GIST Support International

GIST Talking!

http://www.gistsupport.org

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Special points of interest:

- What comes after Sutent?
- Bob Spiegel 2nd Opinion Fund
- CME Meeting
- Book recommendations
- Voices of GSI
- Spring is a'coming in!

Inside this issue:

NIH Clinic

Becky Bensenhaver, PT

From left to right: Dr. Michael LaQuaglia, Dr. Constantine Stratakis, Dr. Lee Helman, Dr. George Demitri, Phyllis Gay, Dr. Katherine Janeway, Dr. Su Young Kim, Trish McAleer, Dr. Alberto Pappo.

The National Institutes of Health hosted the Second Pediatric and Wildtype GIST Clinic on January 22-23, 2009. Su Young Kim, MD of the NIH Pediatric Oncology unit deserves accolades for his outstanding work with planning and coordinating the event.

The first Pediatric GIST clinic held last June was established to gather data pertaining to Pediatric GIST in an effort to facilitate research and the development of innovative new treatments. It brought together world renowned GIST specialists with children and young adult pediatric GIST patients for the first time.

The second Clinic in January incorporated the participation of adults with Wildtype GIST. This expansion was made as older Wildtype GIST patients resemble Pediatric GIST patients, with both groups lacking mutations in either the KIT or PDGFRA genes. This time the Clinic included 12 patients, 5 of whom were pediatric.

The patient participants and their families travelled from all over the USA as well as Canada. The patients underwent a thorough history and physical examination. Information was obtained from each so that it may be added to the database, including clinical history, response to prior treatments, histopathologic results, radiographic assessments and genetic/molecular analyses.

Continued on page 4

What's next after Sutent?

Julie Royster, PhD

GIST patients whose disease progresses on treatment with Gleevec and Sutent need to make sense of the clinical trials available.

GSI's website maintains a table of current trials at **www.gistsupport.org/treatments/clinical-trials/current-trials.php**, and descriptions of the trial drugs are available at **www.gistsupport.org/treatments/emerging-treatments.php**

Single-agent trials

The drugs with the most available track records include:

Sorafenib (Nexavar) is in a Phase II GIST trial for which preliminary results were reported in 2008. So far there has been a 76% disease control rate: 4 partial response, 18 stable disease, 7 progressive disease. The mean progression-free survival for patients resistant to both imatinib and sunitinib was 5.7 months. Mutation analysis, newly available for 22 patients (5 with imatinib resistance only, and 17 with resistance to both imatinib and sunitinib), revealed 14 of the 22 to have exon 11 KIT gene mutations. Two exon-9-mutant patients both had stable disease for longer than 6 months. One patient displayed the PDGFRA mutation D842V (which is imatinib resistant) and had stable disease for greater than 6 months on sorafenib. Sorafenib is already approved for kidney cancer and so could be prescribed off-label for GIST patients. Link to the trial at **http://www.clinicaltrials.gov/ct/show/NCT00265798**

Retaspimycin (IPI-504) is a heat shock protein 90 inhibitor now in a Phase III trial (the Ring Trial) with sites planned worldwide. (**http://clinicaltrials.gov/ct2/show/NCT00688766**). In a Phase I trial 78% of GIST patients derived clinical benefit from this drug (usually stable disease).

Insulin-like Growth factor receptor 1 (IGF-1R) inhibitors are another option that patients with Wildtype GIST should consider. A number of these drugs are in trials described at **www.gistsupport.org/treatments/clinical-trials/current-trials.php#4** . A trial of R1507 specifically for Wildtype GIST patients (pediatric and adult) will be opening soon, organized by SARC with the cooperation of NIH.

Dasatinib (Sprycel) is in a Phase II sarcoma trial, but it is already approved for CML (and so could be prescribed off-label). In the SARC009 trial, so far 22 GIST patients have enrolled who are all either resistant to imatinib or imatinib-intolerant. Some have previously taken sunitinib. The trial also includes many more patients with other sarcomas. A third of patients have needed a dose reduction due to adverse effects. It is too early yet to predict results, but dasatinib is hoped to have activity against primary and secondary mutations that are resistant to imatiniib. Medical papers indicate that dasatinib should work against activation loop mutations (KIT exon 17 or PDGFRA exon 18) including PDGFRA D842V. Link to the trial at: **http://clinicaltrials.gov/ct2/show/NCT00464620**

Nilotinib (Tasigna), which is already approved for CML, is in several trials for GIST, with more to come. There are no published papers about the first two GIST trials of nilotinib, but one ASCO 2007 presentation indicated that 68% of patients achieved stable disease lasting from 6 weeks to 6 months. In cell studies nilotinib inhiibits Wildtype KIT better than sorafenib, dasatinib, and imatinib. Link to the trial at **http://clinicaltrials.gov/ct2/show/NCT00464620** . In addition, other nilotinib trials are listed at clinicaltrials.gov but are not open yet (see NCT00751036 and NCT00633295 and NCT00785785).

