



PEDIATRIC GIST



May 2006

In memory of Jonathan Montague

Vol. 7, No. 4

Reflections on lessons learned from First Pediatric Weekend

By Sue Cohen

Note: Cohen is the Supervisor of Creative Arts Therapy from Tomorrows Children's Institute at Hackensack University Medical Center in New Jersey.

I look out the window and admire the new blossoms on the trees, the bright green of the grass, the clear light blue sky, and the early spring flowers. I am reminded that through the changes of the seasons come opportunities for reflection, contemplation and renewal. These blessings seem the most richly taught by young people with chronic life threatening illness, because it is through their wisdom, that we can truly experience the essence of what it means to live honestly and fully.

Clearly people who do not have GIST can never really understand the challenges that are placed from experiencing ongoing treatments, being poked and prodded, and having to discuss intimate physical details with hospital staff. However, if those of us

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Membership meeting will include Pediatric GISTers

By Elizabeth Braun

As September approaches, plans are being laid for Life Fest 2006, the LRG's third general membership meeting. It will take place in Dallas from September 15th to 17th. Special sessions and events for pediatric patients and their families will be included in the meeting. This will be the second pediatric family gathering. There will be many activities specifically for our pediatric

families.

Holding the meeting at Life Fest 2006 will allow those Pediatric GISTers that are at a crossroads between childhood and adulthood the opportunity to meet other adults that are struggling with GIST, while still participating in the pediatric-related activities.

There are activities planned specifically for the pediatric families. For starters, there will be a slumber party on Friday evening. Movies, food and fun along with time to chat, will give our families

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Adams Mark hotel hosts Life Fest 2006, Sept. 15-17



Understanding pediatric GIST may provide important clues

By Jerry Call

Gastrointestinal Stromal Tumors (GIST) in young people is known as pediatric GIST. It is thought to be very rare. But is it as rare as we think? Are the 27 young members of The Life Raft Group a significant portion of the pediatric GIST patients in the world? As we try to answer that question, let's also take a closer look at some of the different types of pediatric GIST.

Like adult GIST, pediatric GIST can be further divided into subgroups. The most familiar and perhaps the most common type does not seem to have a distinct name so let's just call it "Pediatric GIST." It most commonly affects girls between the ages of about 6 to 18 and almost always starts in the stomach.



DR. CARNEY

The second well-known type of GIST affecting young people is called "Carney's Triad." It is named after Dr. P. Aidan Carney who first described it in 1977. Patients with Carney's triad

may have several different types of tumors including GIST, pulmonary chondroma, and/or functioning extra-adrenal paraganglioma. If any two of these tumors are present, a diagnosis of the "triad" can be made, particularly if age and sex factors are supportive. It is important that patients less than 35 years of age who have any one of the three tumors be examined periodically in search of the others according to Dr. Carney. By 1983, 24 cases had been reported and, by 1999, 79 cases had been reported. Carney's triad affects mostly younger females but there is one report of an 84 year old man who was found to have Carney's triad during an autopsy.

In 2002, Dr. Carney and Dr. Constantine Stratakis reported on a new syndrome that was similar to, yet distinct, from Carney's triad. They had found 12 patients in 5 families with two parts of the "triad," paraganglioma and GIST. Since this condition appeared to be inheritable and the "true Carney's triad" did not, Carney and Stratakis concluded that this syndrome was different than Carney's triad and called it "Familial Paraganglioma and Gastric Stromal Sarcoma" (GIST is sometimes called "Gastric Stromal Sarcoma"). The patients varied in age from 9 to 46 years old at diagnosis with 9 of the 14 patients under the age of 23.

When looking at multiple medical reports, it appears like there may be one more type of pediatric GIST. The youngest GIST patients of all may be born with GIST and need surgery soon after birth. This type of GIST, called neonatal or congenital GIST, appears to affect both boys and girls (although

girls are more common) and seems to start in the intestines instead of the stomach. We found 6 cases described as GIST in newborns, however there seems to be some doubt about whether or not these are really leiomyosarcomas or GISTs.

A search of the internet found seven scientific papers that report more than one pediatric GIST patient from a single institution. These papers provide important insights into the mysteries of pediatric GIST. The Life Raft Group pediatric GIST database forms an eighth source of this type of data and is the second largest series.

Dr. Sonam Prakash, Dr. Christina Antonescu and others of Memorial Sloan-Kettering Cancer Center (MSKCC) in New York reported on 15 cases of young people with GIST. Of the 350 GIST patients in the MSKCC database there were 5 patients less than 18 years old (1.4% of all of their GIST patients) and 10 patients between 18 and 30 years old. Dr. Antonescu is the principal pediatric GIST researcher for The Life Raft Group research project.

The MSKCC team wanted to look at the differences between the younger patients (below 18) and the older patients (18 to 30 years old). They found that the younger patients tended to fit the "classical" pattern of pediatric GIST. The older group had characteristics of both adult GIST (such as a high rate of KIT mutations) and pediatric GIST. The tumors of patients in the older group tended to express genes in patterns that were similar to the younger pediatric GIST patients rather than the adult GISTs. Two of the

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the time and opportunity to share experiences and develop friendships. We are also looking into the possibility of a skating event and some fun local activities.

