

Medicare: what many GISTers need to know

By Marisa Bolognese
LRG Director of Planning & Development

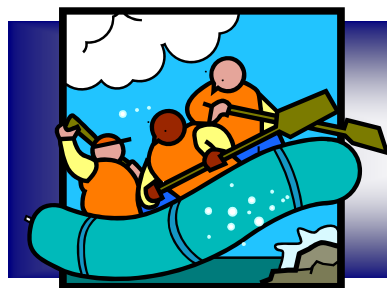
Navigating the medical world as cancer patients is a difficult and stressful experience, often made more exhausting by insurance and prescription drug providers. While some of our members have health insurance through private insurance companies, many others deal with the federal Medicare system and its daunting regulations and guidelines.

Questions about Medicare coverage come up frequently for both new and existing members. Often people have questions about what's covered, who's eligible for what, how Medicare coverage works for those on disability and a host of other issues related to Medicare Part D prescription coverage. Due to the enormity of the issues and the often individualistic nature of the questions, we will only be able to provide an overview.



See MEDICARE, Page 7

Battling gastrointestinal stromal tumor



LIFE RAFT GROUP

May 2008

In memory of Robert Spar & Cherie Ashburn

Vol. 9, No. 5

Interpreting research: dilemmas facing patients and physicians

By Norman Scherzer
LRG Executive Director

Recently, GIST discussion groups have debated the value of the LRG study that examined dosage levels and survival rates. It is important for us to have this debate in the patient community; yet it is equally necessary to spur debate among scientists and physicians. But we should be clear about what exactly we are debating. No current study, neither the MetaGIST Project study nor the LRG study, can offer definitive answers on the correct dosage levels of Gleevec, but both do provide information that can help us ask the right questions. Informing patients and empowering them to question and challenge the orthodoxy of the medical community is precisely what the LRG is all about. Many GIST patients would not be alive today were it not for the shared willing-

ness of the GIST community to question their healthcare providers when their needs were not being adequately heard or met.

The LRG study never purported to prescribe the appropriate dosage for every individual with GIST. Rather, it examined the relationship between dosage level and survival rates among a specific subgroup of patients: 169 metastatic GIST patients who had demonstrated initial tumor shrinkage in response to Gleevec therapy and remained progression free for at least one year (See Figure 1). However, what distinguishes the LRG study from the MetaGIST Project study is that the data collected and analyzed for the LRG study represents actual dosage (as opposed to starting dosage) taken by these 169 patients. By focusing on the actual dosage the LRG study was able to show



SCHERZER

See DILEMMA, Page 6

PI3Ks: a new target in GIST and new drugs in trials

By Jim Hughes
LRG Science Team Member

Since 2001 GIST treatment has benefited from blocking a single mutant protein, c-KIT. Targeting c-KIT with Gleevec and Sutent has led to years of extended survival for many GIST patients. Unfortunately cancer is an adaptive disease.

Adaptive c-KIT mutations can bypass current therapies in one common mechanism of GIST resistance. As researchers observe this phenomenon, the need arises to seek and block new proteins in the GIST cell signaling pathway.

PI3K proteins have been identified in crucial signaling paths of multiple cancers. They can become over-active via a variety of mechanisms including up-

stream signaling. PI3Ks have recently been identified as active downstream signal points in the c-KIT pathway in GIST. A November 2007 paper authored by researchers at Brigham and Women's Hospital (Bauer et al.) reported that imatinib resistant GIST cell lines underwent substantial cell death when treated with a PI3K inhibitor, but not with

See PI3K, Page 4



Life Fest 2008 will be held September 14-16 In Chicago. Look for more details next month!

MRI, CTs and PETs examined and clarified

By Elizabeth Braun

LRG Research Projects Coordinator

Recently, concerns about exposure to radiation during scans have stirred significant discussion in the LRG email community. Although this is a decision that must be made between each individual and their treatment team, it is important to have a strong knowledge base when approaching the issue.

What is an MRI?

MRI stands for magnetic resonance imaging. Using a strong magnetic field, radio waves and a computer, detailed pictures of tissue, bone and other internal structures are produced.



A doctor may request that a contrast material be utilized during the process; this may be either oral or intravenous. It is possible that an allergic reaction could occur from these substances. Kidney disease may also limit the use of contrast materials. The presence of some metals in the body (such as found in some defibrillators and other implants) may preclude the use of MRI's.

Benefits:

- No exposure to radiation.
- May be able to better characterize and identify abnormalities and other focal lesions.
- May enable the detection of abnormalities that could be obscured by bone in other techniques.
- Contrast materials used in MRI's are less likely to cause a reaction than contrasts used in other imaging techniques.

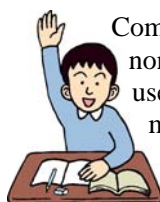
Risks:

- Patients that experience claustrophobia may require a sedative.
- Metals can interfere with the quality of the scan.
- Patients must remain perfectly still to ensure high-quality images. Breathing and bowel motion may cause artifacts or distortions when examining the chest,

abdomen and pelvis.

- MRI's are more expensive and take longer to perform than other techniques.

What is a CT scan?



Computed Tomography (CT) is a noninvasive test that may be used to diagnose and monitor many diseases. CT scans provide higher quality images of internal organs, tissue and blood vessels than x-rays.

Specialized x-ray equipment produces multiple images of the body, called "slices". A computer then joins the images into cross-sectional views that may be printed or viewed on a monitor.

Once again, a contrast material may be used during the procedure. A patient may be asked not to eat or drink anything for several hours before the exam. It is possible for some patients to have an allergic reaction to the contrast material since it contains iodine.

Benefits:

- High quality images may eliminate the need for more invasive testing.
- Images of bone, soft tissue and blood vessels may be produced simultaneously.
- Images are produced quickly and easily.
- Scans can be performed regardless of the presence of any implants.
- CT scans are less expensive than MRI's.
- Scans are less sensitive to movement than MRI's.

Risks:

- Exposure to radiation, although small, does occur. Cumulative exposure may be a concern.
- Allergic reactions are more common with the contrast materials used in CT scans, however they are still rare.

What is a PET scan?

