSI sponsored pediatric/Carney Triad list serv. Some of these Moms were able to connect in person and meet each other and the daughters that they speak of so often when posting on the GSI pediatric list serv.

The pediatric GIST/Carney Triad list serv has become not only a source of vital medical information and treatment comparison tool for ped GIST patients/family members, but truly an emotional support group with increasing tendencies towards a true internet family support group for this very small group of rare pediatric GIST patients/family members.

Recently at the first pediatric GIST clinic held June 19, 2008 some of the Moms who have been posting regularly were able to connect and see the faces that match all of the "typing" over the internet. Jennifer Boa said several times that she was just amazed at "how pretty/ and good looking all of the ped GIST patients were".

Phyllis Gay- Ped/GIST and Carney Triad list serv coordinator
GSI Pediatric Coordinator

Most of the group repeated over and over that they immediately could tell who the person was when they saw them for the first time from their personalities coming through over the internet.



Dr. Stratakis- NIH, Nora Lynn, Stefani Peck, Sile Bao, Jacqui Ryan, Liz Skree, Jason Delorenzo, and Stephanie Kast-



Jennifer Bao and daughter Sile, Toni Young and daughter Ashley, Stephanie Kastner with Mom Patty, and Phyllis Gay with daughter Kara

IGF: Treatment Potential for GIST

Insulin-Related Growth Factor (IGF) signaling appears relevant to GIST, including wild-type GIST for which the activating mechanisms have been unknown. Three 2008 papers describe a relationship:

- Braconi et al in Italy found that strong expression of either IGF-1 or IGF-2 was correlated with risk group, mitotic rate, and actual recurrence on follow-up. IGF-2 expression was strong in 70% of the exon-9 GISTs in this study. All GISTs expressed the receptor IGF-1R.
- Agaram et al from Memorial Sloan-Kettering compared tissue from pediatric GIST to adult wild-type GIST and found higher expression of IGF-1 and receptor IGF-1R in the pediatric tumors based on microarray analysis of transcriptional profiles.

Tarn et al from Fox Chase found amplification (extra copies) of the IGF-1R gene in wild-type adult GISTs and a single Carney Triad GIST and paraganglioma. The investigators found an anti-IGF-1R drug (NVP-AEW541) to be effective in controlling two GIST cell lines and recommended that drugs targeting IGF-1R be investigated in GIST.

Drug treatments targeting the IGF growth factors and receptors are already in trials for certain sarcomas and other solid tumors. Because the IGF pathway seems to impact several common carcinomas, continued development of drugs for controlling it seems likely. Additional research regarding IGF pathway relevance to GIST should provide treatment directions soon.

Trials for pediatric GIST and other wild-type GIST may soon be planned by NIH and Fox-Chase. For more details link to our website story. <http://www.gistsupport.org/posts/igf-signals-in-gist134.php>

By Julie Royster PhD, GSI Science Committee Coordinator



ESMO—May 2008 by Anna Costato

GSI member and Italian GIST Patient Group Coordinator Anna Costato attended the annual Meeting of the European Society of Medical Oncology Meeting and reports some highlights. Anna has a daughter with pediatric GIST who is in college and doing well, 7 plus yrs. now.

Italian GIST Website <http://www.gistonline.it/>

The new ESMO guidelines state:

“Mutational analysis has predictive and prognostic value, so that it is strongly recommended in the diagnostic work-up of all GIST.” This statement is a new addition into the guidelines and baseline mutational analysis is always advised. On the contrary, mutational analysis of progressing disease (secondary resistance) is not recommended and it has no therapeutic value because:

- progressing lesion or lesions bear different secondary mutations (you can find different mutations even within the same mass);

- in theory, all visible masses should undergo biopsy (with the risk to biopsy non progressing/responding lesion, too)

- the finding of different mutations may have a scientific value but no benefit for the patients as it will not change the therapeutic approach as, in principle, it should lead to a different drug approach for each mutation.

During one panel discussion the above was emphasized as doctors said many patients believe that mutational analysis should be performed even in case of progression for secondary drug resistance.