Sue Cohen, of Tomorrow's Children at Hackensack University Medical Center in New Jersey, hopes to join us again after spending last May with families at the Pediatric GIST Weekend. She will run activities so everyone can get to know each other. There will be time for creative expression, discussion and empowerment.

We are also planning an educational program with lectures from world-renowned GIST experts who will address pediatric GIST-specific issues. Additionally, there will be an update on the pediatric GIST component of the Life Raft Group Resistance Research Project.

We are hoping to provide a program for pediatric GIST families that addresses their needs and interests. If anyone has suggestions for the pediatric

program, please e-mail Elizabeth at ebraun@liferaftgroup.org or call the office at (973)837-9092. The best way to create a program for your needs is to let us know what you want to discuss at the meeting.

There will be opportunities for the pediatric families to join the rest of Life Fest 2006. They are welcome to attend any of the seminars focused on adult GIST. They will also have the opportunity to join the other Life Fest attendees on Friday evening when there will be a dinner for our entire membership.

Dr. Jonathan Fletcher, our lead researcher, has penciled the event into his calendar so that he may join us. He will provide an update on the entire Resistance Research Project. The first set of progress reports should be coming in from our researchers at the time of the meeting, so there should be some exciting updates for our membership to hear and learn about.

There will also be updates on clinical trials and the latest treatments available.

Information on access to treatment will be presented. Educational workshops for both caregivers and patients will be highlights. Most importantly, there will be time and opportunity to meet with others that are struggling with the same issues on a daily basis and to discuss common obstacles and triumphs.

Meeting in a central location such as Dallas will allow GISTers from all over the country to attend. Many factors went into choosing the location, including the cost of airfare and hotel accommodations. Sarah Buch, who planned our previous Life Fest meeting, has worked hard to find us both the ideal city and hotel. Located in the heart of Dallas, the hotel provides access to many different sightseeing locations.

With September so close, much effort is being put into organizing the events of the weekend. We are all looking forward to meeting the members of the Life Raft Group that we talk with so frequently via phone and e-mail.

Antonescu helps break ground on pediatric GIST

By Norman Scherzer

One area focus for the Life Raft Group Resistance Research Project is pediatric GIST. Dr. Cristina Antonescu from the Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City was selected as the group leader for this vital segment of the project. Dr. Antonescu and MSKCC will also be hosting the pediatric tissue bank.

Dr. Antonescu became interested in pathology while she was studying in Romania. Although she started her pathology residency at Bucharest University in Romania, she was forced to restart when she chose to move to the Lenox Hill Hospital in New York. As a fellow under the guidance of Dr. Marc Ladanyi at MSKCC, Dr. Antonescu focused on the detection and

molecular characterization of prognostic markers in sarcomas. She shifted her focus to GIST when the opportunity arose. With the support of Dr. Ronald DeMatteo and Dr. Peter Besmer, she was able to start her own lab. Currently her lab specializes in the pathogenesis of GIST. She spends much of her time troubleshooting molecular techniques and supervising the work of her team composed of three very dedicated individuals, Tianhua Guo, Grace Wong and Narsi Agaram. Her team has been a leader in the characterization of the genetic aberrations that are responsible for GIST, including pediatric GIST. Dr. Antonescu has worked assiduously and meticulously to develop her outstanding reputation. She is well-regarded as both pathologist and researcher. She feels that it is



Dr. Antonescu will host the first pediatric tissue bank at Memorial Sloan-Kettering Cancer Center in New York.

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patients in the older group had characteristics that strongly resembled those of the younger group, and the MSKCC doctors noted that at least one of these cases may have developed in childhood and not detected until adulthood.

Some of the things the MSKCC team and others have noted to be typical of pediatric GIST include:

- Affects mostly females.
- Almost always occurs in the stomach, often as multiple nodules.
- Tumors do not usually have the KIT or PDGFRA mutations that occur in the vast majority of adult GISTs.
- Metastases to the lymph nodes appear to be more common than adult GIST.
- The tumor cells tend to be shaped differently. Pediatric GISTs tend to resemble “epithelioid” cells (more rounded and more similar to typical non-sarcoma type cancers), while adult GISTs tend to have a “spindle” shape.

Dr. Victoria Price, Dr. Alberto Pappo and others from the Hospital for Sick Children in Toronto, Canada reported on six young GIST patients. They reviewed hospital records that covered an 11 year span. They had treated five of the patients at their hospital and had acted as a consultant for the pathology of the sixth patient. Four of the patients were girls and two were boys. One of the boys and one of the girls had additional tumor(s) that were typical of “Carney’s Triad.” Another boy (age 13) did not fit the usual pattern of pediatric GIST because of his gender (male) and the fact that he had a mutation in the c-kit gene (which is more typical of adults with GIST).