Positron emission tomography, a PET scan, is a type of nuclear medicine imaging. This means that a small amount



See SCANS, Page 9

The Life Raft Group

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.

May 2008 international clinical trial update

By **Jim Hughes**

LRG Science Team Member

AMN107 Phase III: Novartis has informed us that Phase III enrollment is complete.

Multi-Bacteria Vaccine MBV Phase I: This trial tests patient response to a multi-virus vaccine administered subcutaneously twice weekly. Initially response will be measured through body temperature. GIST patients who have failed Gleevec and Sutent are eligible. Tumor samples must be available and test positive for NY-ESO-1 (a tumor-associated antigen belonging to the family of immunogenic testicular proteins.)

AMN107 (nilotinib, Tasigna®)
Efficacy and safety of AMN107 compared to current treatment options in GIST patients who failed imatinib and sunitinib

Phase: III
Conditions: GIST
Strategy: Inhibit KIT
NCT#: NCT00471328
Contact: Novartis gives a central contact #
Telephone: 862-778-8300
Sites: Phase III enrollment is completed.

Imatinib (Glivec) or Sunitinib (Sutent)

Safety and effectiveness of daily dosing with sunitinib or imatinib in patients with GIST

Phase: III
Conditions: GIST
Strategy: Inhibit KIT and/or impede tumor vascularization
NCT#: NCT00372567
Telephone: 1-877-369-9753
Sites: Milano, Italy, 20133

Dasatinib (BMS-354825)

Dasatinib as first-line therapy in treating GIST patients

Phase: II
Conditions: GIST
Strategy: Inhibit KIT
NCT#: NCT00568750
Telephone: 41-21-314-0150
Sites: **Hospitalier Universitaire Vaudois**, Lausanne, Switzerland CH-1011
Michael Montemurro, MD

Read "PI3K drugs in phase I trials" on page 5 for more information on trials for PI3Ks. Check out page 1 for a brief overview and history.

Imatinib + RAD001 (everolimus)

Treatment with everolimus + imatinib in progressive GIST and imatinib-resistance

Phase: II
Conditions: GIST
Strategy: Inhibit target KIT downstream signaling (mTOR)
NCT#: NCT00510354
Telephone: 41 6 1324 1111
Sites: Clinicaltrials.gov lists 9 sites as open in Germany. We could not independently verify this at the time this newsletter was published. Use the Novartis number above for specific site information or go to the German Novartis site at www.novartis.de.

Radiation Therapy as Palliative Treatment of GIST (GIST RT)

Phase: I/II
Conditions: GIST
Strategy: Kill GIST cells (Radiation)
NCT#: NCT00515931
Telephone: 947173208 Ext. 358
Sites: **Helsinki University Central Hospital**, Helsinki, Finland

Dasatinib (BMS-354825)

Study of dasatinib(BMS-354825) in patients with solid tumors

Phase: I
Conditions: Tumors
Strategy: Inhibit KIT
NCT#: NCT00339144
Contact: Email Clinical.Trials@bms.com. First line of email **must** contain NCT# & Site #.
Contact Site 00, Koto-Ku, Tokyo, Japan, 135-0063.
Contact Site 02, Osakasayama City, Osaka, Japan, 589-0014

Glivec + Interleukin 2 (IL2)

Phase I trial in solid tumor and GIST resistant to imatinib and/or sunitinib (IMAIL-2)

Phase: I
Conditions: Solid tumors and GIST
Strategy: Kill GIST cells (Immunotherapy)
Contact: Dr. Nathalie Chaput nathalie.chaput@igr.fr
Telephone: +33(0)1 42 11 50 05
Sites: **Institute Gustave Roussy** Villejuif, France

LBH589

LBH589 in patients with advanced solid tumors or cutaneous T-Cell lymphoma

Phase: I
Conditions: Tumors
Strategy: Destroy KIT + Inhibit cell cycle + Induce apoptosis (HDAC)
NCT#: NCT00412997
Telephone: +81-3-3797-8748
Sites: Tokyo, Japan

Multi-Bacteria Vaccine

A Phase I study of mixed bacteria vaccine in patients with tumors expressing NY-ESO-1 Antigen

Phase: I
Conditions: GIST
Strategy: Immune response attacks tumor
NCT#: NCT00623831
Contact: Antje Neumann, 069 7601 4161 neumann.antje@khnw.de
Sites: **Krankenhaus Nordwest** Frankfurt, Germany

OSI-930

Dose escalation study of daily oral OSI-930 in patients with advanced solid tumors

Phase: I
Conditions: Solid Tumors/Sarcoma
Strategy: Multiple Targets
NCT#: NCT00513851
Contact: ContactUs@emergingmed.com
Telephone: (877) 601-8601
Sites: **Dept. of Cancer Therapeutics Institute of Cancer Research** Sutton, Surrey, United Kingdom

XL147

Study of safety and pharmacokinetics of XL147 in adults with solid tumors

Phase: I
Conditions: Cancer
Strategy: Target KIT downstream signaling (PI3-K)
NCT#: NCT00486135
Contact: Gemma Sala
Telephone: +34 93 489 4158
Sites: **Hospital Universitario Vall d'Hebron**, Barcelona, Spain, 08035
Jose Baselga, MD, PhD

LBH589

LBH589 in patients with advanced solid tumors or cutaneous T-Cell lymphoma

Phase: I
Conditions: Tumors
Strategy: Destroy KIT + Inhibit cell cycle + Induce apoptosis (HDAC)
NCT#: NCT00412997
Telephone: +81-3-3797-8748
Sites: Tokyo, Japan

PI3K

From Page 1

imatinib. Therefore, PI3K inhibition was proposed to be a promising therapeutic strategy in imatinib-resistant GIST.

c-KIT is a tyrosine kinase. It's often depicted as a spark-plug protruding through the cells surface sending signals down into the cell nucleus. Two c-KIT proteins pair up with each other (homodimerize) and are normally activated when the part outside the cell attaches to a circulating growth factor. This leads to

activation of the part of the KIT protein inside the cell, which then attaches phosphates to tyrosine residues on multiple downstream proteins. PI3Ks are part of these downstream proteins.