The GSI telephone number is: 215-340-9374

For a comprehensive overview of which clinical trials are available see:
www.gistsupport.org/treatments/clinical-trials.php . See also www.ringtrial.com/

Combination Trials after Sutent

Julie Royster, PhD

Many oncologists feel that combinations of drugs will eventually have better results. There are numerous combination trials listed at: **www.gistsupport.org/treatments/clinical-trials/current-trials.php#4.5** Most of these are Phase I trials. A few of the more interesting ones include:

Sunitinib combinations with:

- imatinib
- bortezomib (a proteasome inhibitor)
- CP751,871 (an IGF-1R inhibitor)

Imatinib combinations with:

- sunitinib
- everolimus (an mTOR inhibitor)

Dasatinib combinations with:

- ixabepilone (a cell cycle inhibitor that targets tubulin)
- bevacizumab (an angiogenesis inhibitor)

Other combinations:

- vorinostat and bortezomib
- deforolimus (an mTOR inhibitor) and MK6446 (an IGF-1R inhibitor)
- IMC-A12 (an IGF-1R inhibitor) plus temsirolimus (an mTOR inhibitor)
- pazopanib (a KIT inhibitor) and temsirolimus
- vatalanib (a KIT inhibitor) and everolimus

Sorafenib combinations with:

- RDEA119 (an inhibitor of MEK and MAPK)
- sirolimus (an mTOR inhibitor)
- bortezomib (a proteasome inhibitor that disrupts protein availability, leading to cell cycle arrest, apoptosis, and inhibition of angiogenesis)
- vorinostat (a cell cycle inhibitor that targets histone deacetylase)

The Bob Spiegel Memorial Second Opinion Travel and Treatment Fund

Because GIST is a very rare Sarcoma,, it is sometimes necessary for a patient to travel to a sarcoma expert for a second opinion or treatment. Realizing the importance of getting patients the best care possible, GIST Support International offers a one-time grant to those who need financial help with expenses for this travel and treatment.

The seed money for this fund comes from the Buffalo Chips Restaurant / Brad Clark Golf Tournament played in Bonita Springs, Florida in December 2008. This event was held in honor of GSI Board member Brad Clark by his many friends in his home town. GSI hopes to be able to add to this fund continuously by accepting donations specifically directed to it.

The fund is named for a very special member of the GSI community and Board, Bob Spiegel, who died very suddenly from complications of GIST surgery. Bob had become an integral part of the GIST community with his always supportive communications. He started and implemented the Healing Through Music program for GSI (which continues in operation) and very generously helped members privately when he found a need.

Bob was very much a proponent of this second opinion project as it was being developed, and it was an easy decision for GSI's Board of Directors to **name** it for him after his untimely death.

For full details of the fund and for an application form, please see:

http://www.gistsupport.org/financial-assistance/assistance-from-gsi.php

The 2nd NIH Clinic, cont. from Page 1

by Becky Bensenhaver, PT

Three-dimensional videography was performed in order to collect information about their facial compositions in the hope of pointing researchers toward previously unidentified gene specific phenotype commonalities. The services of pain management specialists, dieticians, dermatologists and psychosocial experts were also made available.

Dr Kim, and Dr Janeway as she prepares to speak

The GIST specialists collaborated in a round-table forum to discuss each patient's case, followed by an opportunity for the patient and family members to ask questions to the panel of physicians. Finally, the consortium of experts met to discuss some of the findings in general terms, and to define ongoing goals.

Phyllis Gay (Pediatric Coordinator, GIST Support International) and Becky Bensenhaver (Science Committee Member, GIST Support International) were able to attend this organizational and planning meeting as representatives of the GSI Listserv Group.

Identifying mechanisms

A major goal of the Pediatric and Wildtype Clinic is to identify the molecular mechanisms that underlie Pediatric and Wildtype GIST. Some patients with Pediatric GIST also have paragangliomas, both of which may or may not be passed on to their children (Carney-Stratakis Syndrome).

Examination of the DNA of Carney-Stratakis patients has shown mutations in genes that code for subunits of the succinate dehydrogenase (SDH) gene.

Participants in the Clinic were offered the option of having a genetic test to determine if they have a mutation in the SDH gene in order to develop the knowledge base in this area.

IGF-1R

Another area of interest pertains to the recent discovery that IGF-1R is overexpressed in Wildtype and Pediatric GISTs. It is suspected that abnormal regulation of IGF-1R may be driving the growth of these GISTs which lack c-KIT and PDGFRA activating mutations. The NIH is one of many sites that will launch a national clinical trial utilizing an IGF-1R monoclonal antibody as a therapeutic regimen in the treatment of Pediatric and Wildtype GIST.

Phase III Trial

During the Welcome Session at the Children's Inn, Dr. Katherine Janeway, MD (of Children's Hospital Boston, Dana-Farber Cancer Institute) presented a summary of the upcoming Phase II trial. The anticipated launch date is expected to be within the next 6 months. It will consist of two arms: a Pediatric group (those under 18 years of age when diagnosed) and an Adult group.

Participants would receive an IV monoclonal antibody at a frequency of once every three weeks. Therapeutic effects would be monitored with CT, MRI or PET scans after start.

Administration of the antibody would continue until progression or interference from side effects of the drug. Criteria for admission into the trial include, but are not limited to, having advanced unresectable GIST (unremovable GIST tumors present) and no prior IGF-1R therapy. Adult Wildtype trial participants must have previously used imatinib. A video link to Dr. Janeway's presentation will soon be available through the NIH website. News of its release will be posted on the GIST Support International list.