Dr. Monica Cypriano, Dr. Najat Daw and others from St. Jude Children’s Research Hospital in Memphis, Tennessee reported on seven young GIST patients. This series was somewhat

unusual in that only two of the seven patients had tumors that started in the stomach. The patients in this study were diagnosed over a 40 year time span between 1962 and 2002.

There are reports of two cases from Ireland and three cases from Atlanta, Georgia in the United States. All five of these cases started in the stomach.

A 1999 report by Dr. Jody Z. Kerr and others reported four cases of Gastrointestinal autonomic nerve tumors (GANTs). GANTs are tumors that are very similar to GISTs. The authors noted many features that were similar to pediatric GISTs. Given the incomplete understanding of GISTs in 1999, the question that arises is whether these tumors would have been classified as GISTs if they were examined using today’s standards.

The largest case series comes from the Armed Forces Institute of Pathology (AFIP). This study looked at 44 cases of pediatric GISTs that were submitted to the AFIP from the United States and Canada between 1970 and 1996. Patients in this study ranged from 5 to 21 years old at the time of diagnosis. Only GISTs with a primary tumor in the stomach were included in this study. These 44 cases represented 2.5 percent of the stomach GISTs submitted to the AFIP in this time frame (44 of 1782 patients).

The AFIP series is particularly striking in its gender distribution according to age. They report 24 females between the age of 6 and 15 and no males. Between the ages of 16 and 21,



Sile Bao, age 16, is one of the pediatric GIST patients that benefits from this research.

however, the gender distribution is completely different with 11 males and 8 females. They did report one 5 year old male.

When you combine all of the reports some patterns begin to emerge (subject to the considerable limitations of this review). Patients seem to form several groups according to age and primary tumor location:

- **Newborns**-primary tumors tend to be located in the intestines.
- **1 to 3 years old**- We were unable to find any reports of patients diagnosed between the ages of one to three.
- **4 to 5 years old**- Three of four were located in the intestines, only one in the stomach.
- **Summary-Newborns to 6 years old**-Seems to affect both females

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| Age Group | Miscellaneous Sources | AFIP (Stomach only) | Total |
|---------------------------|-----------------------|---------------------|------------|
| Less than 1 yr old | | | |
| <i>Female</i> | 4 | 0 | 4 |
| <i>Male</i> | 1 | 0 | 1 |
| <i>Unknown</i> | 1 | 0 | 1 |
| 1 to 3 yrs | | | |
| <i>Female</i> | 0 | 0 | 0 |
| <i>Male</i> | 0 | 0 | 0 |
| 4 to 5 yrs | | | |
| <i>Female</i> | 2 | 0 | 2 |
| <i>Male</i> | 2 | 1 | 3 |
| 6 to 15 yrs | | | |
| <i>Female</i> | 36 | 24 | 60 |
| <i>Male</i> | 9 | 0 | 9 |
| 16 to 21 yrs | | | |
| <i>Female</i> | 10 | 8 | 18 |
| <i>Male</i> | 2 | 11 | 13 |
| Over 21 yrs | | | |
| <i>Female</i> | 7 | 0 | 7 |
| <i>Male</i> | 5 | 0 | 5 |
| GRAND TOTAL | 79 | 44 | 123 |

and males with a tendency towards intestinal primary (includes small intestine, cecum and colon). Probably needs more expert GIST pathology review to verify that these are true GISTs and not leiomyosarcomas.

- **6 to 15 years old-** The vast majority are females and the vast majority have a stomach primary. This group appears to be the largest and probably comes closest to being representative of "Pediatric GIST." It is interesting to note that 8 of the 9 males in this group had primary tumors in the stomach, just like the girls.
- **16 years and up-** Although still

dominated by females and a primary tumor location in the stomach, we start to see a transition towards adult GIST with both more males and more non-stomach primary tumors.

Some observations and questions

It is interesting to note that there are more cases of Carney's triad reported in the literature than pediatric GIST; but in the eight reported series of patients (including The Life Raft Group series) Carney's triad seemed to be a distinct minority. This raises the question of the ratio of pediatric GIST to Carney's triad. Are there a lot more pediatric GIST patients than the 79 reported Carney's triad patients?

Questions

1. Are the newborn GISTs really GISTs?
2. Is the intestinal location of GISTs in patients below six years old an important clue or a red herring?

Limitations

There are some differences between these series of patients. The AFIP series looked only at GISTs with a stomach primary. The pathology expertise almost certainly varies considerably; some of these cases may have incorrectly been classified as GIST. Some series used different age cutoff points (29 for The Life Raft Group, 21 for the AFIP and 18 and 30 for the MSKCC series).

There are also some limitations to this newsletter article on pediatric GIST. It is based on a cursory review of the literature. Many articles were only reviewed in abstract form. It is very possible that some patients have been counted more than once (such as in a series and in an individual article).

Conclusion

Six years ago GIST was very poorly understood. The basic research that found a molecular target (KIT) and an excellent targeted drug (Gleevec) has sparked tremendous advances in the understanding of GIST. Today adult GIST can be divided into many different groups. Although in its beginning stages, therapy is beginning to be optimized for these different groups. The Life Raft Group research team includes many of the top GIST researchers in the world. This group has led the way, doing research that has revolutionized the treatment of GIST and they are working to understand and develop more effective therapies for pediatric GIST. Understanding pediatric GIST may provide important clues to help them understand adult GIST as well.