PI3K is short for "Phosphoinositide 3-kinase". PI3Ks come in two parts, a regulatory component and a catalytic component. The two must pair up (heterodimerize) in order to work. PI3Ks do not protrude through the cell membrane, instead they are entirely within the cell and migrate between the cell

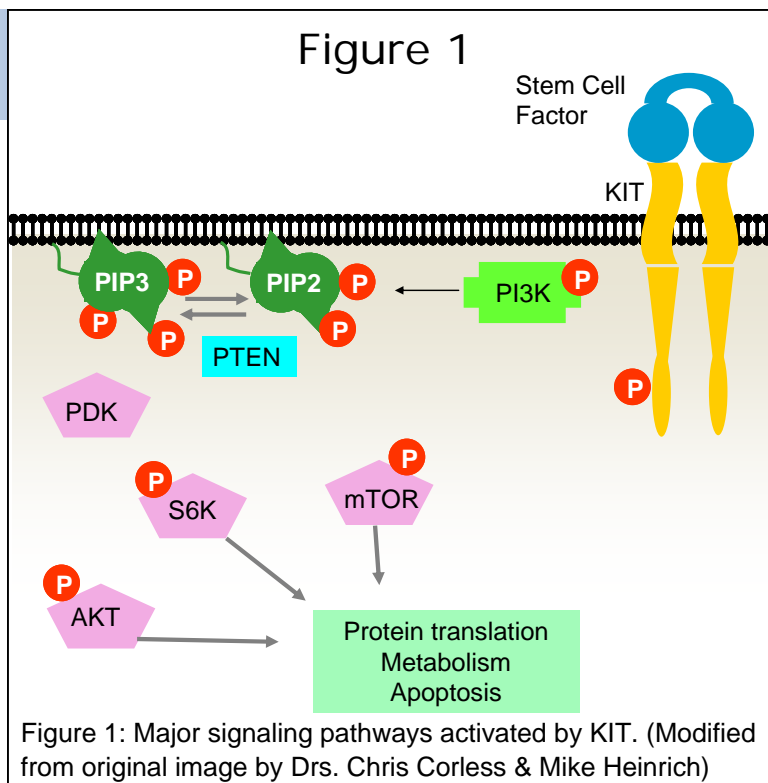


Figure 1: Major signaling pathways activated by KIT. (Modified from original image by Drs. Chris Corless & Mike Heinrich)

surface and the cell interior. When activated, PI3Ks work by attaching a phosphate to proteins called phosphatidylinositols (PtdIns or PI) at the cell surface. Activation of the PI PIP3 leads to the activation (phosphorylation) of AKT at the cell membrane. Activation of AKT then leads to alterations in protein translation, metabolism, cell survival, and proliferation (See Figure 1).

PI3Ks differ from c-KIT in ways that have implications for targeted therapy.

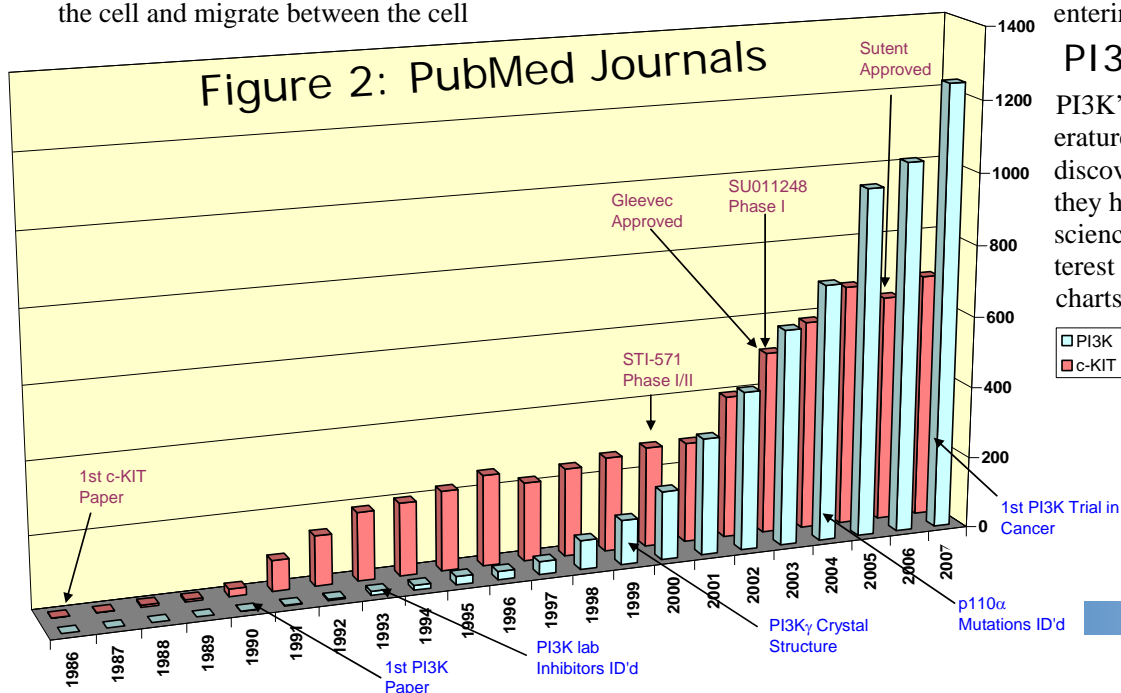
PI3K's comprise a group of about 15 proteins with very similar structures. They are organized into three closely related classes. The Class I PI3Ks are the only group to activate AKT downstream and are the main focus of GIST researchers. As a group, Class I PI3Ks are involved in a variety of life-sustaining functions, including immune system response and glucose metabolism. For instance, PI3Ks are key components in insulin regulation and diabetes. Some Class I PI3Ks are ubiquitous (found in every cell type) which presents a challenge to researchers designing and selecting Class I PI3K inhibitors for testing. It is preferable to have a drug that targets only one isoform (a form similar with small differences) of PI3K to avoid "collateral damage" and to unambiguously assess the effects of pathway inhibition.