After Dr. Janeway's talk, patients and family members were able to socialize and have dinner together at the Children's Inn. It was a pleasure for everyone to meet and support each other.

The NIH Pediatric and Wildtype GIST clinic encourages everyone with pediatric or Wildtype GIST to contact the NIH and register for subsequent clinics. The next clinic is scheduled for June 17-19, 2009.

You may visit their website at http://www.pediatricgist.cancer.gov/. Dr. Kim, Pediatric GIST Clinic Coordinator may be reached at:

ncipediatricgist@nih.mail.gov.

By attending these clinics, patients will help advance basic science and clinical research for GIST. Your information and medical history will add to a valuable database that acts as a foundation for continued advances in Pediatric GIST.

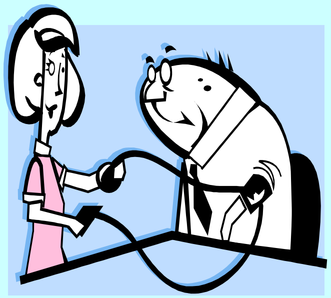
Project FLAG
Families Learning About GIST

Dr. Judy Garber, Dr. George Demetri, and Dr. Suzanne George of Dana-Farber Cancer Institute in collaboration with Memorial Sloan-Kettering Cancer Center, GIST Support International and others are inviting you to a new study for ***all*** GIST patients, regardless of family history. Project FLAG hopes to better understand the rare type of GIST that can occur in families. You can help us by sharing information about your medical history and your family's medical history. This study is conducted by phone and mail. You must be 18 years or older to participate and do **not** need to have a family history of GIST. Go to www.ProjectFLAG.org or call 1-800-828-6622 option #1

Management of hypertension in angiogenesis inhibitor-treated patients

Article by H. Izzedine et al. reviewed by Barbara Doré

From the Annals of Oncology Advance Access, Jan 15, 2009



"Hypertension (HTN) is one of the most frequent side effects of systemic inhibition of vascular endothelial growth factor (VEGF) signaling. Its incidence and severity are dependent on the type of drugs, dose, and schedule used."

The authors did a Medline search to obtain all relevant papers on the use of VEGF-inhibitors in humans since 2000, a meta-analysis of which "revealed a 22.5%-57.7% incidence of HTN under angiogenic inhibitors associated with a 7.5, 6.1 and 3.9 relative risks for developing HTN with Bevacizumab, Sorafenib and sunitinib respectively."

In other words, patients were 7.5 times more likely to have HTN when taking Bevacizumab than otherwise, 6.1 more likely if taking Sorafenib and 3.9 times more likely with sunitinib.

Thus "clinicians must recognize the growing consensus that these drugs may exacerbate cardiac risk factors. On the other hand, HTN induced by anti-VEGF agents may be a predictive factor of oncologic response. Knowledge of this clinical toxicity and /or therapeutic target or novel biomarker of drug activity can aid clinicians choosing the optimal and least toxic regimen suitable for an individual patient."

Some of the recommendations made after reviewing the evidence gathered by meta-analysis of the papers found reporting on patients taking VEGFR-inhibitors were:

- "Patients should be assessed at baseline for existing kidney disease before VEGFR-inhibitors are given. Repeat screening should be carried out every week for the eight week first weeks."
- "Proactive introduction or even prophylactic use of antihypertensive drugs can allow maintenance of therapy despite the onset of HTN."
- "B.P. lowering drugs should be individualized to the patient's clinical circumstances;

- Angiotensin-converting enzyme (ACE) inhibitors or angiotensin 2 receptor antagonists (ANA) should be preferred for those patient with proteinurea, chronic kidney disease risks, or metabolic syndrome;
- Nondihydropyridine calcium channel blocker (CCB) should be avoided in treating patients receiving CYP450 inhibitors.;
- Dihydropyridine CCB should be preferred in elderly or black patients."

- "One test dose of 5-10 mg isosorbide dinatrate may be administered in case of *de novo* HTN or added to previous antihypertensive treatment in case of disequilibrium of previously controlled BP. Prompt return of pretreatment BP in spite of continuous anti-VEGFR treatment may justify long-acting oral nitrates prescription"
- "Angiogenic inhibitors should be withheld only from patients who experienced hypertensive crises."

Also see Ask the Professional at: www.gistsupport.org/ask-the-professional/sunitinib-and-hypertension.php

Team Sarcoma July 18-26th 2009

The 2009 Team Sarcoma Initiative (i.e., the 2009 International Sarcoma Awareness Week) will take place during July 18-26, 2009. Please consider being a part of it. Our goal this year is to have over 10,000 people involved worldwide.

Please see www.team-sarcoma.net and then contact Bruce Shriver if you'd like to discuss this possibility of planning a Team Sarcoma event. Given the downward spiral of the worldwide economy we need all the help we can get to continue funding sarcoma research and increasing public awareness of sarcoma.