Adjuvant Gleevec after surgery and surgery after metastasis

It was re-confirmed that adjuvant Gleevec is investigational, thus far.

Whether it has efficacy in Overall Survival and whether it does not precipitate secondary resistance will be answered not earlier than 2016-2018, when current trials will start showing some results.

Clinical trials are being continued on 1y, 2y and 3y efficacy of adjuvant Gleevec both in progression free survival and overall survival .

Discontinuation of Gleevec:

The first French studies regarding Gleevec discontinuation after 1 yr and 3 yrs showed that it leads to progression; and a clinical trial is now investigating on effect of discontinuation after 5y (results are still unknown).

Surgery of residual disease following Imatinib in metastatic, responding GIST is also investigational. It is unknown if it has value in progression free survival or overall survival if compared to drug therapy only.

A phase 3 randomized clinical trial will start this coming Summer, with the participation of Italian, French, German, Scandinavian and English cancer centres plus others in Australia.

Micro GISTS



Micro-GIST (dimension 1 to 10 millimeters) are incidentally found with unexpected frequency in general population (in 35% of stomach surgeries and in 23% of autopsies).

This phenomenon is common in the case of other cancers (such as colon cancer) where this setting is considered as pre-cancerous condition. However, this has no explanation in the case of GIST and it is inconsistent with its rarity as a disease.

These small nodules are real GISTs, as confirmed by pathology result, but it is unknown why many of them (the majority?) never develop into diagnosable disease and, in fact, they have only been found incidentally so far.

This subject needs further study.

Potassium balance by Shirley Beck

One of the possible side effects of taking Gleevec is the alteration of the body's fluid balance, causing fluid retention. The common treatment for this problem is to prescribe a diuretic. The action of the diuretic may deplete potassium levels in the body. This is not true of all diuretics and if you ask your pharmacist, he can tell you about your diuretic.



minerals controls the rate and force of it's contractions.

Potassium loss is increased by diarrhea OR loss of part of the colon (whose job is to re-absorb salts and minerals). If potassium loss is severe it can cause heart failure.

Your potassium level can be found by testing your blood. Normal level is a narrow range of 3.5 - 5 mEq/liter. Potassium is excreted by the body through urine and sweat.

In order to maintain potassium balance, you must consume potassium via food or medicinal supplement. In normal health and activity, most Americans will consume an adequate amount of potassium in their diet.

Potassium plays an important role in muscle function and nerve conduction. The heart is a muscle and potassium along with other

While most of us are concerned with low level potassium, the potassium level in the body can also become elevated and cause heart problems. The most frequent cause of high potassium levels are kidneys that function poorly and are not excreting proper amounts of fluid. The other common cause is uncontrolled diabetes.

The principal sources of potassium in the diet are oranges (juice), bananas, potatoes, tomatoes and dairy foods. Here is a link to other high-potassium foods.

<http://www.health.gov/dietaryguidelines/dga2005/document/html/appendixB.htm#appB1>



Shirley Beck is a retired nutritionist

Potassium plays an important role in muscle function and nerve conduction



Gina Z. D'Amato, MD, recently joined Emory University in Atlanta as Director of the Sarcoma Medical Oncology Program at Emory Winship Cancer Institute based at Emory Crawford Long Hospital. In addition to overseeing and managing Winship's Sarcoma Program, Dr. D'Amato sees sarcoma patients at Emory Crawford Long Hospital. Her interests also include sarcoma research and clinical trials.

Meeting Dr. D'Amato, by Donna Capps

We flew to Atlanta for my husband, Ronnie, to see Dr. D'Amato, since Dr. Blanke left for Canada. We had a FABULOUS experience with the office staff. The front desk people were friendly, personable, helpful, and FUNNY!! They made us feel really at ease. Felicia, the nurse practitioner was also professional, caring and helpful. She asked questions and answered ours. She had obviously read the chart.