Until recently, clinical researchers have only had compounds that inhibited all Class I PI3Ks. These have been called pan-PI3K inhibitors. Most have poor drug qualities or are too toxic. Using molecular design and novel drug delivery techniques, researchers have recently been able to design newer PI3K inhibitor candidates that more selectively inhibit Class I PI3Ks and/or deliver a pan-PI3K inhibitor selectively to tumor tissues. These drugs are just now entering Phase I trials for solid tumors.

PI3Ks: A Short History

PI3K's were first identified in the literature in 1990, four years after the discovery of c-KIT. For many years they have been the subject of basic science and in the last three years, interest has grown greatly. Figure 2 charts the scientific papers referring to either c-KIT or PI3Ks that have been entered into PubMed.

Inhibitors for PI3Ks have been available in the lab since 1993 when wortmannin, a metabolite of a penicillin fungus, was discovered. Wortmannin is a



Campaign 2008

Candidate's histories concerning healthcare



This month, we will continue looking at the healthcare histories and plans of each candidate (in alphabetical order). This month is Senator John McCain.

The LRG does not endorse or promote any candidate.

Senator McCain differs from his democratic counterparts on the subject of healthcare in certain definable ways.

At the GOP debate in December 1999, McCain proposed a federal match to the amount senior citizens spend on prescription drugs. McCain's position was that due to fixed incomes, "They make too much for Medicare and not enough to pay for their prescription drugs".

In her book, *Citizen McCain*, Elizabeth Drew, points out that, in 2001 McCain joined the struggle over the "Patients' Bill of Rights" to regulate HMOs, and helped it to pass through the senate.

John McCain believes not in universal healthcare but in individual responsibility for health care. In an October 2007 Republican primary debate, McCain voiced a hope to take insurance out of hands of employers and make it individual-bought.

He also stated in a December 2007 debate that he wished to keep the quality of care high while keeping costs down. Senator McCain believes a large part of healthcare problems are caused by inflation. To help with this he has proposed a health savings account and a \$2,500 tax credit.

Much more information regarding Senator McCain's healthcare plan can be viewed online.

Also, view our new Advocacy page at www.liferaftgroup.org/advocacy.html

PI3K drugs in phase I trials

By **Jim Hughes**
LRG Science Team Member

Phase I trials usually determine pharmacological and metabolic actions of drugs administered for the first time in humans. They are also called safety studies because they try to determine the "maximum tolerable

dose" (MTD) of the new drug. This is true of all six PI3K drugs on our list.

Additional similarities for all six:

- Are sponsored by the manufacturer
- Specify either cancer or solid tumors
- Do not specify GIST
- Are for adults only
- Do not exclude prior therapies (they may, but they do not specify)

The main differences are in the PI3K isoforms these drugs inhibit and how well. These are important because:

- A multi-PI3K inhibitor is more likely to block a pathway relevant in GIST. All trial drugs here inhibit multiple Class I PI3K isoforms. Most manufacturers have published data on which isoforms are inhibited and how strongly. Some have not.
- A multi-PI3K inhibitor may also be more risky. PI3K's are heavily involved in the immune system and in glucose metabolism; inhibiting multiple PI3Ks may risk inhibition of these vital functions. These risks would be worth inquiring about prior to trial participation with any of the drugs here.

mTOR is a closely related PI4K protein that is inhibited by some of the drugs in these Phase I trials. mTOR inhibitors have now been approved for use in transplant rejection and renal cell cancer. The prescribing information for these drugs warns about hyperglycemia, secondary cancers and opportunistic

infections. These risks may also be worth exploring when evaluating trials that include an mTOR inhibitor.

PI3K inhibitor based strategy differs in several respects from c-KIT inhibition. PI3Ks are part of the

Maximum tolerable dose— the maximum safe dose determined for a group of patients.

PI3K/PDK/Akt/mTOR pathway that promotes cell survival in many cancers. By inhibiting this pathway researchers hope to increase the effectiveness of existing therapies that can lead to cell death. PI3K inhibitors may therefore be combined with one or more other therapies in future trials.

In the order of the date the trial started:

BEZ235: This oral drug from Novartis targets Class I PI3Ks and mTOR. It is one of two PI3K inhibitors from Novartis currently in phase I. This is a combined Phase I/I trial, with an accrual goal of 80 patients. The trial design will admit solid tumors in Phase I. However, Phase II is limited to breast cancer patients. It is currently available at The Nevada Cancer Institute, Las Vegas, Nev. and at Sarah Cannon Research Institute in Nashville, Tenn.

SF1126: Semafore Pharmaceuticals, a small company in Indianapolis, Ind. has developed a broad spectrum PI3K inhibitor based on the lab drug LY294002. SF1126 is a Prodrug that inhibits Class IA PI3Ks and DNA-PK and mTOR. A Prodrug is given in one form and converted into a different, active form by metabolic action in the body. Semafore has designed SF1126 to have an affinity for the vascular forming areas of tumors.

See TRIALS, Page 9

Table 1: Current Phase I trials using PI3K inhibitors for solid tumors

Drug	Target(s)	Delivery	Phase	Started	Accruing
BEZ235	PI3K, mTOR	Oral	I/II	12/1/2006	80
SF1126	PI3K, DNA-PK, mTOR	IV	I	3/26/2007	n/a
XL147	PI3K	Oral	I	6/1/2007	63
XL765	PI3K, mTOR	Oral	I	6/1/2007	63
BGT226	PI3K	Oral	I/II	12/1/2007	130
GDC-0941	PI3K	Oral	I	3/1/2008	n/a

DILEMMA

From Page 1

a link between overall survival and higher doses. These results point to some significant weaknesses in the MetaGIST Project study; weaknesses that are reflected in the current, rather inflexible treatment guidelines. The LRG study's results represent a major challenge to the medical and research community to re-examine the data of earlier clinical studies as well as the treatment consensus which derives from them. It may not always be comfortable to look at new ways of interpreting things but doing so may save someone's life.

What do we know?