The Liddy Shriver Sarcoma Initiative website has been moved to

www.SarcomaHelp.org

Support
Research
Hope

One event at a time
One week of the year
All over the world

Team Sarcoma
Sarcoma Knows No Borders

The 2009 Team Sarcoma Bike Tour of western Maryland's Allegany Mountains will also take place during July 18-25, 2009 and you and your family are welcomed to join us on it as well; see

http://tinyurl.com/9qxbf3

If you are planning to attend and need a shuttle from the BWI airport out to the starting point in Cumberland Maryland (200 miles) and/or a return shuttle from the finish in Washington D.C. back to the airport (60 miles): Annapolis Mike is offering a shuttle to 4 (approx) GSI members planning to attend this event (Friday 17/Saturday18th). This offer includes transporting bikes if required.

Please email gsi@gistsupport.org to pass on your requests.

Reactions to Attending a GIST CME Event

by Nancy Berezin

These are my thoughts after attending "Evolving Molecular Medicine in GIST Management: a 2009 Update" (held January 14, 2009). I am just going to add a few personal notes to the one Genny Fox has provided .

To recap the event: on the evening of January 14, Genny, Vicki Zuber, their husbands, and I attended a satellite meeting titled "Evolving Molecular Medicine in GIST Management: a 2009 Update," which took place at the glitzy San Francisco Marriott Hotel during the 2009 Gastrointestinal Cancers Symposium. The event was chaired by Dr. George Demetri of Dana-Farber and included slide presentations by three top GIST experts—Dr. Jonathan Fletcher (Brigham and Women's Hospital, Boston), Dr. John Vetto (Oregon Health & Science University—Knight Cancer Institute, Portland), and Dr. Robert Benjamin (MD Anderson Cancer Center, Houston).

The symposium was designed for medical oncologists and oncology team members; however, our little group was warmly welcomed. Since this was an uncrowded, evening satellite meeting rather than one of the official sessions, there was no awkwardness about our lack of conference badges, and the lavish buffet provided by Novartis was open to all. (Warning: If you ever attend one of these events in your area, do not eat beforehand.)

One of the best parts of the experience for me was having the opportunity to meet my fellow Bay Area GISTers and learn something of their personal histories. Vicki observed that we all have different mutational status—an Exon 11, an Exon 9, and a wild type—so we really were representative of the broad spectrum of GIST!

Another positive aspect of the evening was discovering how well informed we are about our disease, thanks to Julie, Marina, and the other dedicated folk who continuously update the GSI web site and share the latest journal abstracts with us by email. While the experts did present cutting-edge information (see Genny's report), they also spent considerable time reviewing older findings that were familiar to us but news to many of the oncologists in the audience.

All continuing medical education (CME) programs have a pre-test (which gives the sponsors an idea of how much the audience knew about the subject before the presentation) and a post-test (which gives them a rough idea of how much information was absorbed). In the old days, these were paper-and-pencil tests, but today's spectators receive hand-held electronic devices on which to punch in their answers. Based on the percentage of correct responses to the pre-test, many of the oncologists did not know (for example) the expected differences in treatment outcome with imatinib vs sunitinib in patients with Exon 11 vs Exon 9 KIT mutations. Now, these were general oncologists, not GIST experts, so some lack of familiarity is understandable. But the difference in kinase inhibitor response is a basic aspect of dealing with GIST, and if they had gone to the GSI web site, they would have known the correct answer! (Note: the audience did somewhat better on the post-test, but they still didn't hit the ball out of the park.)

The continuing "knowledge gap" between general oncologists and GIST specialists underscores the importance of consulting a real expert whenever a major treatment decision is called for—even if it means driving many hours or flying from one city to another. I hope I live to see the day when it no longer is necessary for any of us to work with multiple doctors and institutions, but based on this experience, that day has not yet arrived. Fortunately, most local oncologists recognize this fact and are willing to work in tandem with a GIST specialist. If yours refuses to do this, find another doctor ASAP!

One final note: in his introductory remarks, Dr. Demetri noted that the close collaboration between GIST patients and their physicians was one of two main factors contributing to rapid progress in the field. (The other was the unusually close cooperation between clinical oncologists and bench scientists.)

Having worked as a medical reporter during the early years of the HIV/AIDS epidemic, I saw firsthand the difference that engaged patients can make in the pace of medical research. So let's keep on educating ourselves and one another about GIST—and buying cookbooks and riding bikes and participating in Project FLAG. And if you have an opportunity to attend a similar meeting in your area, get to know some of your fellow patients, and talk to visiting experts, then by all means do it! By putting a human face on the disease, we are encouraging the medical community to go that extra mile toward finding a cure.

Regards to all, Nancy

See webcasts of the presentations at www.cancerlearning.com/index.cfm/fuseaction/lecture.showOverview/id/7/lecture_id/263

Evolving Molecular Medicine in GIST Management: An Update

by Genever Fox, DVM

I was fortunate to attend this 2 hour session on Wednesday evening, January 14, and to meet 2 list mates from GIST Support International, Nancy Berezin and Vicki Zuber, and Vicki's husband. It is so interesting and fun to put faces to the posts we read each day. I am sure we all took home some "pearls" of knowledge from the very interesting lectures in this continuing medical educational seminar held in conjunction with ASCO's GI Cancers Symposium.

The session was chaired by Dr. Demetri (from Dana-Farber). Drs. Jonathan Fletcher (Brigham & Women's), John Vetto (Oregon Health Sciences University), and Robert Benjamin (MD Anderson) all spoke about their respective areas of expertise in the GIST arena. They reviewed the history of GIST treatment and some of the early and still ongoing studies. I will try to summarize the points that I found the most interesting.