When Dr. D came in, she had also read the chart and was able to quote from it, without notes!! She was great, taking time to explain, ask questions and listen to and answer our questions and concerns. She spent over an hour with us, and NEVER looked at the clock once. She outlined her observations and we decided TOGETHER on a plan for the future, with tests, follow up, etc. She said to contact her by phone or e-mail if there are any changes or if we have any other questions. She is personable, down to earth and quite easy to talk to. You do not feel like she is talking at you, which is very refreshing. It was well worth the trip across the country to see her.

To read Donna's interview with Dr. D'Amato – http://gistsupport.medshelf.org/Emory_Winship_Cancer_Institute

Marina Sez!

Cancer Explained—the Gas Pedal and the Missing Brakes

Marina Symcox, PhD , Bio-Chemist ; GSI co-manager



CANCER MADE EASY...You too can be a cyberspace scientist, researching from the University of Google, and taking graduate courses from Entrez Pub Med.

Lesson 1: "The Perils of Stuck Gas Pedals and Broken Brakes:"

1) Cells are planes, trains, and automobiles. 2) Gas pedals make the car go. A stuck gas pedal is not a good thing but the car will not wreck if the brakes still work. 3) Brakes make the car stop. Provided that the gas pedal is not stuck and is used judiciously, then the car won't wreck if the brakes are functional--not broken.

KIT is a gas pedal. When KIT becomes mutated in key regions (exon 11) it can become a stuck gas pedal. A stuck gas pedal all by itself is not enough to cause the cell to behave out of control provided the brakes in the cell work.

Making sense of an abstract: what the heck is it telling you? Oh my, it is full of words that I don't know! Well you need lesson #2 first. Then you are ready for the abstract, and you really don't need to understand the specialized words.

Lesson #2 "Doublemint fun, two, two mints in one:" (oh boy, tell me more)

1) Cells have two copies of everything. One from the mom, one from the dad.

2) Cells have two copies of the gas pedal KIT. If you think about it, only one of the two sets needs to become mutated "stuck in the on position" to force a problem with acceleration around tight bends on mountain roads.

3) Brakes--two sets of brakes. Tumor suppressors are a fancy name for cell brakes. There are a lot of different braking systems in a cell. But for GIST, probably certain braking systems are more important than others.

4) If one copy of KIT becomes a stuck gas pedal (exon 11 mutation), and both copies of the brakes work, then you are probably okay. You might have this situation for years, and never know it because the brakes are keeping things in check. BUT, what happens if one or both sets of brakes go out? If both sets of brakes go out, the car is gonna crash big time. The car might be okay with one set functional, but it is a precarious situation...braking is not as forceful, and if the second set fails, then again...disaster--a car out of control. A car, train, or plane crash. Or a tumor.

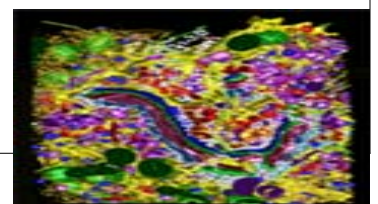
Back to the abstract with the techno jargon. All it is telling you is that a lot of GIST tumors seem to have lost one of the two copies of parts of chromosome 22. "LOH" "Loss of Heterogeneity" (Heterogeneity means you still have both copies of chromosome 22--the one from your dad and the one from your mom). So, the term LOH means that one of these two parental copies is gone.

The assumption is that chromosome 22 must contain an important set of brakes in GIST. When KIT is mutated to be a stuck gas pedal (exon 11 mutations again), you still don't have GIST. You need broken brakes also. It seems that one or more genes on chromosome 22 must be the important braking system, due to the fact that a lot of GIST seem to have lost certain regions of their second copy of chromosome 22. NF2 is mentioned...

With LOH, there is still the other copy of the chromosome...but only one copy. It is possible that the braking gene on this remaining chromosome is defective and doesn't work too well. Or it might be a dosage problem, in that one gene copy doesn't make enough of the braking protein to keep the stuck gas pedal KIT under control.

Hint: When looking at abstracts---read the first sentence and then skip to the end and read the conclusion. Don't read the stuff in the middle until AFTER you have figured out what the first sentence and the conclusion are saying. Or you can even skip the stuff in the middle, because it is details that you won't remember anyway.