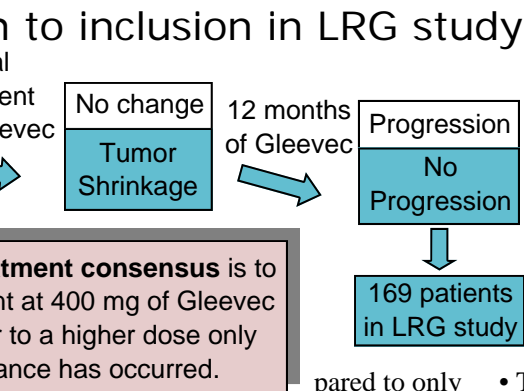
Let's continue the dialogue we began when we presented our data on the relationship between Gleevec dosage levels and survival, and re-examine what we know and what we don't know.

☑ The LRG study demonstrates a strong correlation between dosage levels and progression, and between progression and death. In fact, the LRG study shows that the single most important factor in long-term survival for metastatic patients is staving off progression. In the study, which included 169 metastatic patients who had shrinkage and who

were stable on Gleevec for at least one year, 81 percent of the patients who had progressed by 2004 died by 2007, com-

pared to only 11 percent of the group that remained stable in 2004.

paring to only 11 percent of the group that remained stable in 2004. For some patients, a lower dosage of Gleevec is enough to maintain stability but at the current time we have no conclusive way of predicting which patients fall into this category and which will progress. The reliability of LRG's patient-derived data has been demonstrated by the following:



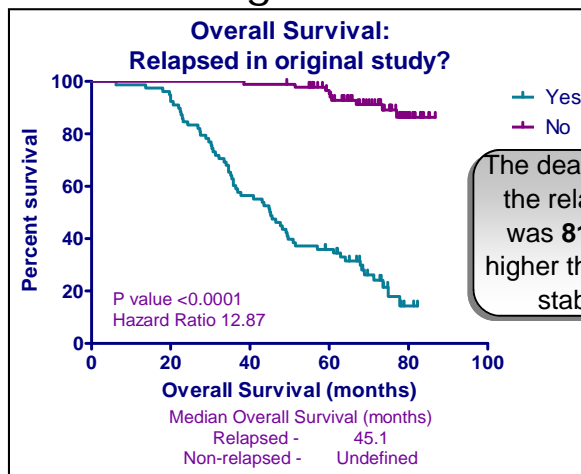
What are the weaknesses of the MetaGIST Project Study?

- The most serious concern was the exclusive use of starting (intent to treat) dosage levels. The MetaGIST Project study considered only these starting doses, and ignored the actual dose taken by patients if it changed. The fact is that of the patients originally assigned to the higher 800mg dose, 62 percent could not tolerate that dosage and were dropped to a lower dose. However, these patients were included in the 800 mg group analysis.
- No 600mg arm was included in the study. The only two doses examined were 400mg and 800mg.
- There was no dose escalation strategy employed to get patients to a higher dose. As a result, the study was not able to determine the impact of increasing doses. Had it included such a strategy, the MetaGIST Project study might have established much earlier what is now known. Namely, that side effects ease over time and that patients are more able to tolerate higher doses after first adjusting to lower doses.

What are the weaknesses of the LRG study?

- The LRG study sample was non-random and was relatively small compared to clinical trials.
- The LRG patients who submitted data for the study may not be representative of the entire population of GIST patients.
- The use of patient-reported data and subjective progression criteria may have introduced a bias into the progression-free data; however, neither would affect overall survival data.

Figure 2



There is no one dosage study that answers all of our questions. While we could choose to wait for more definitive data, there are no studies that will soon address the issues brought up by the LRG dosage study or the recent blood level study presented by Dr. George Demetri at the Gastrointestinal American Society of Clinical Oncology meeting. In his study, Dr. Demetri found that a higher concentration of Gleevec in the blood correlates with better clinical outcomes and a longer time to progres-

MEDICARE

From Page 1

Please see www.liferaftgroup.org/treat_finance.html about Medicare and a more thorough guide to online resources.

The Basics

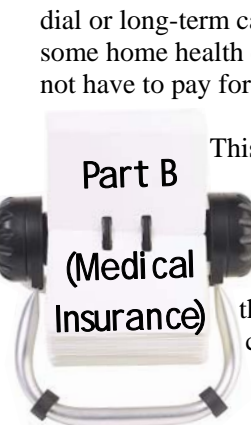
First, it's worth reviewing some basics about Medicare coverage. The Medicare Insurance Program is available to

- ☑ People age 65 or older.
- ☑ People under age 65 with certain disabilities.
- ☑ People of all ages with End-Stage Renal Disease (permanent kidney failure requiring dialysis or a transplant).

Medicare Parts A & B:



This pays for care in hospitals as an inpatient, critical access hospitals (small facilities that give limited outpatient and inpatient services to people in rural areas), skilled nursing facilities (not custodial or long-term care), hospice care, and some home health care. Most people do not have to pay for Part A.



This part pays for doctors' services, outpatient hospital care, and some other medical services that Part A doesn't cover, such as the services of physical and occupational therapists, and some home health care. Part B helps pay for these covered services and supplies when they are medically necessary. Most people pay monthly for Part B.

You can choose different ways to get the services covered by Medicare. Depending on where you live, you may have different choices. In most cases, when you first get Medicare, you are in the Original Medicare Plan. You may want to consider a Medicare Prescription Drug Plan to add drug coverage. Or, you

may want to consider a Medicare Advantage Plan (like an HMO or PPO) that provides all your Part A, Part B, and often Part D coverage. You make a choice when you are first eligible for Medicare. Each year you can review your health and prescription needs and switch to a different plan in the fall.

Medicare Coverage and Disability

You are automatically enrolled in Medicare after you receive disability benefits for two years. The 24 months begins from the month you were entitled to receive Disability, not the month when you received your first check. If you qualify for disability retroactively, you may be entitled to Medicare immediately. It is important to know your qualifying date at the time you receive your disability approval.



Social Security disability benefits are available under two programs:

The Social Security disability insurance (SSDI) program pays benefits to you and certain family members if you worked long enough and paid Social Security taxes.

The Supplemental Security Income (SSI) program pays benefits to disabled adults and children who have limited income and resources.

Note that SSI benefits also are payable to people 65 and older without disabilities who meet the financial limits.