1. Although most GIST's are primarily driven by gain of function mutations in KIT (or less frequently in PDGFRA,) within each tumor there are small numbers of cells with other mutations. TK inhibitors are not effective on some of these mutations, especially the ones affecting the activation loop part of KIT (as opposed to mutations affecting the ATP-binding portion which tend to be sensitive to TK inhibitors.) Determination of the primary mutation will help prognosticate the initial response to therapy.

2. After a TK inhibitor knocks out the cells being driven by the primary mutation, the cells being driven by the less sensitive mutations are still able to grow into resistant tumors. Within one individual, there may be multiple resistant tumors each driven by different mutations. Some of these may be sensitive to a different TK inhibitor, such as Sutent or Nexavar, and some may not be sensitive to these drugs. That is why the response to the second and third line TK inhibitors is so variable among different patients. Mutation testing of the resistant tumors would be helpful in selecting the next drug to try but there may be multiple mutations found within a single patient.

3. Ultimately other targets within the resistant cells will have to be attacked for therapy to be effective. There is a lot of research going on looking at these potential targets (HSP-90, mTOR, PI3K, etc.)

4. All of the speakers seemed to feel that multiple drug therapy will ultimately be necessary to effect a long-lasting remission or cure in non-resectable GIST. Eventually new patients will be started on multiple drug regimes, similar to what is done with conventional chemotherapy.

5. Surgery is still the best shot at a cure now and the surgeons are getting better and more aggressive in excising tumors. Using a TK inhibitor (usually Gleevec) prior to surgery when the tumors are big is very helpful as long as you choose the right time to go to surgery. (An oncologist and surgeon with experience in this type of approach is likely to be crucial in getting the best outcome.)

6. Recurrent/metastatic tumors should be managed both surgically and medically if possible. For example, if a patient has multiple tumors and only 1 or 2 are growing while on a TK inhibitor, then the rogue masses should be removed if possible and the patient should stay on the TK inhibitor that is still controlling any remaining tumors.

7. For patients with tumors larger than 6 cm, 1 year of adjuvant Gleevec prolongs the interval before disease recurrence and is now FDA-approved. Studies where the adjuvant Gleevec is given for 2 years and 3 years are ongoing.

8. CT imaging is very good for monitoring response to treatment. PET scanning is also very helpful but doesn't need to be done on every patient. The speakers felt that PET scans are best used when CT results don't make sense or don't give the clinician the information they need to make appropriate therapeutic decisions.

9. The Exon 9 mutation is not as responsive to imatinib and requires 10 times as much imatinib at the cellular level in order to respond. Exon 9 patients should be taking more than 400 mg per day, ideally 800 mg if they can tolerate it, even if they are taking it in an adjuvant setting. When these patients progress, it is usually because they just aren't very sensitive to imatinib, not because of other mutations. That is why Exon 9 patients usually do well on sunitinib (Sutent.) When the Exon 9 patients progress while on sunitinib, it is because of other mutations.

Vitamin D Gets its Day in the Sun

by Carolyn Grobe, HHP

Scientists are now beginning to understand how sunlight activates the body to produce vitamin D and produces far-reaching health benefits. Vitamin D is not actually a vitamin, but a potent repair and maintenance neuro-steroid hormone responsible for the regulation of over 2000 genes. Vitamin D deficiency may lead to cancer, type I diabetes, multiple sclerosis, rheumatoid arthritis, cardiovascular disease, osteoporosis, and autism development (caused by prenatal deficiency).

A 2006 paper, Solar ultraviolet-B exposure and cancer incidence and mortality in the United States, 1993–2002**,** by Francis Boscoe and Maria Schymura, concluded there is an inverse relationship between solar ultraviolet-B (UV-B) exposure and non-skin cancer mortality, including gastrointestinal cancers. "The evidence is clear that exposure to solar UV-B affords protection against numerous cancers, and that current public health recommendations that advocate little or no sunlight exposure should be revisited."

Exposure to UV-B rays in the form of sunlight is the way nature intended us to get vitamin D: Sunlight converts a compound in skin cells into vitamin D3. The liver converts D3 into 25-hydroxyvitamin D (or calcidiol), which is the major circulating form of vitamin D that clinicians use to determine vitamin D status. This is then converted by the kidneys to the hormone 1,25 dihydroxyvitamin D (or calcitriol).

Adequate vitamin D is different for everyone and depends on where a person lives, their lifestyle, skin color, age and overall health. A young, light-skinned person in a bathing suit on a sunny summer day synthesizes as much as 20,000 or 30,000 units of vitamin D. People with very dark skin need about 10 times as much sun exposure to synthesize the same amount.

Tips for safe sun exposure to optimize Vitamin D levels:

1. Start slowly with sun exposure. There are many medications which may cause sensitivity to sunlight. For some, Gleevec has increased sunburn potential, possibly due to the report of thinning skin, especially for those who have taken the drug for longer periods. At the beginning of the season, go out gradually, exposing as much skin as possible, working up to 15 minutes a day. Never get a sunburn. You do not need to be out during peak sun times in order to synthesize vitamin D.