> End of lesson ----- http://gistsupport.medshelf.org/Marina_Sez



Why Music? By Bob Spiegel

Former Disney marketer and Jazz musician

One day in September, 2005, I returned home from five music-less weeks in two hospitals in Gainesville, Florida after having a huge GIST diagnosed and removed. Being a lifelong jazz fan and NEVER being without music in my home or car (except when sleeping), I have a CD collection of many hundreds and subscribe to XM Satellite Radio to make sure my life is devoid of 'white space'. Well, as I gingerly sat down in my white recliner after being delivered from those institutions of higher experimentation and clicked on my stereo as XM was playing Count Basie's "Kid From Red Bank", I cried.

I'm Cured

Just a few days later, I attended a big band concert featuring a band that recreates the sound of the Stan Kenton Orchestra. At the end of the encore, I thrust my arms into the air and proclaimed, "I'm CURED!"

Music does that to me. And later, I started to think that maybe music of some other kind might mean as much to somebody else and have the power either to soothe their



Music does that to me

rattled nerves, break their unwelcome boredom, or lift them up after perhaps weeks of silence and inattention. Then, I wanted to enlarge the program and GSI was the most logical place to turn because it fit in so well with their mission. Hospitals everywhere have learned of the value of 'holistic' healing; that patient well-being is not entirely the responsibility of surgeon's hands or medication's effects. Injecting art, music, animals and crafts have equally starring roles in bringing patients back to normal life. Now, Tufts University has released a report claiming proof that listening to music after surgery is as effective as 325mg of acetaminophen.

Healing Through Music is born!

So that's how "Healing Through Music" was born. It's now a service of GSI and you are encouraged to take advantage of it. There's no fee, return is not required, and we probably have music in our growing library that will help YOU. Just go to the GSI website, find "Healing Through Music", click on it, fill out the form, and the worker bees will fulfil your request.

Just another way GISTers are helping GISTers cope.

www.gistsupport.org

Handy Tips

GIST SUPPORT WIKI – A Wiki for Everyone to use!! http://gistsupport.medshelf.org/Main_Page

DID YOU KNOW

For those EARLY or LATE appointments at MDA (Houston) when your motel's shuttle bus isn't running, call the University of Texas Shuttle Service (713) 792-2890 about an hour before you need to depart your hotel.



A little bit of what you fancy does you good

Fun Hospital Gown

Katherine Somervell created the great idea of making hospital gowns in fun fabrics for lengthy hospital stays. Kathy says it was easy to follow the simple pattern on the web. The pattern includes velcro at the shoulders and even a front slit and pocket for a heart monitor. See:

www.lazygirldesigns.com/

Living to Ninety *By Brenda Bannon GIST patient*

In March 2002 at age 36 my boys were 7, 4, and 1. Ready to leave my verbally and mentally abusive husband, I hardly expected my doctor to find “innumerable, inoperable, malignant liver tumors”. My cancer journey began with a neuroendocrine cancer misdiagnosis and staying with my husband.

Gleevec just in Time

Unlike most GISTs, my tumors grow very slowly and most doctors suspect I've had them for decades. In God's perfect timing, my tumors weren't discovered until one month after FDA approval of the first successful treatment for GIST (Gleevec). Getting premier treatment meant 3-4 hour car trips to Dana Farber Cancer Institute in Boston, MA. Escaping the clinical trial visit-intensity enabled me to continue working. 800 mg daily stabilized my tumors for 2 years. Side effects were bearable, though worsened the longer I took it.



From Gleevec to OSI-930

Leg two of my journey was two years of stability on Sutent. My team at DFCI worked diligently on dosing to keep tumor growth at bay. A few side effects, but by the end my bone marrow (even with transfusions) couldn't keep my hemoglobin much above 8 and my white counts were very low. Despite this, I managed to leave my husband in August 2006 with my boys.

With pneumonia and tumor growth in December 2006, and disqualifying for AMN-107, in March 2007 I was the first GIST patient on OSI-930.