ANTONESCU

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vital to work as both in order to maintain the link between the lab and patients. It allows a researcher to see and bridge the gap between the science and its applications.

The goals of the LRG Pediatric Project are the identification of the activation mechanisms for KIT in pediatric GISTS and understanding the reasons that these mechanisms do not respond to imatinib inhibition. This is vital because pediatric GISTS are especially resistant to imatinib therapy. Few pediatric patients have a significant response to the medications currently available and some suffer severely from the side effects of the medications. This leaves pediatric patients with few options besides surgical man-

agement of the tumors. Surgical management of the tumors often means balancing the desire to remove the tumors as quickly as they appear against the frequency of surgery. Although instinct is to remove the tumors, it is hard for a person to have repeated, frequent surgeries every time there is a recurrence. Fortunately pediatric GIST tends to be slower growing which may allow doctors to reduce the number of surgeries.

The new pediatric tissue bank will collect frozen tissue samples as well as paraffin blocks. This will allow the researchers participating in the project more options as they work towards finding treatments and a cure for pediatric GIST. The entire research team

will collaborate to fully annotate each of the tissue samples. This type of cooperation is unusual in the research field where tissue samples are as valuable as gold. Since pediatric GIST is such a rare sarcoma, it is even more vital that this type of collaboration occur.

It is the hope of the Life Raft Group that this research project can accelerate the development of treatments and a cure for pediatric GIST. Although the funds available to the project may not be sufficient, strategic use of these funds provides the Life Raft Group with the ability to speed up research in areas that provide the most hope for the future.

A wedding in the Life Raft Group

By Meredith Simmons

Brad and I met in high school in 1996. He was a sophomore and I was a freshman. The funny part is that I already knew who he was, having heard of him through mutual friends and seeing him in community theater shows over the years. Secretly, I had always had a little crush on Brad, but never let him know that, until years later. He was a charming and confident guy, with a really outgoing personality... something that I was drawn to early on, probably because I lacked so much of that myself. Because I didn't feel that Brad's relationship with the Lord was much of a priority to him in high school, it wasn't until college that we actually began dating.

I was a freshman at Oakland University. Brad had already been there a year as a sophomore study-

ing theater. He pursued me for awhile before I finally gave in and realized that the Lord had brought Brad back into my life for a reason—he was going to be my husband someday!

Brad and I have been together now for almost five and a half years. He has seen me at my worst, sick and unable to get out of bed; and he has seen me at my best, ready to serve a God that has showered me with an abundance of His blessings in my life. Together, we've been through a lot of ups



Brad Ellison proposes to Meredith Simmons. Meredith is the first pediatric GIST patient to become engaged.

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Stephanie Kastner shares her trip to the Western Caribbean

Oh, the places you'll go—Life with pediatric GIST still allows travel to exotic spots

By Stephanie Kastner

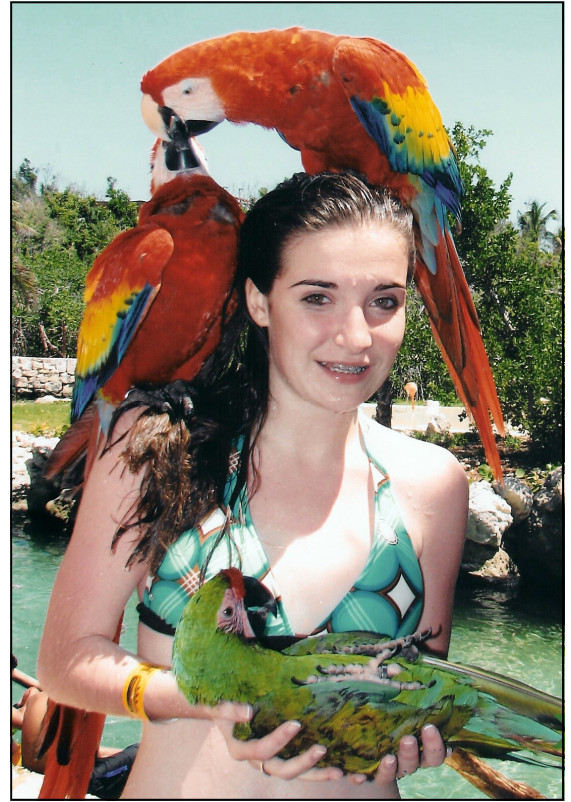
This year for spring break I went on a cruise to the Western Caribbean with my Aunt Debbie, Uncle Jim, and Cousin Megan. We set sail from Galveston, Texas on April 7th. The first stop on our adventure was to the island of Playa Del Carmen. Here we visited a resort called X-Caret. During our tour we saw different animals and even a butterfly farm. After that we went tubing down a river. At the end of the river there was a place where you could hold and get your picture taken with parrots. The parrots were a little scary. Before returning to the ship, we enjoyed an authentic Mexican lunch.