2. Don't put on hats, clothing or sunscreen until you've been in the sun 15 minutes. SPF-15 sunscreen will absorb 99.9% of beneficial UV-B rays. Also, car and home windows block the majority of UV-B.

3 Don't shower immediately after sun exposure. Since the conversion is made within your skin cells up to 30-60 minutes after exposure, it is possible that soap may interfere with this process.

It is imperative that your vitamin D levels be monitored, and it is recommended that your doctor also check serum calcium levels as a rise may indicate vitamin D toxicity.

The most accurate test to measure vitamin D is a blood test which measures total 25-hydroxyvitamin D. Another option is a home test kit where a blood spot is sent back to the lab. Either of these tests, which require a prescription, are more accurate than the measurement of 25-hydroxyvitamin D2 and D3 separately, which on average are 40% higher and may falsely reassure that your levels are optimal when they are deficient.

The appropriate values are somewhat controversial, but these general guidelines are currently used in monitoring 25-hydroxyvitamin D levels:

Deficient:	Under 40-50 ng/ml*
Optimal range:	50-65 ng/ml*
With Cancer:	65-90 ng/ml*
Excess:	Over 100 ng/ml*

*1 ng/ml = 2.5 nmol/l (if your measurement is in nmol/l)

Relying on dietary sources alone will most likely not raise vitamin D levels significantly. There's essentially no naturally-occurring vitamin D in our diet, and very few foods are fortified with vitamin D. Eating wild salmon will contribute as much as 1,000 units a serving, but you'd have to eat it every day. The addition of cod liver oil to your diet will increase your intake of vitamin D3 as well as provide the well-documented health benefits of omega 3 fatty acids.

So, eat lots of wild salmon or take cod liver oil and have your doctor check your total 25-hydroxyvitamin D to see if you require further supplementation to bring you up to therapeutic levels. If you are in a sunny climate, take advantage of prudent sun exposure. If you are living through a winter season, take that tropical vacation of your dreams!

A Kauai vacation bolsters our levels of Vitamin D. Even though Jeff had been on Gleevec for 18 months, he was fortunate to not have any photosensitivity!

This is an extract from a much fuller article : see the full text at

www.gistsupport.org/learning-center/nutrition/vitamin-d-and-cancer.php

Book Recommendations from GSI Listmates

Julie wrote: There is no need to wait 'til "everything is sorted out" to live your dreams. None of us have guarantees, but we all have today. The book "Cancer As A Turning Point" by Lawrence LeShan focuses on this.

Vicky writes: I recently read Randy Pausch's The Last Lecture and thought it was great. On September 18, 2007, computer science professor Randy Pausch stepped in front of an audience of 400 people at Carnegie Mellon University to deliver a last lecture called "Really Achieving Your Childhood Dreams." Randy was youthful, energetic, handsome, often cheerfully, darkly funny. He seemed invincible. But this was a brief moment, as he himself acknowledged.

Randy's lecture has become a phenomenon, as has the book he wrote based on the same principles, celebrating the dreams we all strive to make realities. Sadly, Randy lost his battle to pancreatic cancer on July 25th, 2008, but his legacy will continue to inspire us all, for generations to come.

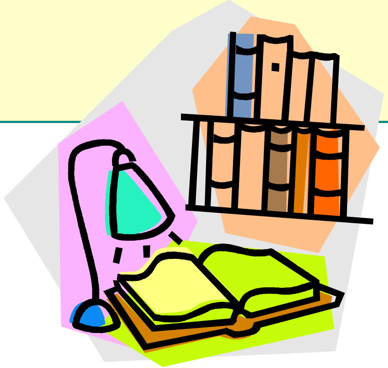
I'm reading a book - "Anticancer - A new Way of Life" by David Servan- Schreiber and found it interesting. The author is an MD and PhD and has had brain cancer. His book talks a lot about diet - which ones are good and not so good. Thought others might be interested in this….. Paul

"At the Will of the Body, Reflections on Illness" by Arthur Frank.

This is one of the very best books about the sociology/cultural impact of major illness. There is more than psychological coping,, there is sociological coping.

Illness is shunned in our society...If you act well, then by gosh to those around you...you are as good as well...and they don't have to deal with the stress that your illness causes them… Marina

I have been reading "Crazy Sexy Cancer Tips" by Kris Carr. It is fabulous, gives many tips, some in a humorous way, on how to be a survivor. I highly recommend it.. Darce



For further book recommendations from GSI members, please see (use underscores between the words Book recommendations from GSI Listmates)

http://gistsupport.medshelf.org/Book_Recommendations_from_GSI_Listmates

Carolyn says she would like to recommend a book by Allen Carr (founder of international Easyway Clinics) called The Easy Way to Stop Smoking. Of the 475 reviews on Amazon, 415 people gave it a five or the top rating. I noticed that our library has the book and CD. Allan Carr has also authored The Little Book of Quitting and The Easy Way to Stop Drinking.

Carr knows most smokers realize the health implications and so he doesn't preach. He also thinks most smokers want to quit. What he does is debunk many of the myths about smoking: smokers enjoy smoking, smokers choose to smoke, smoking is a social habit, smoking relieves boredom and stress and smoking aids concentration and relaxation.