3 Boys 2 dogs and a Bunny

The trial began with weekly Boston trips, then every three weeks. A single mom working full-time with three boys, two dogs, three cats, a bunny, a guinea pig, and divorce proceedings, going to Boston every three weeks challenged me. But within 3 weeks my belly shrank, blood counts rose, and I felt great. No side effects.



I became the Original OSI-930 GIST Guinea Pig Pioneer (OOGGPP). In March 2008, my team convinced the trial folks to let me come every 6 weeks!!

I turned 43 in April. Most who know me know I plan to outlive GIST and live to 90 (with the Lord's help) sliding into my 90th birthday all "lived out" and ready to go home. I have lots to do between now and then, including getting my boys through college, into careers, and married, and spoiling my grandbabies. Most importantly, I expect to raise three strong men of Christ. I know that isn't "politically correct" and I mean no offense – but my boys are my heart, and teaching them to know, love and follow Christ is my most passionate life goal

“I plan to outlive GIST and live to be 90”

The First Edition of GIST Talking!

Welcome to this first edition of GIST Talking, the newsletter for GSI. This is to be a quarterly production, and we hope that you will all have a hand in contributing to it. We welcome news, tips, jokes, and messages of hope. Most of all this publication is meant to be a window on the wonderful community of GISTers that thrives on the internet.

GSI has an actively maintained website with all the latest scientific, treatment and clinical trials news. But there is also a very active email group of over 1000 members from all over the world—the biggest such group of GIST patients. And these GISTers do much to help each other with experience, advice, a listening ear, a sympathetic shoulder. We also have a wealth of dedicated scientists who go to the conferences, meet the experts and question them, have good contacts in the pharma industry, who are working for the membership. This is a truly interactive self-help group who are one for all and all for one. Come join us!

Email to join or send newsletter contributions to:

gsi@gistsupport.org





HISTORY of GSI

by

Lee Ann Lamb , GSI Co-manager

In the spring of 2002, a small group of patients and caregivers shared a dream about a free and open support group that welcomed anyone with an interest in GIST, without any requirement to share any personal information. Through a truly grass-roots effort a new support group, GIST Support International (GSI), began to take shape.

GSI went live on the Internet in March 2003. Since that time, GSI has grown to be the largest GIST patient group in the world with over 1000 members in over 28 countries. Today, the GIST Support International web site, www.gistsupport.org, is the source of the most up-to-date scientific and medical information about GIST to be found in one place. It is also full of patient information about coping with cancer from diagnosis on. GSI has remained committed to its original ideals of a volunteer organization, with no one receiving a salary or gaining personal profit. The main goal is to empower each individual touched by GIST to be his or her own best advocate. Whether caregivers, family members, or patients, GSI provides support and education to anyone who needs help. Thanks to everyone on the mailing list who shares their experiences, or answer questions daily and all the others who volunteer quietly to keep GSI functioning as a successful non-profit group, this goal is being met.

- Email: gsi@gistsupport.org
- Lee Ann Lamb, Co-Manager
 - Marina Symcox, PhD, Co-Manager
 - Ginger Sawyer, Treasurer
 - Joan Marie Hayno, Secretary
 - Yvonne Blixt, List manager
 - Donna Capps, Wiki Team
 - Bradley Clark, Newsletter
 - Bill Davis, Newsletter
 - Barbara Doré, Newsletter Editor
 - Bob Spiegel, Healing Through Music
 - Julie Royster, PhD, Sci. Coordinator
 - Phyllis Gay, GSI Pediatric Coordinator

GSI is run entirely by volunteers without salaries or personal gain

Volunteers from GSI attend medical conferences and pharmaceutical meetings, usually at their own expense. GSI has earned the respect of many medical professionals, aided, in part by the face-to-face interactions during these meetings. Our reputation as a fair and impartial GIST support group helps ensure that these professionals are willing to help when we need guidance or assistance.

GSI members come up with both ideas and implementation, and we are always open to new ideas and new volunteers!