Medicare Prescription Drug Coverage

Under Medicare, prescription drug coverage is now provided under Medicare Part D. First, you need to decide whether to:

- ☑ Stay with original Medicare (which covers your doctor, hospital, and some other services) and enroll in what is called a stand-alone Part D plan or Prescription Drug Plan (PDP). Hundreds of plans are available and vary state-to-

THE BASICS

☞ Find out about current Medicare benefits in **Medicare and You: 2008** at www.medicare.gov/publications/pubs/pdf/10050.pdf

☞ Get an overview on how Medicare is structured, who it serves, and how it works, with **Medicare: A Primer** at www.kff.org/medicare/7615.cfm

DisABILITY

☞ You might want to start with an **Adult Disability Starter Kit**. Go to www.ssa.gov/disability/adult_StarterKit_fact_sheet.pdf for a copy.

☞ If you need some facts, go to "What You Should Know Before You Apply For Social Security Disability Benefits." at www.ssa.gov/disability/Applyforbenefits

PRESCRIPTIONS

☞ Make sure you stop by www.ssa.gov/prescriptionhelp for an online tool to help decide if you qualify for help with Medicare prescription drug costs.

I Need HELP!

There are many advocacy organizations focused on Medicare and prescription drug coverage. Keep yourself informed about important legislative action and ways to help yourself by visiting any number of action-oriented websites.

☞ **The Center for Medicare Advocacy, Inc.** www.medicareadvocacy.org is an organization which provides education, advocacy, and legal assistance to help elders and people with disabilities obtain necessary healthcare.

☞ **Fair Medicare** www.fairmedicare.org is an organization that identifies and promotes advocacy solutions to ensure elders and people with disabilities get access to Medicare and health care.

☞ **The Medicare Rights Center** www.medicarerights.org is very similar; its website offers helpful and reliable Medicare information for all.

Please see www.liferaftgroup.org/advocacy.html for many more helpful organizations and sites.

DILEMMA

From Page 6

What does this mean for patients?

The data gathered in the LRG study clearly suggest that the MetaGIST Project study results do not justify an overly rigid insistence on a dosage level of 400mg. This is supported by research demonstrating that all patients do not metabolize drugs at the same rate, and that absorption rates may change over time. We need to optimize dosages for GIST patients through individualized treatment plans that take the following four key factors into consideration:

1. The Gleevec levels in the blood
2. Utilization of a dose escalation strategy to determine the best tolerated dosage level
3. Adequate control of side-effects
4. Mutational data

Over the last few years, the LRG has frequently found itself ahead of the curve when tracking information and trends. This was the case with our initial data on response rates to Gleevec and with our side effects survey. We find

PI3K

From Page 4

highly effective inhibitor of PI3K and related proteins, but don't look for it on the pharmacy shelf. Wortmannin is highly unsuited as a drug; it is toxic, with a poor solubility and a ten minute half-life in tissue samples. However, the availability of wortmannin and a synthetic version, LY294002, opened up the study of the PI3K pathway in the lab. These inhibitors and others enabled researchers to better understand the signal components and the pathways.

In the late 1990s, researchers were able to identify different isoforms or versions of PI3K proteins. In 1999, the crystal structure of one PI3K catalytic component, p110 γ (gamma) was documented. Throughout this period, PI3K-related proteins were being identified as active in different cancers. There are now 15 regulatory and catalytic components

Since 2004, PI3K mutations have been

ourselves in this situation again with the LRG dosage study. We recognize it as our obligation to share what the study

"We have a responsibility to ourselves, to our loved ones and to our fellow GISTers to do our homework..."

results tell us about how to best survive this disease.

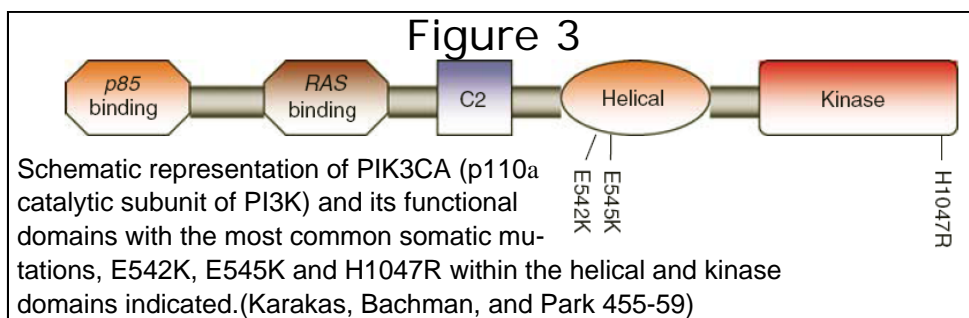
The Empowered Patient's Responsibility

One of the consequences of becoming empowered patients is that we enter into the world of medicine and science where there are sometimes more questions than there are answers. In addition to the burden of dealing with a life-threatening illness, many of us have taken on the additional responsibility of educating ourselves, supporting each other and ultimately making life-changing medical decisions. We have a responsibility to ourselves, to our loved ones and to our fellow GISTers to do our homework, to ask questions, to read the studies and to

stay abreast of the latest scientific developments and medical breakthroughs. As informed patients, we often find ourselves in uncharted territory with respect to the medical community, sitting in the unfamiliar seat of making critical treatment decisions that may go

against physician recommendations. Likewise, physicians may be uncomfortable allowing their patients to call the shots and choosing treatment options that are not part of the current medical consensus.

Ultimately, what makes data reliable or unreliable is an understanding of what they are based upon and whether they can stand up to rigorous and unbiased methodological and statistical scrutiny. No data and no study should be considered "untouchable"; but neither should they be ruled out in advance. We would hope that the patients, caregivers and physicians reading the LRG dosage study would find it more than just a "good read" and would have the objectivity and the wisdom to decide for themselves what this data means and what actions to take.



associated with a wide range of cancers. This discovery leveraged the significant body of science that had been building around the PI3K family of proteins since they were first documented in 1990.

Mutation is one of several reasons for that increased PI3K signaling. In 2004 and 2005, multiple papers identified the gene PIK3CA (See Figure 3) as generally mutated in cancer. PIK3CA encodes the PI3K catalytic subunit p110 α . This subunit is responsible for cell survival and glucose metabolism.