Our next stop was to Belize. I had a lot of fun in Belize. We took a cave tubing excursion. We hiked 45 minutes through the forest until we came to a deep river that we jumped into and floated through caves. Along the

river we saw different kinds of bugs and learned how the caves were formed.

The third island we cruised to was Costa Maya. This was a tremendous learning experience for me. We went to Mayan ruins and then went to a Mayan village. Here we got to see how the people on the island lived. Most of them were poor and they lived in grass huts. The little kids sold us bracelets that they made and then gave their parents the money to buy food. After seeing how they lived, our tour brought us to a lagoon where many children from the island were playing in the park. They sold most people souvenirs and we used our best Spanish to communicate with them. Most of the time they could only afford to eat one to two meals a day, so we gave them our sandwiches and drinks. They were very thankful and pleased.

The last island we went to was called Cozumel. This was my favorite island. We went snorkeling and saw many bright colored fish and different kinds of coral. We returned to the beach and went kayaking and swimming in the ocean.



Stephanie plays with the parrots at the resort on the island of Playa Del Carmen.

My trip was so much fun. I would definitely recommend taking a cruise if you have never been on one. It was one of the best vacations I have ever been on and I'm looking forward to going on another one as soon as possible.

PROPOSAL

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and downs. On March 3rd, 2006, after asking my parents permission to marry me, Brad proposed to me in a beautiful candlelit room, decorated with dozens of my favorite flowers and soft music in the background. I cried through a large part of the proposal, and responded with a "yes please," at the end.

We are so thrilled to be able to start our lives together, as husband and

wife, and have set a date to marry on October 7th of this year (fall is my favorite time of year). I have experienced moments when I didn't think marriage was ever going to be a possibility for me. Who would want to marry a girl with SO many complications, physically, and along with that, financially? Brad did! I had found someone that loved me just the way I was—an 18-year-old cancer patient! I

am 23 now, and my family and I are so excited preparing for this wedding and this new time in our lives when I will be moving on and eventually moving out. I am a lucky girl and I am thankful for the Lord's provision in my life. Brad, myself and my family want you to share in this celebration with us as I am living proof that cancer cannot stop us from experiencing all that life has to offer.

COHEN

From Page 1

around these precious youngsters can open ourselves to be alert students, we will come away having learned some of the most valuable lessons of all. Young people who come face-to-face with illness tap into aspects of human existence that offer tremendous guidance and insight. Some of these gems include the following. These themes are reciprocal and mutual in nature for all readers; for those who are patients (our teachers), and for all of us who avail ourselves to their invaluable lessons;

Give it your all. Whatever the interest, challenge, activity or goal, go for it. The fruits of your actions can only be discovered by fully investing in those potentials.

Insight. Reflect on your experiences in order to find what is meaningful to you. It may not be the same as another person's expectations for you. Discover the difference.

Special. Explore your uniqueness, no matter what stage of life you are in. Teach people about what makes you tick so that others can try to understand what you are going through. When the going gets tough, identify your special ways of coping. See where creativity and joy can fit in.

Teach. Teach and be open to learning. Realize that part of each person's life experience cannot be fully understood by another human being. This can feel empowering and this can feel lonely. Be ready to help others get as close to your experience as possible. Be open to always learning.

Let these tools serve as gateways to our own reflection and renewal. May we continue to be open learners so that our teachers will keep teaching us what it means to proceed through such a sacred journey.

And go round and round in the circle game



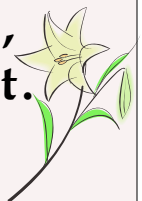
Cohen, pictured on far left, leads Pediatric GIST Families in an ice breaker at the First Pediatric Family Weekend last May.

What Cancer Cannot Do

Cancer is so limited . . .

It cannot cripple love,
It cannot shatter hope,
It cannot corrode faith,
It cannot destroy peace,
It cannot kill friendship,
It cannot suppress memories,
It cannot silence courage,
It cannot invade the soul,
It cannot steal eternal life,
It cannot conquer the spirit.

Source unknown



We all have different ways of coping with cancer

By Rachel Gilbert

At first when I heard the news from the doctor I put a brave face on and tried to stay positive. I have stayed positive ever since then. But that doesn't mean not to cry. Everyone needs to cry; crying is an outlet for all your worries and fears. A good cry, or whatever, helps you release your anxiety.

There are other materialistic ways of coping. One of my favorite things is shopping – they do say retail therapy works and I have to say it definitely does (at least until you get your bank balance). One of the other things that really helps me escape is reading. I read loads of books. It's a good way to think about something else – to travel into another world.

A good way to cope with having cancer is to take each day at a time. Do what you want to and if you need to sleep or rest, then do it. Do what your body is telling you to; to cope with

fighting this horrible disease your body needs lots of rest, relaxation and sleep.

Another good way of coping is confiding in someone, talking everything through – like what your doctor has just said or your worries. Sometimes it's nice to talk to someone just to get their opinion of what's going on. They do say a trouble shared is a trouble halved and I really believe that. It's good just to get things out. If you bottle them up inside they become bigger and bigger and worry you even more.