Kath's cookbook to raise money for GIST research using recipes garnered from friends and fellow GIST patients. has been a wild hit. It is stuffed with personal favorite recipes from many of the folks you read online every day (including two of Fla. Bob's). Kath says there are still some books available, so hurry along and snap up your copy now!.

The cookbooks cost $12 each and $3 for shipping. All profits from the cookbook will be donated to Dr. Trent at M.D. Anderson to go towards GIST research.

You can contact Kath at katharine_kimball@hotmail.com for further information or to order your copies now. Checks or money orders should be made out to Katharine Kimball, with 'Cookbook' in the memo field and mailed to Kath Kimball

Voices of GSI members: Hello from Larry Richardson

Hello, my name is Larry Richardson. I currently reside in Bridgeport, New York on the beautiful shores of Lake Oneida. I am 64 years old, and am an Electrical Engineer by profession. I look forward to retirement in a couple of years. Until recently, I have enjoyed excellent health.

I am married to the lovely Penelope Richardson, my bride of 15 years. Between us we have six children and three grandchildren. Our youngest has just received his PhD from The University of California in San Francisco in the field of geno-pharmacology, a field which combines genetics and pharmacology. Since my diagnosis, he is becoming interested in this disease. His dissertation dealt with cell receptor recycling, and the effect this has on the bioavailability of drugs.

Larry with Jocko

Hobbies, of course, include boating and fishing. I have a small 19-foot cuddy hull runabout which has been in storage since my surgery last year. I really look forward to getting it back in the water this summer. I am also interested in amateur radio (call sign is KD5WRN), and get on the air whenever my schedule permits. I am interested in health issues and medicine from a layman's standpoint, and do a lot of reading about the subject.

Larry with grandson Merrick

My GIST journey actually started on the morning of December 27, 2007, which started out for me like any other morning, with my getting out of bed to make coffee. This morning was very different, in that I was very dizzy and could not maintain equilibrium. I lay down on the couch, thinking if I could rest a bit more, I would be OK. My wife found me asleep on the couch when she got up, and being an RN, she knew something was amiss. When she saw my color, she knew immediately I was probably bleeding internally, and insisted I go to the emergency room, which probably saved my life. From there, I was admitted to Saint Josephs Hospital in Syracuse, where they determined I had lost half the blood in my body.

During my stay there, I received five units of packed blood cells, and finally got my hematocrit count up from 19 to an acceptable range in the 30s (normal for men is 47). My attending physician for this was the one who had performed a recent colonoscopy on me, so he knew the source of the bleed was probably not my colon, and it was decided to perform an endoscopy. During this procedure, they saw the source of the bleed was a 2cm mass in the upper part of my stomach. This was cauterized and a fine needle biopsy was performed. The results of the FNA showed no malignancy.

After my release from the hospital, I was referred to the head of the GI department at SUNY Upstate Medical School, Ron Szyjkowski for management of my conditions. He made a good decision that the offending mass should come out for a closer look, and we scheduled surgery for June 24, 2008. Howard Simon was the surgeon, and he did an excellent job. The mass was removed and clean at the edges, so we are very optimistic about the outcome. I had the opportunity to go to Sloan Kettering in NYC, but since my tumor was small and the mitotic rate is only 1-2/50hpf, I have decided to go on the adjunct 400 mg Gleevec treatment for a year with CT scans every six months and keep my treatment local.

Has GIST changed my life? You betcha! I tend to live a day at a time now. I am looking around locally for opportunities in retirement to help others as a volunteer, and I am no longer planning to continue working as a consulting engineer after retirement, but plan to enjoy more time with my family and more time out on the "clear blue water" as the Little River Band put it in their song "Time for a Cool Change".

State help with prescriptions

Louise writes that she "is grateful to ConnPACE, a state program for those of us who aren't well off. If you don't have a high income, check if there are state programs available that you haven't heard of."

Hospital performance info

To find out how a specific hospital performs in treating certain illnesses or doing certain operations, the Government web site:

www.hospitalcompare.hhs.gov provides information

Some states require hospitals to publish their infection rates, this information can be found at **www.hospitalinfection.org**

Voices of GSI members: Hello from Barbara Bruce

I am now 76 years old now and have been playing tennis since I was 40. I love the game and play 3 to 5 times a week and play competitively on our club's A team and have played in many tournaments. There is nothing more rewarding than coming home tired from a tough tennis match. I am so very lucky that my team members are all so wonderful, especially our Captain and they are truly my life line. They will not let me slow down, or think of quitting the game, and all of them support me in every way, even though most of them are my daughter's age.

In 2000, I was getting ready to go out for a tennis game when I felt something I thought might be heart burn, but it wasn't in the right place. I even thought I might be having a heart attack, so I took an Aspirin and went out and played anyway. I continued to feel this in the mornings and late afternoons and had self diagnosed it (with the help of the Internet) as an ulcer, and finally decided it was check-up time.

When I told my Doctor he sent me for an Endoscopy. They took several biopsies and determined it to be a benign mass that must come out. The surgery ended up lasting 8 hours and when I woke up I was told I had GIST and that they had removed 1/3 of my stomach and had to rebuild my esophagus. Not only that, but it had metastasized to my liver and I would have to have liver surgery after I recovered. Two months later I had 2/3 of my liver removed, but there was still a tumor too close to the hepatic vein to be removed. My Oncologist told me I would die, because GIST always returned. However, my surgeon was not about to give up. He sent me to City Of Hope. They were wonderful; told me to come back in 3 months and maybe a new medicine would be available.