The first PI3K inhibitor trials in humans began in early to mid 2007. Interest in PI3Ks in GIST began with the

publishing of a June 2007 identifying PI3K proteins as promising therapeutic targets in resistant GIST signaling.

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HAPPY CANCER-VERSARY TO LAURA KUKUCKA!



"Seven years ago I heard those words that no one EVER wants to hear: **"You have cancer."**

Insert sound of squealing brakes *here* as you realize that life as you knew it is now a chapter in history, as you will never be quite the same person, ever again. Over the years I just kept surviving...surviving cancer, and surviving life. I'm looking forward to another 7 years...and another 7 beyond that...and I know in my heart that I will continue to face adversity, yet I will continue to overcome those adversities & come out stronger and smarter.

Just passed your own GIST milestone? Email us at liferaft@liferaftgroup.org and you might see *your* name in print.

SCANS

From Page 2

of radioactive material (called a radiotracer) is used during the exam. PET scans do not provide pictures or images of structures. The pictures produced by PET scans reflect the levels of chemical activity in different areas. Areas of greater intensity, or hotspots, indicate higher concentrations of the radiotracer and greater chemical activity.

The radioactive material critical for this type of imaging may be swallowed, injected or inhaled. This material collects in specific areas of the body and emits gamma rays, a type of energy. This energy is detected by a special device and a computer producing specialized pictures that demonstrate both function and structure of organs and internal structures.

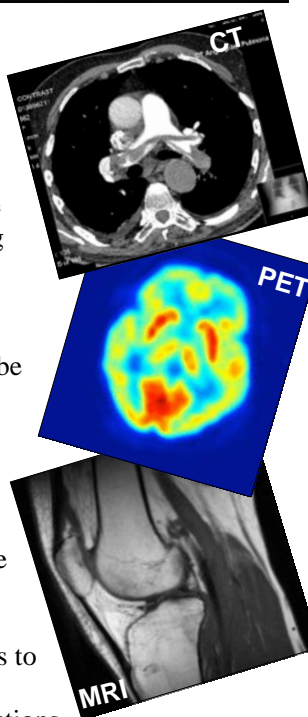
PET scans measure blood flow, oxygen use and sugar metabolism. In GIST, the measurement of metabolism may provide a gauge of tumor activity or growth or response to treatment. Indolent GISTs may not be visualized accurately on PETs.

Benefits:

- ☑ The unique images produced provide information that may not be attainable using other techniques,
- ☑ Response to treatment may be measured.

Risks:

- ☑ The use of a radiotracer means exposure to radiation. It takes approximately 24 hours to leave the body.
- ☑ Allergic reactions may occur to the radiotracer.
- ☑ Diabetics may need to take special care when considering PET scans.
- ☑ Scans are time consuming and expensive.
- ☑ Resolution may not be as clear as in CTs or MRIs.
- ☑ Timing and scheduling are important to ensure accurate results.



TRIALS

From Page 5

This design is intended to concentrate the effect of a broad spectrum inhibitor within the tumor. Of the six PI3K inhibitors listed here, SF1126 is the only one administered intravenously. Current trial sites include Arizona Cancer Center, Tucson, Ariz. and Indiana University, Indianapolis, Ind.

XL147: A second PI3K inhibitor from Exelixis. XL147 is a more selective PI3K inhibitor. It inhibits Class IA and IB PI3Ks. It is also administered orally. Trial sites currently include Dana Farber (under Jeffrey Shapiro, MD), Mary Crowley Medical Research Center, Dallas, T.X. and Hospital Universitario Vall d'Hebron in Barcelona, Spain.

XL 765: Exelixis is a drug development company based in San Francisco, Calif.. Exelixis has 13 drugs in Phase II or earlier stages of development. XL765 is one of two oral PI3K targeted drugs in development. XL765 inhibits Class 1A and 1B PI3Ks as well as DNA-PK and mTOR and is administered orally. Trial sites currently include Karmanos in Detroit, Mich., South Texas Accelerated Research therapeutics (START) in San Antonio, T.X. and Hospital Universitario Vall d'Hebron in Barcelona, Spain.

BGT226: This is a second PI3K inhibitor from Novartis, which inhibits Class I PI3Ks. This trial is classified as a combined Phase I/II. Initially patients with solid tumors will be accepted, but the phase II expansion part will enroll only advanced breast cancer patients and Cowden syndrome patients. Cowden syndrome is an inherited disease in which the PTEN gene is defective leaving the survival signal from the PI3K pathway un-attenuated. The only current trial site is Nevada Cancer Institute, Las Vegas, Nev.

GDC-0941: This drug was initially developed by Piramed in the United Kingdom. GDC-0941 selectivity has not yet been published, so this information is unknown. We have been told informally that this oral drug inhibits multiple class I PI3K's. It is currently in trial at Dana Farber in Boston, Mass. under George Demetri, MD.

Pediatric GIST webcast highlights treatment elements & spring clinic

By Sara Rothschild
LRG Program Coordinator

On April 15, Dr. Lee Helman, the Director of the Pediatric Oncology Branch of the National Cancer Institute, and Dr. Alberto Pappo, Pediatric Oncologist of Texas Children's Hospital, discussed a new initiative for pediatric GIST patients.

The webcast provided an opportunity for listeners to learn about a new NIH-based clinic scheduled for June 19, 2008. For the first time in history, doctors will come together to explore pediatric GIST hands-on, in the hopes of discovering viable treatment options for these patients. An overview about the event was discussed by Dr. Helman. Dr. Pappo presented and discussed valuable information about the genetic and clinical



Ashley and LRG Director of Operations, Trish, prepare for the webcast. Ashley Young and Jacqui Bromberg, Life Raft Group pediatric GISTers and Co-chairs for the NIH Clinic Planning Committee, were the moderators for the session. Jacqui was unable to moderate this session but we want to thank her for her continuing dedication in planning the NIH clinic. Ashley was able to visit the office for the event and she did a great job introducing the panelists and presenting questions to them.

The recording of the event is available on our website: http://www.liferaftgroup.org/library_videos.html

We look forward to having more participation among our pediatric GIST community to help spread awareness about this rare disease. If you would like to volunteer in any capacity, please e-mail ebraun@liferaftgroup.org.