Having fun doing your favorite things, whatever they may be, is also good to take your mind off things and give you something to concentrate on.

Everybody has their different ways of coping. It's really good to do these things. Cancer, especially one that is so rare for people of our ages, is very hard to deal with. We have to grow up very fast and deal with things



Gilbert shares her advice with the rest of the pediatric GIST community.

that nobody should have to deal with so young or ever. So do whatever you think will help. There is no right or wrong way. Just be yourself and get on with getting better!!



YOUNG

Living life to the fullest

Young finds activities to help her cope with cancer and 'live strong'

By Ashley Young

I always seem to go through ups and downs and lose interest in everything that I love to do. My favorite things to do in life are shooting, hunting, fishing, four-wheeling in my truck, archery, cooking and riding snowmobiles and quads (type of off-road vehicle). I came to a

point where all I wanted to do were activities that I knew wouldn't hurt me. Riding slower and not wanting to go fishing. Staying inside and sleeping all day. My neighbor across the street said to me, "You know I see that you are scared but you really need to not let this disease run your life and ride as hard and as fast as you can." That stuck in my mind for a while. And then finally the trip of a lifetime came up, I mean one I have been wishing for my entire life. My whole family going to Northern Vermont and riding our quads. I didn't want to go. I would've rather stayed home and watched televi-

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sion. Then I was forced to go. I had no desire to be there at all. But my brothers made me take my quad out anyway and go. I was so scared to get hurt. I remembered what my neighbor had said to me and, as I put on my helmet, I looked down at my bracelet—"LIVESTRONG"—I said to myself what is living strong? You know what, I am going to ride as hard and as fast as I possibly can. I have never ever been a sissy and now I'm letting some stupid disease run my life? NO WAY! I hopped on my quad and went for it—through the mud, all over huge rocks and bouncing everywhere almost falling off on every rock I went over. I rode over everything going between 45 and 75 mph. Now when I am scared of anything I just remind myself of what living strong really is.

Ashley Young enjoys times with her family in Northern Vermont while riding 'quads'



May 2006 clinical trial update for GIST patients

By Jerry Call

AMN107 + Gleevec

The trial has reopened for accrual at both Dana-Farber and Fox Chase Cancer Center after it temporarily stopped patient enrollment while the protocol was having some dose-related amendments. International trial sites include: Dr. P. Schoffski in Leuven, Belgium; Dr. Paolo Giovanni Casali for Lyon, France; Dr. Peter Reichardt in Berlin, Germany; and Dr. Paolo Giovanni Casali in Milan, Italy. The original intention was to evaluate doses as high as 800 mg of AMN107 plus 800 mg of Gleevec. Our understanding it that the current intention is to evaluate doses as high as 800 mg of AMN107 and 400 mg of Gleevec. A total of about 45 patients are expected to be enrolled in the phase I trial and 200 to 300 patients are expected for the phase II

trial. The phase II portion of the trial has a projected start date of mid-September.

The combination of AMN107 and Gleevec may have a broad spectrum of activity against primary and secondary mutations in GIST. The generic name for AMN107 is nilotinib and our understanding is that the brand name will probably be Tasigna.

IPI-504

The IPI-504 phase I trial is open and accruing patients at Dana-Farber. IPI-504 is an inhibitor of Heat Shock Protein 90 (HSP90) and has been the subject of articles in the November 2005 and January 2006 editions of The Life Raft Group newsletter. This is an intravenous drug which is administered twice a week. Dose escalation continues. Our understanding is that 90 mg/m² was the initial dose and 225 mg/m² is the current dose.

RAD001 + Gleevec

Both RAD001 and Gleevec are manufactured by Novartis. RAD001 is an mTOR inhibitor that may improve the effectiveness of Gleevec. This trial is moving into the phase II.

The phase II trial will have two stratum:

- 1) Patients progressing on Gleevec
- 2) Patients progressing on Sutent (2nd-line).

Both stratum are open for enrollment. In the U.S., only the Dana-Farber site (Boston) is open at this time.

The additional sites planned are:

- Dr. Blanke-Oregon Health & Science University- Portland, Oregon
- Dr. Hecht- University of California-Los Angeles- Los Angeles, California
- Dr. Trent- M.D. Anderson- Houston

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ton, Texas

- Dr. Taub- Columbia University- New York, New York
- Dr. Von Mehren- Fox Chase Cancer Center- Philadelphia, Pennsylvania

Sites participating/recruiting in Europe are:

- Dr. Patrick Schöffski- Leuven University Hospital- Leuven, Belgium
- Dr. Peter Reichardt- Charité University- Berlin, Germany
- Dr. Marcus Schlemmer- Univ. Klinikum Grossharden- Munich, Germany

We also understand that Dr. Jean-Yves Blay in Lyon, France will participate and that additional sites in Germany (not yet known) are also planned.