In the meantime, the tumor continued to grow, but I was back playing tennis again. If I hit the ball hard enough maybe it would go away. When I went back to City of Hope they told me there was a Clinical Trial that I could get into for a new medicine. I wasn't told much about it, but it was my only choice.

I filled out the paper work, they gave me the pills and I went home with a little hope. A friend called when I got home and suggested that I watch World News Tonight with Peter Jennings because they were going to talk about a new cancer treatment. I did watch and was so excited to see them saying my new medicine was, as they called it the new "wonder drug". That was April 1, 2001 and I am still on 400 mg a day. The tumor having shrunk 50%, it has remained stable all this time.

The best part of all this is that I am still able to play tennis. Oh yes, I do have side effects: I wake up with muscle cramps in the middle of the night, I have blood shot eyes from time to time (I wear Sarah Palin glasses to hide them). My stomach has pain spasms sometimes after eating, and I thought I would never get over the dumping syndrome. I would not eat before playing tennis to avoid that on the tennis court, but as years go on the side effects have lessened. I now eat a banana and a teaspoon of Peanut Butter before playing.

Besides tennis, the best thing in my life has been GSI. I am continually amazed by the kindness and helpfulness of this whole group. How lucky I was to find these wonderful people.!

Keeping busy is very important to overcome the side effects from Gleevec and I manage to do that by working on Genealogy and working with Youth Tennis. We have a huge Ojai Tennis Tournament in our area every year that has been going on for 108 years and both my husband and I work on that. I have attended the 3 walkathons for Gist in California and hope and pray that we find a cure for this soon. We have lost far too many wonderful people from this disease and nothing makes me happier than to read that someone has remained "stable" for one more scan. I pray that we will all be stable soon.

Barbara Bruce

Barbara with daughter Diane

U.S. Medicare Proposes Wider Cancer PET Scan Coverage

The Centers for Medicare & Medicaid Services recently said they propose to allow most Medicare patients to undergo one PET scan without registering in the Oncologic PET Registry program but would have to enroll for future scans. This should make it easier for doctors to order the initial scan. though the changes would not apply to breast cancer, prostate cancer and melanoma. This is to help doctors decide the initial course of treatment in some cancer patients,

CMS plans to issue a final decision in April. It posted its draft report on its website at: www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?id=218

Currently the Oncologic PET Registry program is still in place: See http://www.gistsupport.org/posts/pet-scans-medicare54.php?p=20

See the full article on the proposed changes at:

http://www.medscape.com/viewarticle/586446?src=mpnews&spon=7&uac=62982PT

GIST— becoming History

by Marina Symcox, PhD, Co-Manager

GIST receives quite a bit of research attention. Especially so since the year 2000, as can be seen by the explosion of GIST articles in PubMed...before that date...there wasn't much.

The FLAG Study is looking into heritable GIST and patterns with other cancers. An NIH consortium is looking into Pediatric GIST, a different disease than adult KIT driven GIST. Yes, researchers are looking into what causes a GIST.

Interestingly, it seems that "microGISTs" in stomachs are rather common...even, extremely common. They are small grain sized GIST masses that never grow larger, never threaten the life of the individual who grew them, and yet they contain KIT mutations. A KIT mutation could be a random event that happened long ago in your life. DNA is sometimes randomly damaged and there was nothing in the environment that particularly caused it. At that point the cell is primed for trouble though the cell is still not out of control. Years may pass before other genetic damage happens randomly, and the cell becomes uncontrollable. No one yet knows why so many people walk around with micro-GISTS and never know it, or why in others the GISTS develop.

So research into the possible heritability of GIST progresses alongside research into therapies using combinations of drugs, into adjuvant therapy to prevent metastases, into different lines of attack against GIST— targeting amongst others IGF-1R, VEGF and its receptors, PDGFRA, HSP90 — and finally into surgery to remove individual metastases that are proving drug resistant.

GIST is at the cutting edge of research

In a way we are fortunate that GIST is a relatively simple cancer—the genetic mutations that causes it are pretty well understood even if it is not understood exactly why these GISTS develop in some people and not in others. At least GIST is proving to be a testing ground for drug targets that may be models for treating other cancers with more complex biochemistry at their basis. This means that GIST is often right at the cutting edge of research, and so is benefiting from the finest minds and the will to find, if not a cure, a way to make GIST a chronic and not a terminal disease.

Hang on in there folks, Spring is a'coming in!

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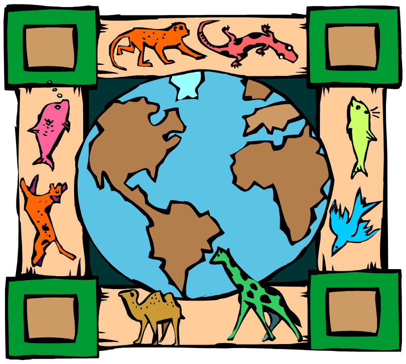

GSI needs you—please volunteer !