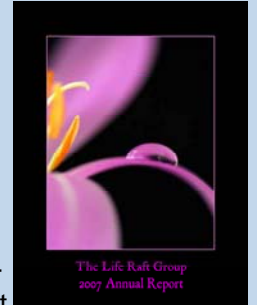


Ashley and mom, Toni (bottom row, second from left), pose with the LRG staff.

Did you Know...



Fatigue getting you down? Want to know about muscle cramps? Check out the LRG's new Side Effects pamphlet. Order your copy today at www.liferaftgroup.org.



Be sure to check your mailboxes next month for our 2007 Annual Report. This year's cover features art by Pediatric GIST patient and Life Rafter, Rachel Gilbert.

Want to shop 'til you drop?



Do it online...

...and donate to the LRG!

If you shop at igive.com you can donate a portion of your purchase to your favorite cause while browsing through over 680 stores, including Lands' End, Staples, JCPenney, Barnes & Noble, Expedia, & Best Buy.

P.S. Don't forget that



surfing the web via GoodSearch also raises money for the LRG.

WEBSITE OF WORTH

By Erin Kristoff
LRG Newsletter Editor

Roger and Kathy Cawthon were diagnosed with cancer within weeks of each other. After many hardships, including chemo, surgery and radiation, they decided to become proactive. Four years later, they completed the Marine Corps Marathon. They also started www.thecancercrusade.com, a website dedicated to "fighting cancer with hope and humor".

On their site you will find the "Meditation Room", where a soothing female voice guides you through meditations like "Overcoming Fear" and "Finding Hope".

Check out the "Healing with Humor" section for laughter tips, jokes and comic strips for cancer patients, like the one featured on the right.

Want to know recipes for cancer patients? Get on over to the "Kitchen" for a Fatigue-Fighting Smoothie.

Don't forget to take a peak at the Hopemobile on your way out.

Snapshots at jasonlove.com



"You really need to stop doing that."

MEDICARE

From Page 7

state. You can use Medicare.gov’s prescription plan finder to evaluate which plan is right for you (www.medicare.gov/MPDPF/Public/Include/DataSection/Questions/SearchOptions.asp).

OR

Enroll in a private health insurance plan that has contracted with Medicare to provide the full range of Medicare covered health care, including drug benefits.

This second option is known as Medicare Advantage (previously known as Medicare+Choice). Medicare Advantage plans may be health maintenance organizations (HMOs), preferred provider organizations (PPOs), or private fee-for-service plans. There are also some Medicare Advantage plans designed for people with special needs, such as long-term care needs. The Part D drug benefit offered with a Medicare Advantage plan is known as a Medicare Advantage Prescription Drug plan or MA-PD.

The Annual Enrollment Period for Part D runs from November 15 to December 31. During this period people with Medicare can enroll in a plan or change their enrollment from one plan to another. Plans and coverage under these plans may differ in each state and may change each year. It is advisable to review your options each year as your medications may change and new plans may be available. State Health Insurance Assistance Program (SHIP) counselors

can provide individualized counseling and help you assess what drug plan—if any—might be best for you given your situation (www.healthassistancepartner.org/ship-locator/).

The Coverage Gap or “Doughnut Hole” under Part D

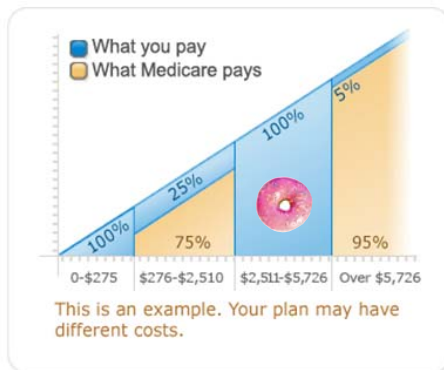
The “Doughnut Hole” is the gap in coverage when an enrollee must pay 100 percent of the discounted price. It is the period after spending exceeds the initial coverage limit and before costs reach the “True Out of Pocket” cost or TrOOP limit. Your total drug costs include what you and the plan pay for your prescriptions. If these are greater than \$2,510 per year, you will hit the “coverage gap,” or “doughnut hole”. During this period, you will pay 100 percent of your drug costs until your out-of-pocket costs reach \$4,050 (or your total drug costs hit

\$5,726.25). After that, you will pay 5 percent of the costs, and the plan will pay 95 percent.

If you qualify for extra help with costs, you will not have a coverage gap. You will continue to pay reduced or no co-pays or co-insurance for each prescription. Depending on how much income you have, your co-pays or co-insurance may get even lower when your total drug costs (what you and your plan pay for your drugs) reach \$5,726.25.

Medicare Part D vs. Medicare Part B

Medicare Part B pays for certain oral anti-cancer drugs if that drug has the same active ingredients as a non-self administrable drug. The injectable and oral drug must have the same chemical and generic name, and be approved for the same indications. Acknowledging recent advances in drug technology, Medicare now allows for coverage of certain oral anti-cancer drugs, called Prodrugs, which have the same active ingredients in the body as injectable anti-cancer drugs. The oral drug may have a different chemical composition from the injectable drug at the outset, but once metabolized the oral drug has the same chemical composition as the injectable drug. This broader interpretation permits coverage of alternative forms of administration of the same drug. The seven oral cancer drugs covered by Medicare Part B do not include any medications for GIST. Medications that are covered under Part B are paid 80 percent by Medicare and 20 percent by the patient.



Midwestern GIST patients meet!



Over 50 patients and caregivers showed up for the April 26 Midwestern GIST patient meeting in St. Louis, Missouri. Please go to <http://giststlouis.blog.spot.com> for pictures and comments.

Mark your calendars!

- Camp Mak-A-Dream will hold a free Young Adult Cancer Survivors Conference in Missoula, Mont., from **May 14 to May 19**. See http://campdream.org/camp_schedule.htm for details.
- The Chicago-area Life rafters are meeting Sunday, May 4 at 12:30 PM at the Wellness Place in Palatine, IL. Please contact Jim Hughes at tjhughes43@comcast.net for details.

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