BAY 43-9006 (known as Sorafenib and by trade name Nexavar)

This drug was approved in December 2005 for kidney cancer. BAY 43-9006 inhibits several kinases including KIT, VEGFR-2, VEGFR-3, PDGFR- β , RAF, FLT3, and RET. The phase II trial for BAY 43-9006 is open and recruiting patients. Three trial sites are open in Illinois and one in New York:

- Univ. of Chicago- Chicago, Illinois.
- Decatur Memorial Hospital- Decatur, Illinois.
- Oncology/Hematology Associates of Central Illinois- Peoria, Illinois.
- Memorial Sloan-Kettering Cancer Center- New York, New York.

Sites are pending in the following places:

- Univ. of Southern California/Norris Comprehensive Cancer Center- Los Angeles, California
- City of Hope-Los Angeles, California
- Univ. of California at Davis/Davis Cancer Center- Davis, California
- Central Illinois Heme/Onc Center- Springfield, Illinois

- Univ. of Maryland- Baltimore, Maryland
- Univ. of Michigan- Ann Arbor, Michigan (This site may be delayed more than others)
- Duke University Medical Center- Durham, North Carolina
- University of Pittsburgh Cancer Institute- Pittsburgh, Pennsylvania
- Medical College of Wisconsin- Milwaukee, Wisconsin

Sutent

In the United States, Sutent is now available by prescription for patients failing Gleevec or those who can't tolerate Gleevec. In addition, Sutent continues to be available to patients via the "Treatment Use Protocol," which is "four weeks on/two weeks off" (50 mg). There are many sites open throughout the world. Site information changes frequently; for the most current information contact EmergingMed at 1-877-416-6248 (outside the United States) or at 1-800-620-6104 (inside the United States). If international patients have problems with the listed number use email at:

sutent@emergingmed.com. Sutent is also available in a phase II "continuous dose" trial (at 37.5 mg) in the following locations: Dana-Farber Cancer Institute, Boston, MA; Lyon Cedex, France; Villejuif, France; and Milan, Italy.

Genasense + Gleevec

A phase II trial testing the combination of Genasense plus Gleevec in patients with Gleevec-resistant GIST recently opened. Genasense (Genta Inc.) is an antisense drug that inhibits bcl-2. Bcl-2 is a protein involved in cellular survival. This drug is administered intravenously. It is hoped that Genasense may help Gleevec kill tumor cells by making them more sensitive to Gleevec.

This trial is currently open only at M.D. Anderson. Several other trial sites are planned including: Dana-Farber Cancer Institute, Boston, Mass.; University of Michigan Comprehensive Cancer Center, Ann Arbor, Michi-

gan; Mayo Clinic Cancer Center, Rochester, Minnesota; and Memorial Sloan-Kettering Cancer Center, New York, New York.

Perifosine + Gleevec

Perifosine is an oral drug that inhibits the AKT protein. AKT is an anti-apoptosis protein. It is speculated that inhibition of AKT might enhance therapy. Apoptosis is a form of controlled cell death, a type of cellular suicide where the cell issues its own death warrant. The phase II trial, which combines Perifosine with Gleevec is open at M.D. Anderson Cancer Center and accruing Gleevec-resistant GIST patients.

BMS-354825 (Desatinib)

BMS-354825 is a tyrosine kinase inhibitor of Src, abl, KIT, and PDGFR. We understand that this trial may expand to phase II soon. We will update trial sites and the scope of the trial as this information becomes available.

PTK787/ZK222584

This is a phase II study being conducted at the University of Helsinki in Finland. PTK787/ZK222584 was synthesized and developed by Novartis Pharma AG and Schering AG. It is a tyrosine kinase inhibitor and inhibits VEGF receptors as well as KIT and PDGFRB.

Glivec

Also recently added to the ClinicalTrials.gov database is a trial called "Open-Label Trial of Glivec With Unresectable or Metastatic Malignant Gastrointestinal Stromal Tumors." This study has been designed to gain more experience with the treatment of GIST in several Central and Eastern European Countries. The rationale is to assess the clinical and biological activity of Imatinib and to compare the data with historic data. This trial includes sites within the following countries: Austria, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Lithuania, Romania, Serbia and Montenegro, Slovakia and Slovenia. Further information can be found at the ClinicalTrials.gov website.

THE LIFE RAFT GROUP

Life Raft staff

| | | |
|--------------------------|------------------------|-----------------------------|
| Executive Director | Norman Scherzer | nscherzer@liferaftgroup.org |
| Executive Assistant | Tricia McAleer | tmcaleer@liferaftgroup.org |
| Administrative Assistant | Erin Kristoff | ekristoff@liferaftgroup.org |
| Program Coordinator | Sara Rubino | srubino@liferaftgroup.org |
| Research Coordinator | Elizabeth Braun | ebraun@liferaftgroup.org |
| Research Assistant | Pamela Barckett | pbarckett@liferaftgroup.org |
| Science Coordinator | Jerry Call | Jerry.Call@comcast.net |

Board of Directors

Executive Committee

| | |
|---|---------------------------|
| Stan Bunn , President | SBunn@BSTGlobal.com |
| Jerry Cudzil , Secretary-Treasurer | Jerry.Cudzil@DACFunds.com |
| John Poss , Fund-raising | John@PossHaus.com |

Directors

| | |
|---------------------------|-------------------------|
| Robert Book | RMBook2@aol.com |
| Mia Byrne | mebmcb@wowway.com |
| Chris Carley | ccarley@fordhamco.com |
| Jim Hughes | tjhughes43@comcast.net |
| Gerry Knapp | gsknapp@winfirst.com |
| Dr. Arnold Kwart | amkmbp@aol.com |
| Rodrigo Salas | rsalas@webtelmex.net.mx |
| Silvia Steinhilber | nswplas@mb.sympatico.ca |

How to contact the Life Raft Group

40 Galesi Drive, Wayne, NJ 07470
 Phone: (973) 837-9092; Fax: (973) 837-9095
 Web: www.liferaftgroup.org; e-mail: liferaft@liferaftgroup.org

Life Raft volunteers

| | | |
|------------------------|---------------------------|--------------------------------|
| General Counsel | Thomas Overley | guitarman335@msn.com |
| Accountant | Erin Robb | erin@mackeyctas.com |
| List Manager | Mia Byrne | mebmcb@wowway.com |
| Newsletter Editors | Rachel Gilbert | aliveandkickingout18@yahoo.com |
| | Ashley Young | Ayopride2@aol.com |
| Web Designer | Tami Margolis | tami@comcast.net |
| Fund-raising co-chairs | John Poss | John@PossHaus.com |
| | & Gerald Knapp | gsknapp@winfirst.com |

Life Raft area groups

| | |
|------------------------|-----------------------------|
| Linda Martinez | linda.martinez1@cox.net |
| Richard Kinzig | rjkinz@aol.com |
| Jerry Call | Jerry.Call@comcast.net |
| Floyd Pothoven | floyd@keralum.com |
| Ellen Rosenthal | ebrosenthal@comcast.net |
| Dan Cunningham | Daniel.Cunningham2@pseg.com |
| Kerry Hammett | yaloo@gvtc.com |

Life Raft country representatives

| | | | | | |
|-------------------|-------------------------|--------------------------|--------------------|-----------------------|---------------------------|
| Brazil | Vanessa Passos | vanessa@endo.med.br | Malaysia | Yong Choo Sian | ycspj2005@yahoo.com |
| Canada | David Josephy | djosephy@uoguelph.ca | Mexico | Rodrigo Salas | rsalas@maprex.com.mx |
| China | Ruijia Mu | mu_ruijia@yahoo.com | Netherlands | Ton de Keijser | tdk@liferaftgroup.nl |
| Columbia | Jaime Peralta | peraltas@etb.net.co | Norway | Jan Einar Moe | jeinmoe@online.no |
| Costa Rica | Michael Josephy | mjosephy@gmail.com | Poland | Stan Kulisz | listy@gist.pl |
| France | Estelle LeCointe | gist.estelle@laposte.net | Singapore | Yong Choo Sian | ycspj2005@yahoo.com |
| Iran | Negar Amirfarhad | negaraf@sympatico.ca | Switzerland | Ulrich Schnorf | ulrich.schnorf@bluewin.ch |
| Ireland | Carol Jones | roycal@eircom.net | Turkey | Haver Tanbay | tanbay@tanbay.net |
| Israel | Ben Shtang | ehuds@merkavim.co.il | U.K. | David Cook | D.Cook@sheffield.ac.uk |
| Italy | Anna Costato | anna.costato@virgilio.it | | | |

Who are we, what do we do?

The Life Raft Group is an international, Internet-based, non-profit organization offering support through education and research to patients with a rare cancer called GIST (gastrointestinal stromal tumor). The Association of Cancer Online Resources provides the group with several listservs that permit members to communicate via secure e-mail. Many members are being successfully treated with an oral cancer drug Gleevec (Glivec outside the U.S.A.). This molecularly targeted therapy represents a new category of drugs known as signal transduction inhibitors and has been described by the scientific community as the medical model for the treatment of cancer. Several new drugs are now in clinical trials.

How to join

GIST patients and their caregivers may apply for membership free of charge at the Life Raft Group's Web site, www.liferaftgroup.org or by contacting our office directly.

Privacy

Privacy is of paramount concern, and we try to err on the side of privacy. We do not send information that might be considered private to anyone outside the group, including medical professionals. However, this newsletter serves as an outreach and is widely distributed. Hence, all articles are edited to maintain the anonymity of members unless they have granted publication of more information.

How to help

Donations to The Life Raft Group, incorporated in New Jersey, U.S.A., as a 501(c)(3) nonprofit organization, are tax deductible in the United States.

Donations, payable to The Life Raft Group, should be mailed to:

The Life Raft Group
 40 Galesi Dr., Suite 19
 Wayne, NJ 07470

Disclaimer

We are patients and caregivers, not doctors. Information shared is not a substitute for discussion with your doctor. As for the newsletter, every effort to achieve accuracy is made but we are human and errors occur. Please advise the newsletter editor of any errors.